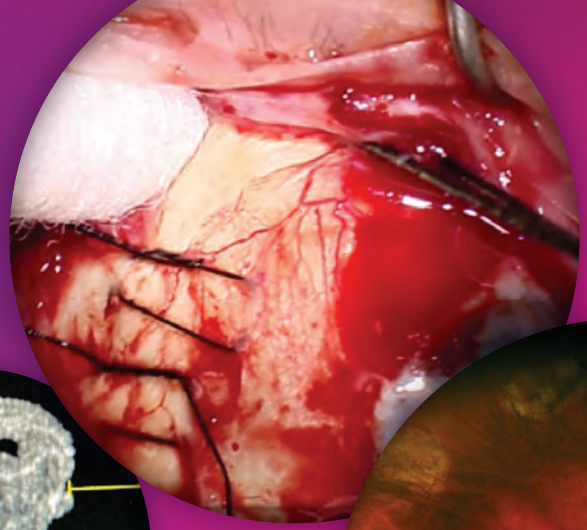
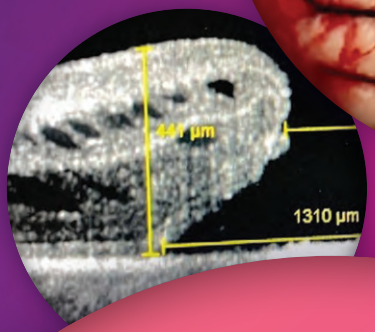
POWERED BY bmc

RT
Retina Today

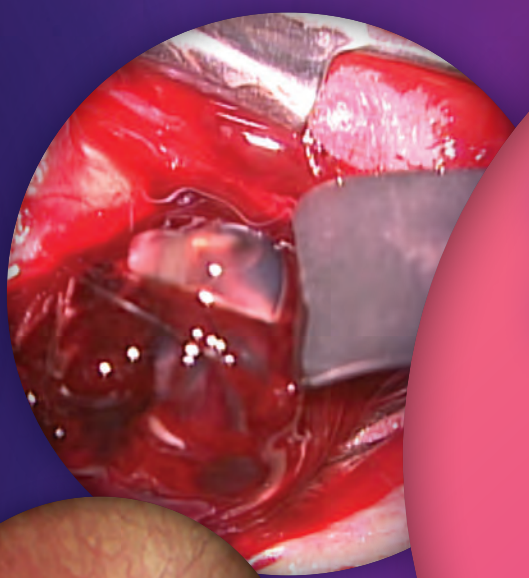
OCTOBER 2023 VOL. 18, NO. 7
RETINATODAY.COM

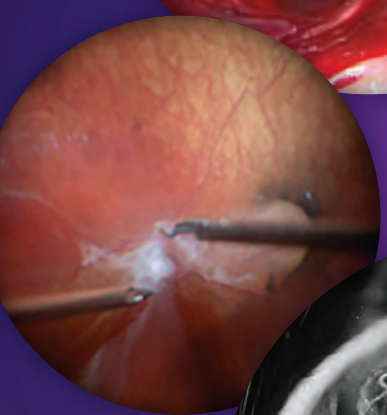


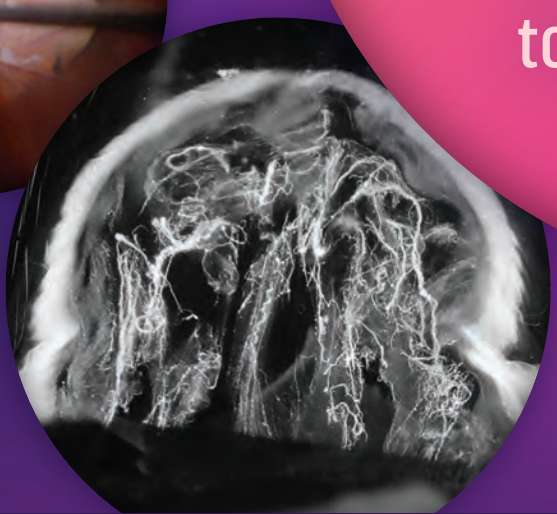


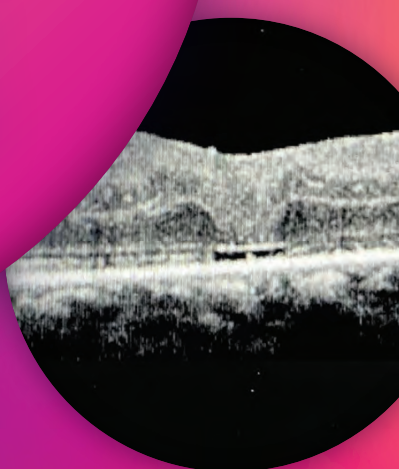
SURGICAL ROUNDS

Novel techniques and tough cases to expand your expertise.









eyetube

EXPLORING NEW CONCEPTS IN PVR

MACULAR HOLE CLOSURE: A NEW CLASSIFICATION

A USEFUL SURGICAL MODALITY FOR MTM

SUBSCRIBE FOR FREE

IZERVAY™ (avacincaptad pegol intravitreal solution) 2 mg

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.

NOW APPROVED

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

To learn more and stay up to date, visit IZERVAYecp.com

- 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.

IVERIC BIO
An Astellas Company

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

Retina Today (ISSN 1942-1257) © 2023 Bryn Mawr Communications LLC is published January/February, March, April, May/June, July/August, September, October, and November/December by Bryn Mawr Communications LLC, 125 East Elm Street, Suite 400, Conshohocken, PA 19428. Subscription is free to all applicable US retina physicians. All others, applicable subscription charges apply. For subscription information call +1 800 492 1267 (US only) or e-mail retinatoday@bmctoday.com. Pending periodical postage paid at Wayne PA and additional entry offices. POSTMASTER Please send address changes to Bryn Mawr Communications LLC, 125 East Elm Street, Suite 400, Conshohocken, PA 19428. Bryn Mawr Communications LLC provides certain customer contact data, which may include customer names, addresses, phone numbers and e-mail addresses, to third parties for promotional and/or marketing purposes. If you do not wish Bryn Mawr Communications LLC to make your contact information available to third parties for any marketing purposes, please contact us at 800-492-1267 or e-mail us at retinatoday@bmctoday.com. This publication is intended for health care professionals and providers only. The information contained in this publication, including text, graphics and images, is for informational purposes only and is not intended to be a substitute for professional medical advice. Bryn Mawr Communications LLC, via its Editors and the Publisher, accepts no responsibility for any injury or damage to persons or property occasioned through the implementation of any ideas or use of any product described herein. While great care is taken by the Publisher and Editors to ensure that all information is accurate, it is recommended that readers seek independent verification of advice on drug or other product usage, surgical techniques and clinical processes prior to their use. The opinions expressed in this publication are those of the authors and are not attributable to the sponsors, the publication or the Editorial Board. References made in articles may indicate uses of medical equipment or drugs at dosages, for periods of time and in combinations not included in the current prescribing information. Inclusion of advertising material in this publication, or in supplements thereof, does not constitute any representation or guarantee by Bryn Mawr Communications LLC of the quality of such products or of the claims made by the manufacturers.

TABLE OF CONTENTS

SURGICAL ROUNDS

Novel techniques and tough cases to expand your expertise.

0.18 mg
YUTIQ®
(fluocinolone acetonide intravitreal implant) 0.18 mg

Discover continuous calm in uveitis[1]

YUTIQ is designed to deliver a sustained release of fluocinolone for up to 36 months for patients with chronic non-infectious uveitis affecting the posterior segment of the eye.[1]

- Proven to reduce uveitis recurrence at 6 and 12 months[1,*]
  At 6 months–18% for YUTIQ and 79% for sham for Study 1 and 22% for YUTIQ and 54% for sham for Study 2 (p<0.01). At 12 months–28% for YUTIQ and 86% for sham for Study 1 and 33% for YUTIQ and 60% for sham for Study 2.
- Extended median time to first recurrence of uveitis[1,2]
  At 12 months–NE[†] for YUTIQ/92 days for sham in Study 1; NE for YUTIQ/187 days for sham in Study 2.
- Mean intraocular pressure (IOP) increase was comparable to sham[1,2]
  Study was not sized to detect statistically significant differences in mean IOP.

*Study design: The efficacy of YUTIQ was assessed in 2 randomized, multicenter, sham-controlled, double-masked, Phase 3 studies in adult patients (N=282) with non-infectious uveitis affecting the posterior segment of the eye. The primary endpoint in both studies was the proportion of patients who experienced recurrence of uveitis in the study eye within 6 months of follow-up; recurrence was also assessed at 12 months. Recurrence was defined as either deterioration in visual acuity, vitreous haze attributable to non-infectious uveitis, or the need for rescue medications.

[†]NE=non-evaluable due to the low number of recurrences in the YUTIQ group.

For more information, visit
YUTIQ.com

INDICATIONS AND USAGE

YUTIQ® (fluocinolone acetonide intravitreal implant) 0.18 mg is indicated for the treatment of chronic non-infectious uveitis affecting the posterior segment of the eye.

IMPORTANT SAFETY INFORMATION

CONTRAINDICATIONS

Ocular or Periocular Infections: YUTIQ is contraindicated in patients with active or suspected ocular or periocular infections including most viral disease of the cornea and conjunctiva including active epithelial herpes simplex keratitis (dendritic keratitis), vaccinia, varicella, mycobacterial infections and fungal diseases.

Hypersensitivity: YUTIQ is contraindicated in patients with known hypersensitivity to any components of this product.

WARNINGS AND PRECAUTIONS

Intravitreal Injection-related Effects: Intravitreal injections, including those with YUTIQ, have been associated with endophthalmitis, eye inflammation, increased or decreased intraocular pressure, and choroidal or retinal detachments. Hypotony has been observed within 24 hours of injection and has resolved within 2 weeks. Patients should be monitored following the intravitreal injection.

Steroid-related Effects: Use of corticosteroids including YUTIQ may produce posterior subcapsular cataracts, increased intraocular pressure and glaucoma. Use of corticosteroids may enhance the establishment of secondary ocular infections due to bacteria, fungi, or viruses. Corticosteroids are not recommended to be used in patients with a history of ocular herpes simplex because of the potential for reactivation of the viral infection.

Risk of Implant Migration: Patients in whom the posterior capsule of the lens is absent or has a tear are at risk of implant migration into the anterior chamber.

ADVERSE REACTIONS

In controlled studies, the most common adverse reactions reported were cataract development and increases in intraocular pressure.

Please see brief summary of full Prescribing Information on adjacent page.

References: 1. YUTIQ® (fluocinolone acetonide intravitreal implant) 0.18 mg full US Prescribing Information. EyePoint Pharmaceuticals, Inc. February 2022. **2.** Data on file.

Alimera

1-844-445-8843. US-YTQ-MMM-0006-01 08/2023

YUTIQ® (fluocinolone acetonide intravitreal implant) 0.18 mg, for intravitreal injection
Initial U.S. Approval: 1963

BRIEF SUMMARY: Please see package insert for full prescribing information.

1. INDICATIONS AND USAGE. YUTIQ® (fluocinolone acetonide intravitreal implant) 0.18 mg is indicated for the treatment of chronic non-infectious uveitis affecting the posterior segment of the eye.

4. CONTRAINDICATIONS. 4.1. Ocular or Periocular Infections. YUTIQ is contraindicated in patients with active or suspected ocular or periocular infections including most viral disease of the cornea and conjunctiva including active epithelial herpes simplex keratitis (dendritic keratitis), vaccinia, varicella, mycobacterial infections and fungal diseases. **4.2. Hypersensitivity.** YUTIQ is contraindicated in patients with known hypersensitivity to any components of this product.

5. WARNINGS AND PRECAUTIONS. 5.1. Intravitreal Injection-related Effects. Intravitreal injections, including those with YUTIQ, have been associated with endophthalmitis, eye inflammation, increased or decreased intraocular pressure, and choroidal or retinal detachments. Hypotony has been observed within 24 hours of injection and has resolved within 2 weeks. Patients should be monitored following the intravitreal injection *[see Patient Counseling Information (17) in the full prescribing information]*. **5.2. Steroid-related Effects.** Use of corticosteroids including YUTIQ may produce posterior subcapsular cataracts, increased intraocular pressure and glaucoma. Use of corticosteroids may enhance the establishment of secondary ocular infections due to bacteria, fungi, or viruses. Corticosteroids are not recommended to be used in patients with a history of ocular herpes simplex because of the potential for reactivation of the viral infection. **5.3. Risk of Implant Migration.** Patients in whom the posterior capsule of the lens is absent or has a tear are at risk of implant migration into the anterior chamber.

6. ADVERSE REACTIONS. 6.1. Clinical Studies Experience. Because clinical trials are conducted under widely varying conditions, adverse reaction rates observed in the clinical trials of a drug cannot be directly compared to rates in the clinical trials of another drug and may not reflect the rates observed in practice. Adverse reactions associated with ophthalmic steroids including YUTIQ include cataract formation and subsequent cataract surgery, elevated intraocular pressure, which may be associated with optic nerve damage, visual acuity and field defects, secondary ocular infection from pathogens including herpes simplex, and perforation of the globe where there is thinning of the cornea or sclera. Studies 1 and 2 were multicenter, randomized, sham injection-controlled, masked trials in which patients with non-infectious uveitis affecting the posterior segment of the eye were treated once with either YUTIQ or sham injection, and then received standard care for the duration of the study. Study 3 was a multicenter, randomized, masked trial in which patients with non-infectious uveitis affecting the posterior segment of the eye were all treated once with YUTIQ, administered by one of two different applicators, and then received standard care for the duration of the study. Table 1 summarizes data available from studies 1, 2 and 3 through 12 months for study eyes treated with YUTIQ (n=226) or sham injection (n=94). The most common ocular (study eye) and non-ocular adverse reactions are shown in Table 1 and Table 2.

Table 1: Ocular Adverse Reactions Reported in ≥ 1% of Subject Eyes and Non-Ocular Adverse Reactions Reported in ≥ 2% of Patients

Ocular		
ADVERSE REACTIONS	**YUTIQ (N=226 Eyes) n (%)**	**Sham Injection (N=94 Eyes) n (%)**
Cataract[1]	63/113 (56%)	13/56 (23%)
Visual Acuity Reduced	33 (15%)	11 (12%)
Macular Edema	25 (11%)	33 (35%)
Uveitis	22 (10%)	33 (35%)
Conjunctival Hemorrhage	17 (8%)	5 (5%)
Eye Pain	17 (8%)	12 (13%)
Hypotony Of Eye	16 (7%)	1 (1%)
Anterior Chamber Inflammation	12 (5%)	6 (6%)
Dry Eye	10 (4%)	3 (3%)
Vitreous Opacities	9 (4%)	8 (9%)
Conjunctivitis	9 (4%)	5 (5%)
Posterior Capsule Opacification	8 (4%)	3 (3%)
Ocular Hyperemia	8 (4%)	7 (7%)
Vitreous Haze	7 (3%)	4 (4%)
Foreign Body Sensation In Eyes	7 (3%)	2 (2%)
Vitritis	6 (3%)	8 (9%)
Vitreous Floaters	6 (3%)	5 (5%)
Eye Pruritus	6 (3%)	5 (5%)
Conjunctival Hyperemia	5 (2%)	2 (2%)
Ocular Discomfort	5 (2%)	1 (1%)
Macular Fibrosis	5 (2%)	2 (2%)
Glaucoma	4 (2%)	1 (1%)
Photopsia	4 (2%)	2 (2%)

(continued)

Table 1: Ocular Adverse Reactions Reported in ≥ 1% of Subject Eyes and Non-Ocular Adverse Reactions Reported in ≥ 2% of Patients

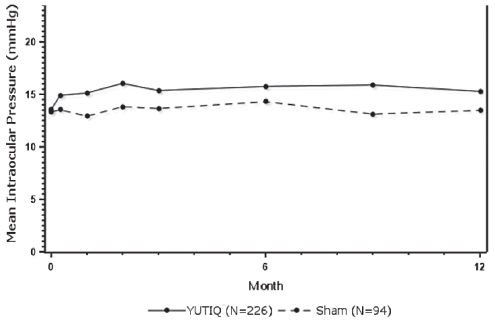
Ocular		
ADVERSE REACTIONS	**YUTIQ (N=226 Eyes) n (%)**	**Sham Injection (N=94 Eyes) n (%)**
Vitreous Hemorrhage	4 (2%)	0
Iridocyclitis	3 (1%)	7 (7%)
Eye Inflammation	3 (1%)	2 (2%)
Choroiditis	3 (1%)	1 (1%)
Eye Irritation	3 (1%)	1 (1%)
Visual Field Defect	3 (1%)	0
Lacrimation Increased	3 (1%)	0
Non-ocular		
ADVERSE REACTIONS	**YUTIQ (N=214 Patients) n (%)**	**Sham Injection (N=94 Patients) n (%)**
Nasopharyngitis	10 (5%)	5 (5%)
Hypertension	6 (3%)	1 (1%)
Arthralgia	5 (2%)	1 (1%)

1. Includes cataract, cataract subcapsular and lenticular opacities in study eyes that were phakic at baseline. 113 of the 226 YUTIQ study eyes were phakic at baseline; 56 of 94 sham-controlled study eyes were phakic at baseline.

Table 2: Summary of Elevated IOP Related Adverse Reactions

ADVERSE REACTIONS	YUTIQ (N=226 Eyes) n (%)	Sham (N=94 Eyes) n (%)
IOP elevation ≥ 10 mmHg from Baseline	50 (22%)	11 (12%)
IOP elevation > 30 mmHg	28 (12%)	3 (3%)
Any IOP-lowering medication	98 (43%)	39 (41%)
Any surgical intervention for elevated IOP	5 (2%)	2 (2%)

Figure 1: Mean IOP During the Studies



8. USE IN SPECIFIC POPULATIONS. 8.1 Pregnancy. Risk Summary. Adequate and well-controlled studies with YUTIQ have not been conducted in pregnant women to inform drug associated risk. Animal reproduction studies have not been conducted with YUTIQ. It is not known whether YUTIQ can cause fetal harm when administered to a pregnant woman or can affect reproduction capacity. Corticosteroids have been shown to be teratogenic in laboratory animals when administered systemically at relatively low dosage levels. YUTIQ should be given to a pregnant woman only if the potential benefit justifies the potential risk to the fetus. All pregnancies have a risk of birth defect, loss, or other adverse outcomes. In the United States general population, the estimated background risk of major birth defects and miscarriage in clinically recognized pregnancies is 2% to 4% and 15% to 20%, respectively. **8.2 Lactation.** Risk Summary. Systemically administered corticosteroids are present in human milk and can suppress growth, interfere with endogenous corticosteroid production. Clinical or nonclinical lactation studies have not been conducted with YUTIQ. It is not known whether intravitreal treatment with YUTIQ could result in sufficient systemic absorption to produce detectable quantities of fluocinolone acetonide in human milk, or affect breastfed infants or milk production. The developmental and health benefits of breastfeeding should be considered, along with the mother's clinical need for YUTIQ and any potential adverse effects on the breastfed child from YUTIQ. **8.4 Pediatric Use.** Safety and effectiveness of YUTIQ in pediatric patients have not been established. **8.5 Geriatric Use.** No overall differences in safety or effectiveness have been observed between elderly and younger patients.

Manufactured by:
EyePoint Pharmaceuticals US, Inc., 480 Pleasant Street, Watertown, MA 02472 USA

A LEGACY LIVES ON


We struggled to put this editorial together, as our community mourns the loss and celebrates the life of Kirk Packo, MD, FACS. Our Editorial Advisory Board members came together to offer their tributes to Kirk, and we encourage you to read through their inspiring words. As you would expect, the outpouring of fond memories, love, admiration, and grief was too much to fit within these pages, so everyone's full comments—and great pictures—are available in the online version (bit.ly/3tawEWM).

But we must focus on the topic at hand: the Surgical Rounds issue. Kirk would have enjoyed this one—it's full of many of the things he loved most in retina. He was passionate about education and conference innovations, and we have plenty of meeting summaries to offer: the Vit-Buckle Society (VBS), Pacific Retina Club, and Aspen Retinal Detachment Society. Kirk was a driving force behind ASRS, and we have that meeting coverage on Eyetube (eyetube.net/meeting-coverage/asr). These days, our retina meetings always include robust programs, surgical videos, and interactive audience polls—all thanks to Kirk's early influence. VBS even has the theatrics we expected from Kirk!

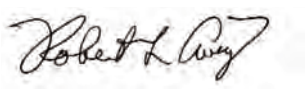
Beyond the robust meeting coverage, the Surgical Rounds issue is just *fun*. It's an opportunity to explore surgical cases that aren't easily categorized, and we encourage our authors to include videos whenever possible (you can access those through QR codes in the articles themselves, or cruise Eyetube to see what other surgeons have shared). The featured articles are chock-full of tips and tricks you can translate to your OR tomorrow, including new approaches for pediatric vitrectomy and myopic traction maculopathy and ways to reduce the risk of postoperative proliferative vitreoretinopathy. Experts also discuss creative ways to address intraoperative surprises and the benefits of managing vitreous floaters surgically. Our classification for full-thickness macular holes needed an overhaul based on novel surgical techniques, and you can find that here, too.

The cases, commentary, and surgical approaches provided by our contributors make it clear that retinal surgery remains a dynamic experience; no two cases are alike, and surgeons must be prepared to implement novel techniques when the tried-and-true doesn't seem to be the best option.

For example, this issue's Fellows' Focus column provides an excellent discussion of when to choose vitrectomy, scleral buckling, or a combined procedure. Linnet Rodriguez, MD, a retina fellow at Wills Eye Hospital, asked five attendings to provide their surgical treatment approach for three different cases of retinal detachment. You might find their answers thought-provoking, and it highlights the value of ongoing peer discussion and education.

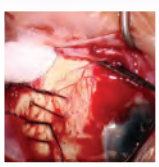
We hope you enjoy these surgical rounds, and we encourage you to reach out if you have your own interesting cases to share. We are always looking for ways to stay connected, grow together, and advance our field. It's what Kirk would have wanted. ■

ALLEN C. HO, MD
CHIEF MEDICAL EDITOR

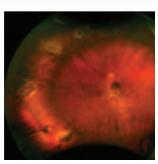


ROBERT L. AVERY, MD
ASSOCIATE MEDICAL EDITOR

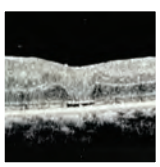
ON THE COVER
(clockwise from the top):



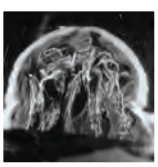
Scleral imbrication.
- Fong May Chew, FRCOphth, MBBS, BSC; David R. Chow, MD, FRCSC; and David Wong, MD, FRCSC



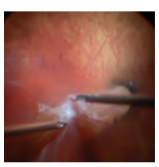
A high-risk retinal detachment repaired with vitrectomy and scleral buckling.
- M. Ali Khan, MD, FACS, FASRS



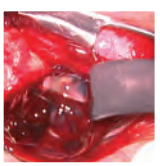
Macular hole closure after wide internal limiting membrane peeling.
- Flavio A. Rezende, MD, PhD



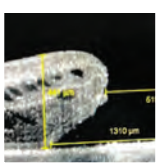
Thickened and tortuous vitreous fibers in the eye of an 88-year-old patient.
- J. Sebag, MD, FACS, FRCOphth, FARVO



Vitrectomy for an 11-month-old girl.
- Vahid Ownagh, MD; Nita Valikodath, MD, MS; and Lejla Vajzovic, MD, FASRS



Intraocular contents prolapsing through a scleral rupture.
- Takumi Ando, MD



A large macular hole with elevated edges.
- Flavio A. Rezende, MD, PhD

TRIBUTES TO A LEGEND IN RETINA

KIRK PACKO, MD, FACS

Photo courtesy of Kevin Caldwell Photography

A long-time member of *Retina Today*'s Editorial Advisory Board, Kirk Packo, MD, FACS, will be remembered for his exemplary surgical skills, drive for innovation, tireless loyalty to family and friends—and a penchant for theatrical flair. Here, *Retina Today* Editorial Advisory Board members share their tributes to their colleague, mentor, and above all, friend.

> "...Kirk was a great friend—generous, joyful, kind—and he valued friendship and family above all. I treasure the Wizard of Oz poster he sent me one Christmas. Thanks, Kirk, for so much, and for bringing joy to our lives and meetings."
>
> **Maria H. Berrocal, MD**

> "There are not enough words to describe Kirk Packo, MD. Doctor, surgeon, teacher, entertainer, creator, mentor, anchor, luminary, legend, husband, father..."
>
> **John W. Kitchens, MD**

> "...As a surgeon, educator, and patient advocate, Kirk embodied the essence of protecting sight and empowering lives every day of his career. He made me laugh more times than I can remember, all while teaching me something new. I was privileged to have him as a friend and colleague..."
>
> **George A. Williams, MD**

> "Kirk Packo was a larger-than-life figure, an icon of retina and medicine, and much more. Creative, pioneering, innovative, and passionate about everything he did and everyone he loved..."
>
> **Julia A. Haller, MD**

To read these and other tributes in full, visit retinatoday.com or scan the QR code.


Photo courtesy of Kevin Caldwell Photography


Photo courtesy of Maria H. Berrocal, MD


Photo courtesy of Maria H. Berrocal, MD


Photo courtesy of J. Fernando Arevalo, MD


Photo courtesy of Kevin Caldwell Photography

NEW RETINA RADIO

LUMINARIES IN RETINA: KIRK PACKO, MD, FACS

John W. Kitchens, MD, interviews Kirk Packo, MD, FACS, about his triumphant career and his decision to retire from practice.

Part 1: Background in acting and directing, residency match, early career, and passion for educating.

Part 2: The creation of AAO subspecialty day and passion for honoring the history of retina and advocating for vitreoretinal surgery innovation.

"I have many fond memories of Kirk Packo… Over the years, we had wonderful conversations about vitrectomy, surgical techniques, and life all over the world. He will never be forgotten!"

J. Fernando Arevalo, MD, PhD

"Kirk Packo, MD, had the most pure talent in all of retina, and this was only exceeded by his big heart. He made us all better by raising the bar in so many ways, professionally and personally…"

Allen C. Ho, MD

"…Kirk will forever remain celebrated in the world of retina. His memory brings a tranquil sigh to my mind and a heartfelt smile to my face. Thank you, Kirk, for your immense and animated leadership."

Carol L. Shields, MD

"Few, if any, have left their mark on retina more than Kirk… He was beloved by his patients and the numerous retina doctors who had the privilege to train with him or learn from him. He added excitement and color to our field, was quite inspirational, and will be terribly missed."

Robert L. Avery, MD

"Dr. Packo's contributions to retina are immeasurable, and his compassion unmatched. An absolute legend who will truly be missed."

Christina Y. Weng, MD, MBA

"Kirk was a retina renaissance man—masterful in the OR, at the podium, in a boardroom, at a keyboard, or in quiet conversation. He was an artist, teacher, physician, visionary, and great friend. Our world was made better by his presence."

Carl C. Awh, MD, FASRS

"As we acknowledge the loss of one of our specialty's true giants, I am reminded of how much he accomplished and how willing he was to give of his own time and prodigious intellect…"

Timothy G. Murray, MD, MBA

"In addition to being a skilled surgeon, a kind and caring clinician, and a remarkably warm and helpful colleague, Kirk almost single-handedly carried ASRS into the digital age…"

Jeffrey S. Heier, MD

OCTOBER 2023
VOL. 18, NO. 7 | RETINATODAY.COM

EYES WITH DR AND PERIVASCULAR LEAKAGE RESPOND WELL TO ANTI-VEGF THERAPY

Researchers recently found that eyes with diabetic retinopathy (DR) and greater perivascular leakage relative to generalized leakage had a rapid, lasting positive response to anti-VEGF treatment with aflibercept (Eylea, Regeneron).[1]

The researchers used ultra-widefield fluorescein angiography (FA) to assess 40 eyes of 40 patients with DR and BCVA of 20/800 or better from the PRIME clinical trial. With the help of a validated, machine learning-based analysis platform, the team assessed the panretinal leakage index and differentiated between generalized and perivascular leakage phenotypes.[1]

They found lower baseline generalized leakage in eyes that attained a 2-step improvement in DR severity scale level in less than 16 weeks (1.9% vs 2.8%, *P* = .026). The baseline macular perivascular-to-generalized leakage ratio significantly correlated with the number of treatment-free days (R = .4, *P* = .012). One year of therapy significantly reduced the mean panretinal (3.9% vs 5.8%, *P* = .002) and macular (6.2% vs 12.2%, *P* = .008) generalized leakage indices compared with baseline, as well as the mean panretinal perivascular leakage index (1.5% vs 2.3%, *P* = .002). The mean panretinal ischemic index experienced a small but likely clinically insignificant decrease from 12.5% at baseline to 11.6% at 1 year (*P* = 0.016).[1]

Assessing quantitative ultra-widefield FA features with a high follow-up frequency in eyes with DR treated with intravitreal anti-VEGF injection allows for a better understanding of biomarker progression and treatment response over time, the authors concluded.[1]

1. Kalra G, Wykoff C, Martin A, Krivastava SK, Reese J, Ehlers JP. Longitudinal quantitative ultra-widefield angiographic features in diabetic retinopathy treated with aflibercept from the PRIME trial [published online ahead of print September 9, 2023]. *Ophthalmol Retina*.

LINK BETWEEN DR AND CHOLESTEROL BUILDUP IN THE RETINA

A research team identified a potential relationship between the buildup of cholesterol in the retina—along with subsequent formation of cholesterol crystals—and the pathogenesis of DR, among other metabolic diseases.[1] Cholesterol crystals contribute to this disease process by inducing proinflammatory and proapoptotic changes and disrupting the blood-retinal barrier in retinal endothelial and retinal pigment epithelial cells.[2]

In their study, published in *Diabetologia*, researchers used scanning electron microscopy and immunohistochemistry to identify hyperreflective crystalline deposits as cholesterol crystals in human donor tissue and animal models. Retinal cell cultures with these deposits showed that treatment with fibrates, statinsm, and α-cyclodextrin effectively dissolved the crystals in vitro. In mice, treatment with α-cyclodextrin reduced cholesterol levels and prevented development of DR.[2]

1. MSU researchers discover link between cholesterol and diabetic retinopathy. Eyewire+. September 11, 2023. September 20, 2023. eyewire.news/news/msu-researchers-discover-link-between-cholesterol-and-diabetic-retinopathy
2. Hammer SS, Dorweiler TF, McFarland D, et al. Cholesterol crystal formation is a unifying pathogenic mechanism in the development of diabetic retinopathy. *Diabetologia*. 2023;66(9):1705-1718.

CRVO EYES WITH PVD HAVE LOWER INJECTION BURDEN

Researchers recently evaluated the status of the posterior vitreous hyaloid on presenting OCT images of the macula in cases of central retinal vein occlusion (CRVO), reporting that eyes with complete posterior vitreous detachment (PVD) at presentation had significantly lower central subfield thickness (CST) and 1-year injection burden.[1]

The study included 102 acute, treatment-naïve CRVO cases, 51% of which had complete PVD at presentation. At the 1-year follow-up, CST was significantly lower in patients with complete PVD (284.9 ± 122.9 µm vs 426.8 ± 286.4 µm); the 1-year intravitreal injection burden was also significantly lower (5.1 ± 3.6 vs 6.7 ± 3.3, *P* = .013).[1]

Based on these study results, the authors concluded that the assessment of the vitreomacular interface in CRVO may serve as a prognostic imaging biomarker for patients presenting with CRVO.[1]

1. Zheng Y, Woodward R, Feng HL, et al. Implications of complete posterior vitreous detachment in eyes with central retinal vein occlusion [published online ahead of print September 5, 2023]. *Retina*.

(Continued on page 48)

RIVALS OF RETINA

THE SURGICAL SHOWDOWN

SATURDAY NOVEMBER 4TH, 2023

Yerba Buena Center for the Arts

The Retina Film Festival is reimagined in 2023!

THE VIT BALLERS

TEAM CAPTAIN:

NINA BERROCAL, MD

THE ENUCLEATORS

TEAM CAPTAIN:

FIRAS RAHHAL, MD

THE VIT VIGILANTES

TEAM CAPTAIN:

CHRISTINA WENG, MD, MBA

Alcon

LET'S GET READY TO RIVAL!

Donald J. D'Amico, MD, will lead the Rivals of Retina Teams in a three-team showdown of exciting surgical case videos.

Join us in San Fran to vote for the winner!

Register online at https://cvent.me/aqED5P

THE PANELS AT ARDS 2023: GA THERAPY AND OR TRICKS

Experts discussed medical innovations, surgical techniques, and what's changing our clinical practice.

BY ETHAN M. STERN, MD

The 2023 Aspen Retinal Detachment Society (ARDS) meeting in Snowmass, Colorado, boasted several panel discussions on all things surgical, medical, and novel. Experts hashed out ways in which we might integrate new therapies for geographic atrophy (GA) and how we are approaching tough cases in the OR. Here, you can catch a glimpse of the conversation. Registration will open October 16 for ARDS 2024, set for March 2-6. Visit aspenretina.com for more information—it's never too early to start thinking snow.

- Timothy G. Murray, MD, MBA

The 2023 ARDS meeting took place during an exciting time—just weeks after the FDA approved the first drug for the treatment of GA, which was a major topic of discussion throughout the meeting. The panels are a long-standing tradition at ARDS, creating a space to discuss the medical and surgical management of various retinal conditions and highlight the diversity of approaches for even common diseases.

SURGICAL MANAGEMENT IN RETINA

The first panel focused on surgery and was moderated by Donald J. D'Amico, MD, with panelists Allen C. Ho, MD; Zofia A. Nawrocka, MD, PhD; Gregg T. Kokame, MD, MMM; and Stratos Gotzaridis, MD (Figure 1). The group used cases to spearhead a discussion of lamellar macular holes, retinal detachments, and proliferative vitreoretinopathy (PVR).

When treating lamellar macular holes, the panel was split regarding whether symptoms or visual acuity should be the primary driver of surgical management. Dr. Kokame noted that he would not operate on a patient with good visual acuity (ie, 20/25 or better), but Dr. Gotzaridis would "if the patient is symptomatic, even if the visual acuity is good, but the patient sees metamorphopsia and it's disturbing." Other panelists suggested worsening symptoms or anatomy as drivers of management, but there was no consensus.

The panelists did, however, unanimously agree on peeling the internal limiting membrane (ILM) for macular pucker caused by epiretinal membrane. Dr. D'Amico was surprised by the total agreement, given the relatively recent advent of this approach. Dr. Nawrocka emphasized the importance of staining and removing the ILM, stating: "Before finishing the case, I give additional staining to be completely sure that the ILM is peeled off; this way, I have [had] no repeated epiretinal membranes [for] 20 years."

Image courtesy of Kevin Caldwell Photography

Figure 1. The surgical panelists shared their approaches to PVR. From left to right: Stratos Gotzaridis, MD; Allen C. Ho, MD; Gregg T. Kokame, MD, MMM; and Zofia A. Nawrocka, MD, PhD.

Next, Dr. D'Amico presented multiple clinical scenarios and asked the panelists to provide their opinion on the best management approach. For a superior break with a retinal hole, the entire panel opted for pneumatic retinopexy. But an additional break, even within the same clock hour, provoked a mixture of answers, including repeat pneumatic retinopexy, vitrectomy, and scleral buckling.

Lastly, the group discussed different surgical approaches to PVR. Dr. Ho said that he prefers PFO and emphasized that if a retinectomy is to be performed, it should be large. "If your retinectomy is less than 120°, you better ask yourself, 'Am I doing a large enough retinectomy?'" Dr. Kokame uses intravitreal methotrexate for cases of PVR, while the European surgeons on the panel recommended staining and peeling of the ILM throughout the fundus to control PVR.

GA AND WET AMD THERAPY

Moderated by Dr. Murray, the second panel discussed GA and wet AMD management with experts Charles

C. Wykoff, MD, PhD; Susan B. Bressler, MD; Tarek S. Hassan, MD; and Steven Yeh, MD (Figure 2).

Pegcetacoplan (Syfovre, Apellis Pharmaceuticals) was the hot topic at this year's conference, and clinicians had many questions about the clinical trial data and the road ahead regarding implementation in clinical practice.

Each panelist described their experience with GA prior to the approval—patients were educated about GA and the likely progression and were prescribed the AREDS2 vitamin formulation. It's no surprise that many on the panel saw the drug as a first step toward a new treatment paradigm.

The panel first discussed how to set patient expectations in GA, given the unknowns that still exist in this disease. Each expert agreed that retina specialists must educate patients carefully about dry and wet AMD. When it comes to wet AMD, it is nearly impossible to predict the treatment outcome and the expected course with and without injections. Research is still unclear about the natural history of any given patient's disease course in AMD. The benefit of monthly pegcetacoplan versus treatment every other month is still up for debate, according to Dr. Hassan.

The data have not given guidance on chronic VEGF suppression, and many specialists wonder if residual intraretinal fluid may be necessary to prevent GA, or if patients need to be kept completely dry. Dr. Wykoff felt that the evidence did not support this conclusion. "I don't think that VEGF suppression at the levels that we're using in the clinic is exacerbating or worsening GA," he noted.

The conversation then pivoted to the combination of anti-VEGF drugs and GA therapy. Because pegcetacoplan is new, retina specialists must make independent decisions in the early management of GA. "All the GA trials actively excluded active wet AMD," Dr. Wykoff pointed out. "We really don't know [and] we have a lot to learn here." Dr. Bressler expressed strong reservations about using pegcetacoplan in patients who developed GA in the setting of wet AMD management. "I would be extraordinarily reluctant to use an agent that was developed and tested on patients [who] had native GA completely in the absence of past or present choroidal neovascularization; I would have no data to say that it was going to be efficacious for them," she explained.

One of the challenges of transitioning from trials to the clinic is the ability to assess treatment success. When treating wet AMD with anti-VEGF therapy, there are known biomarkers. For GA, window defects and autofluorescence findings often are multifocal, and assessing the area of GA is difficult, especially in a busy clinic. Dr. Murray asked, "How are we going to manage treating patients with GA when we don't really have a marker that we can look at? How do you tell your patient whether they're doing well or poorly?" The panelists didn't have a good answer yet. Dr. Wykoff noted that the field needs better algorithms in clinical imaging software to help assess drug efficacy. Dr. Hassan suspects that AI will come into play. Other panelists expressed reservations about the readiness of AI for clinical practice. Dr. Yeh pointed out that clinical metrics in the studies may be a potential avenue for implementation in the clinic, such as low luminance and microperimetry.

Image courtesy of Kevin Caldwell Photography

Figure 2. The medical retina panel included an animated discussion of GA therapy. From left to right: Tarek S. Hassan, MD; Steven Yeh, MD; Timothy G. Murray, MD, MBA; Susan B. Bressler, MD; and Charles C. Wykoff, MD, PhD.

Finally, safety was a primary concern.* Many of the panelists were forward about the 12% risk of new-onset neovascularization in the monthly treatment arm (and roughly 7% in the every-other-month arm) but expressed more concern about the rate of nonarteritic anterior ischemic optic neuropathy (NAION). The panelists said that they would be able to treat neovascularization with well-established paradigms but felt nervous about the risk of NAION. "A 1.7% [risk of NAION] with monthly dosing over 2 years is very high, in my opinion," Dr. Wykoff said.

Ultimately, the panel agreed that the most important thing is to get informed consent when deciding to treat patients with GA. Dr. Bressler summed up the opinion of the entire panel, stating, "The patient needs to understand what we're sharing and then make the decisions that are appropriate to them, their needs, and their expectations."

UNTIL NEXT YEAR

The ARDS panels showed that very few issues are truly settled in the field of retina, and many questions remain to be discussed—likely at the 2024 ARDS meeting in March. ■

**Editor's note: These panel discussions took place before the American Society of Retina Specialists Research and Safety in Therapeutics Committee reported eight cases of occlusive retinal vasculitis after intravitreal injection of pegcetacoplan.*[1]

1. Apellis provides update on review of safety events with Syfovre for geographic atrophy. Eyewire+. July 30, 2023. Accessed August 28, 2023. eyewire.news/news/apellis-provides-update-on-review-of-safety-events-with-syfovre-for-geographic-atrophy

ETHAN M. STERN, MD
- Vitreoretinal Surgery Fellow, Department of Ophthalmology, University of Texas Health San Antonio, San Antonio
- sterne1@uthscsa.edu
- Financial disclosure: None

PACIFIC RETINA CLUB

ALL THINGS RETINA ON THE PACIFIC

The 9th annual Pacific Retina Club meeting boasted mystery cases, expert lectures, and panels.

BY GEORGIA (KAIDONIS) KAMBOJ, MBBS, PHD; MALINI V. PASRICHA, MD; AND MITCHELL J. CHRISTENSEN, BS

The Pacific Retina Club (PRC) was created in 2013 when the Western Retina Study Club merged with the Los Angeles Imaging Conference of Retina Specialists. The founders and program directors of PRC—H. Richard McDonald, MD; SriniVas R. Sadda, MD; and David Sarraf, MD—hosted the 9th annual meeting on June 2-3, 2023, at the University of California San Francisco Mission Bay Conference Center (Figures 1 and 2).

CASE PRESENTATIONS

The first day kicked off with 20 mystery cases presented by residents and fellows. The self-appointed panel sitting in the front row battled it out to guess the diagnosis within the first 2 minutes of each presentation. The presenters felt victorious if their case remained unsolved by the end of the 6-minute time slot. Cases of rare inherited disease dominated the line-up, with a wide range of conditions, such as maternally inherited diabetes and deafness, Shwachman Diamond syndrome, Knobloch syndrome, enhanced S-cone syndrome, and a dual diagnosis of phacomatosis pigmentovascularis of cesioflammea type and *TSPAN12*-associated familial exudative vitreoretinopathy. Infectious, inflammatory, and masquerading cases were thrown into the mix, and the audience was reminded of the differential diagnoses for temporal thinning on OCT, which include sickle cell retinopathy and Alport syndrome.

More than 30 additional cases were presented throughout the day by retina attendings from across the country. Notable topics that spurred enthusiastic audience participation included cases of placoid retinal lesions, acute macular neuroretinopathy following COVID-19 vaccination, and melanoma-associated retinopathy (which Ehsan Rahimy, MD, playfully coined the term "Steve Jobs syndrome"). Gaurav K. Shah, MD, prepared us for the solar eclipse that would take place a few months after the meeting with his case of solar retinopathy, and Prithvi Mruthyunjaya, MD, MHS, concluded the day with a rare case of two genetically distinct choroidal melanomas arising in the same eye. It felt as if half of the Gass Atlas had been touched on by the end of the case presentations.

Figure 1. The PRC faculty and attendees gathered for the 9th annual meeting (from left to right): H. Richard McDonald, MD; Gaurav K. Shah, MD; Robert N. Johnson, MD; Malini V. Pasricha, MD; Anita Agarwal, MD; Judy J. Chen, MD; Ananda Kalevar, MD, FRCS(C), DABO; Joseph B. Alsberge, MD; Emmett T. Cunningham Jr, MD, PhD, MPH; and Brandon Lujan, MD.

THE LATEST IN RETINA

The second day provided a comprehensive retina update and began with a session on basic science and pathology. Two interesting presentations were an "Update on CRISPR Technology for Neovascular AMD," presented by Glenn C. Yiu, MD, PhD, and "Lutein and Zeaxanthin for Prevention of Ocular Disease Throughout the Lifespan," presented by Paul S. Bernstein, MD, PhD. Alexander J. Brucker, MD, and Dr. McDonald then chaired a session on vitreoretinal surgery, during which J. Michael Jumper, MD, shared many excellent strategies on the surgical management of complex retinal diseases. This was followed by a high yield and entertaining rapid-fire panel on surgical cases moderated by Dr. McDonald and including Dr. Jumper; Dr. Shah; Amr Dessouki, MD; Carolyn K. Pan, MD; and Jay M. Stewart, MD.

The morning continued with a session on tumors. William F. Mieler, MD, provided an update on retinal and choroidal vascular tumors, and Jose S. Pulido, MD, MS, MPH, MBA, and Dr. Sarraf touched on the imaging and biomarkers of

Figure 2. (From left to right): Gaurav K. Shah, MD; Robert W. Wong, MD; J. Michael Jumper, MD; Anita Agarwal, MD; H. Richard McDonald, MD; Robert N. Johnson, MD; and Richard R. Roe, MD, on the PRC stage.

vitreoretinal lymphoma. Dr. Mruthyunjaya moderated a session with panelists Armin Afshar, MD, MBA; Robert N. Johnson, MD; Tara A. McCannel, MD, PhD; Dr. Mieler; and Dr. Pulido, who illustrated the breadth of techniques used for the diagnosis and management of choroidal tumors. The attendees were reminded of the importance of monitoring choroidal nevi with B-scan ultrasound to catch the rare case of choroidal melanoma with orbital extension.

Next in line were two fascinating talks on imaging by K. Bailey Freund, MD, and Amani A. Fawzi, MD. Dr. Freund spoke about imaging of the vortex vein system in central serous chorioretinopathy using en face ultra-widefield OCT and touched on key points related to the clinical cases presented the day prior. A highly intellectual panel discussion on imaging followed with Anita Agarwal, MD; Dr. Fawzi; Dr. Freund; Richard F. Spaide, MD; and Robin A. Vora, MD.

In the wet AMD session, David S. Boyer, MD, discussed the therapeutic pipeline, Michael S. Ip, MD, presented 2-year data from the OPTIC trial and the rationale for the LUNA study, and Dr. Sarraf discussed biomarkers for wet AMD. The wet AMD panel cases were moderated by Dante J. Pieramici, MD. Four panelists—Frank L. Brodie, MD, MBA; Judy J. Chen, MD; Dr. Ip; and Dr. Rahimy—provided their insights into treatment approaches for complex and recalcitrant cases.

THE ALEXANDER R. IRVINE LECTURE

The named lecture, in honor of the University of California San Francisco Professor Alexander R. Irvine, was the highlight of the first day. This year's Irvine award recipient, Richard F. Spaide, MD, gave an incredible lecture discussing the concept of foveation in both development and disease.

The afternoon kicked off with a session on dry AMD. Dr. Sadda presented an update on clinical trials for dry AMD, a topic that was further discussed by a panel consisting of Dr. Bernstein; Dr. Brodie; Dr. Rahimy; and Roger A. Goldberg, MD, MBA. Dr. Shah moderated this session and addressed important considerations regarding the practical use of intravitreal injections for dry AMD.

The diabetes and retinal vascular disease session was up next. Andrew A. Moshfeghi, MD, MBA, gave an exciting presentation on potential nonintraocular therapies for the treatment of diabetic retinopathy and diabetic macular edema. An engaging panel discussion on diabetic retinopathy followed, with panelists Diana V. Do, MD; Jesse J. Jung, MD; Caesar Luo, MD; Dr. Ip; and Dr. Pieramici, moderated by Baruch D. Kuppermann, MD, PhD.

Emmett T. Cunningham Jr, MD, PhD, MPH, moderated the uveitis session that included an excellent discussion of complex cases presented by the panelists (Dr. Agarwal; Nisha Acharya, MD, MS; Quan D. Nguyen, MD, MSc; Jessica G. Shantha, MD, MSc; and Edmund Tsui, MD).

The day finished with a session on pediatric retina and inherited diseases chaired by Mary Elizabeth Hartnett, MD, and Aaron Nagiel, MD, PhD. Three excellent presentations preceded a panel discussion moderated by Darius M. Moshfeghi, MD. Topics under discussion included retinopathy of prematurity, familial exudative vitreoretinopathy, and X-linked retinitis pigmentosa.

SEE YOU IN LA

The 2023 PRC meeting was packed with exciting debates, engaging discussions, and a healthy dose of humor and rivalry. Fellows and attendings united with an eagerness to teach and learn. The baton will be handed off to the Los Angeles team for next year's meeting, which will take place on May 30-31, 2024, at the UCLA Luskin Conference Center. It will be followed by the International Retinal Imaging Symposium on June 1, 2024, and we will no doubt see the meeting continue to grow into an international event. ■

MITCHELL J. CHRISTENSEN, BS
- Medical Assistant, West Coast Retina Medical Group, San Francisco
- Financial disclosure: None

GEORGIA (KAIDONIS) KAMBOJ, MBBS, PHD
- Retina Fellow, West Coast Retina/CPMC, San Francisco
- georgia.n.kamboj@gmail.com
- Financial disclosure: None

MALINI V. PASRICHA, MD
- Vitreoretinal Surgeon, West Coast Retina Medical Group, San Francisco
- malini.veerappan@gmail.com
- Financial disclosure: None

THE SUPERHEROES OF RETINA: GLOBAL SPEAKERS AT VBS 2023


Experts from around the world shared their best surgical retina cases.

BY TAKU WAKABAYASHI, MD, AND TINA FELFELI, MD, PHD

One of the highlights of the 11th annual Vit-Buckle Society (VBS) meeting was the international surgical retina session, presented and moderated by experts from around the world. The session included two parts that covered tips and tricks for various surgical techniques and the outcomes of challenging cases (Figure).

ROUND ONE OF CASES

Part one was moderated by Efrem Mandelcorn, MD, FRCSC, from Canada, and Virgilio Morales-Canton, MD, from Mexico. Danilo Iannetta, MD, PhD, from Italy, presented a case of high myopia-associated macular hole and retinal detachment (RD), and he shared a video of amniotic membrane transplantation. To avoid any damage to the retinal pigment epithelium (RPE), he used a preretinal amniotic membrane transplantation. Dr. Iannetta discussed the importance of placing the amniotic membrane with the stromal layer side down for better adherence.

Şengül Özdek, MD, from Turkey, presented two successful pediatric tractional RD surgical repair cases. First, a 10-month-old boy with bilateral leukocoria achieved retinal reattachment after pupillary reconstruction with pupillary membrane removal and synechiolysis and limbal vitrectomy. Second, a 7-month-old boy with persistent fetal vasculature complicated by vitreous hemorrhage and tractional RD required a limbal lensectomy and vitrectomy with membrane peeling. The surgery resulted in retinal reattachment, and the patient was able to fix and follow light. Both cases highlighted the amazing potential of children to respond remarkably well to advanced surgeries.

Nassim Abreu-Arbaje, MD, from the Dominican Republic, presented a case of vitreous hemorrhage in a 43-year-old woman. Upon removal of the hemorrhage with vitrectomy, Dr. Abreu-Arbaje found a vasoproliferative tumor in the periphery. Among the many options, he chose to apply the triple freeze-thaw technique. His video highlighted the role of cryotherapy in effectively freezing the tumor to its apex.

Helen Mi Fang, MBBS, MMed (Ophth), FRCOphth, FAMS, from Singapore, presented a four-point IOL fixation with a transconjunctival snare technique. Dr. Fang mentioned that postoperative transient hypotony rarely occurs, and she recommended massage of the sclerotomies or, if necessary, a cautious sclerostomy suture if the wound leakage is brisk; she also noted that clinicians should avoid cutting the polytetrafluoroethylene (Gore-Tex, W.L. Gore) stitch.

Raul Velez-Montoya, MD, from Mexico, presented a technique for ultrasound-guided vitrectomy in patients with infectious keratitis endophthalmitis in which the fundus cannot be visualized. For this approach, the ultrasound probe was placed sequentially over the eye to monitor the vitreous cavity while performing the vitrectomy. He highlighted the value of this technique in cases where keratoprosthesis or endoscopic vitrectomy is not available.

MORE INTERNATIONAL PERSPECTIVES

Part two was moderated by Dr. Özdek and Gabriela Lopezcarasa Hernandez, MD, from Mexico. Mariam A. Al-Feky, MD, FRCSC, from Egypt, presented challenging pediatric retinal cases. She first discussed her approach to cases of premature infants with bilateral central RDs and extensive persistent fetal vasculature and neovascularization. She opted for bilateral intravitreal anti-VEGF injections followed by vitrectomy. At 5 months postoperatively, the children were able to fix and follow. Dr. Al-Feky also presented a case of a 2.5-year-old girl with a history of ruptured globe repair and IOL implantation who presented with extensive cyclitic membrane. After explanting the IOL and cutting the membrane, she treated the RD with minimal laser power to avoid injury. Despite the guarded prognosis, Dr. Al-Feky reported another good outcome.

Naresh Babu Kannan, MS, FNB, MBA, FASRS, from India, presented his approach to the removal of a thick submacular hemorrhage with extensive fibrotic tissue and RPE patching in a patient with wet AMD. Dr. Kannan injected balanced

Images courtesy of Kevin Caldwell Photography

Figure. Part one of the international session was moderated by Efrem Mandelcorn, MD, FRCSC, and Virgilio Morales-Canton, MD, and presenters included Danilo Iannetta, MD, PhD; Şengül Özdek, MD; Nassim Abreu-Arbaje, MD; Helen Mi Fang, MBBS, MMed (Ophth), FRCOphth, FAMS; and Raul Velez-Montoya, MD (A). Part two included cases presented by Mariam A. Al-Feky, MD, FRCSC; Naresh Babu Kannan, MS, FNB, MBA, FASRS; Maria Ana Martinez Castellanos, MD; Chee Wai Wong, MD, PhD; Dhariana Acon, MD; and Kotaro Tsuboi, MD (B).

salt solution under the retina and performed a fluid-air exchange followed by a retinectomy with diathermy in the periphery. The retina was then retracted nasally to access and remove the blood clot and fibrotic plaque. He placed an RPE graft over the macula and, very cleverly, barriered the blood clot and fibrotic tissue at the graft site.

Maria Ana Martinez Castellanos, MD, from Mexico, gave an excellent talk on approaches to pediatric laser therapy. She has an anesthesiologist sedate patients who are younger than 6 years of age and then performs an ultra-widefield fluorescein angiography. Then, areas of avascular retina are lasered, guided by angiography, at the slit lamp. In children older than age 6, she uses methoxyflurane, which does not alter patients' consciousness while providing good analgesia for up to 20 minutes. Methoxyflurane, although widely used in sports in many countries, is banned in the United States due to its association with acute renal failure with repeated use in cancer patients. However, Dr. Castellanos noted that, with limited use and careful consideration of contraindications, side effects may be minimal.

Chee Wai Wong, MD, PhD, from Singapore, presented on high myopes with macular hole RDs that extended beyond the arcades. He first placed a PFO bubble over the disc and macular hole to prevent the subretinal migration of the dye and provide counter-traction while performing the internal limiting membrane (ILM) peel and flap. He highlighted the importance of repeated staining to ensure all the ILM is peeled up to the edges of the staphyloma. He demonstrated the value of using intraoperative OCT for visualizing and confirming the placement of the ILM flaps over the hole.

Dhariana Acon, MD, from Costa Rica, presented challenging cases of tractional RD in patients with diabetes. She had excellent outcomes despite vitreous hemorrhages and difficulty viewing the retina. She opted to use a chandelier with bimanual surgery to aspirate the bleeding and dissect the thick membranes.

Kotaro Tsuboi, MD, from Japan, gave an informative talk on the anterior chamber fluid-gas exchange technique. The technique combines intraocular gas injection and an anterior chamber tap from a paracentesis wound, where all aqueous is removed through the anterior chamber. Dr. Tsuboi demonstrated that injection of the necessary amount of a nonexpanding gas is done inferiorly 3.5 mm posterior to the corneoscleral limbus. A paracentesis is then performed to remove aqueous in the vitreous cavity through the anterior chamber. Dr. Tsuboi noted that the advantages of this technique include complete filling of the vitreous cavity with gas, which may be helpful for patients with difficultly maintaining strict postures.[1] ■

1. Tsuboi K, Kamei M. Anterior chamber fluid-gas exchange. *Retina*. 2022;42(9):1814-1815.

TINA FELFELI, MD, PHD
- Ophthalmology Resident, Clinician-Scientist Trainee, Department of Ophthalmology and Vision Sciences, University of Toronto, Toronto, Canada
- tina.felfeli@mail.utoronto.ca
- Financial disclosure: None

TAKU WAKABAYASHI, MD
- Attending Surgeon, Wakabayashi Eye Clinic, Kanazawa, Japan
- Former Retina Research Fellow, Wills Eye Hospital, Mid Atlantic Retina, Philadelphia
- taku.wakabayashi@gmail.com
- Financial disclosure: None

WHERE IT ALL BEGAN

As a native of Vancouver, British Columbia, it comes as no surprise that Scott Walter, MD, wanted to be a ski lift architect as a child. It wasn't until his senior year at Stanford that he began to consider medicine as a career. After completing a master's in evolutionary anthropology, he landed at the University of Pennsylvania for medical school. A serendipitous 1-week clerkship in ophthalmology opened his eyes to the breadth of pathology that ophthalmologists treat, and he was hooked. It was the perfect specialty for him, "combining surgery and longitudinal patient care without being tied to the hospital," he said.

Dr. Walter's Advice: Don't rule out private practice, even if you're an academically minded retina specialist. There's tremendous opportunity to thrive in this space.

HIS PATH TO RETINA

Dr. Walter's love of retina was apparent during residency at the Bascom Palmer Eye Institute in Miami. He gained significant experience performing intravitreal injections, lasers, and surgery for patients with advanced stages of diabetic eye disease. Dr. Walter also worked with Harry W. Flynn, MD, to launch the Diabetic Retinopathy Pipeline Project, connecting underserved patients with primary care services. For Dr. Walter, it was an important contribution to the local community and a turning point in his career—the start of "a lifelong passion for all things retina."

SUPPORT ALONG THE WAY

Dr. Walter attended the Duke Eye Center in Durham, North Carolina, for his vitreoretinal surgery fellowship. He connected with Duke faculty member Lejla Vajzovic, MD, a former Bascom Palmer resident. He was inspired by Dr. Vajzovic's growth as a surgeon and the innovative thinking she brought to the OR early in her career. Together, they used intraoperative OCT to create a dynamic 3D model of platelet-rich plasma in complex macular hole surgery.

Sharon Fekrat, MD, was another inspirational mentor. On his VA rotation, Dr. Walter was confronted with an influx of patients requiring secondary IOLs. Dr. Fekrat encouraged him to try not one but three new techniques, and then write about each of them in the Duke Manual of Vitreoretinal Surgery.

Dr. Walter was inspired by Prithvi Mruthyunjaya, MD, MHS, to combine a career in retina with ocular oncology. He returned to Bascom Palmer for additional post-fellowship training in ocular oncology with former research mentor, J. William Harbour, MD, before establishing himself in private practice as the only ocular oncologist in Connecticut.

Dr. Walter was the first "out" resident at Bascom Palmer. He is grateful for the emergence of visible LGBTQ+ leaders within the field, including Vivienne S. Hau, MD, PhD, with whom Dr. Walter worked closely to establish the Underrepresented in Retina Mentorship Program.

AN EXPERIENCE TO REMEMBER

Dr. Walter cherishes "the intensity of the specialty," he said. Recently, he and a visiting medical student performed nine vitrectomies, including two combination cases with an anterior segment surgeon, quickly changed out of their scrubs into suits, and traveled to New York City to give a talk to the fellows and faculty at New York University.

In addition, he loves the variety of complex cases he sees in private practice and the doors they open, including the opportunity to perform the first autologous retinal transplant and retinal gene therapy in Connecticut. ■

Scott D. Walter, MD, MSc, FASRS, is a partner with Retina Consultants PC in Hartford, Connecticut. He is the vice chief of ophthalmology at Hartford Hospital and is on faculty at the University of Connecticut and Yale School of Medicine. He is a speaker for Apellis, Bausch + Lomb, Genentech/Roche, Regeneron, and Spark Therapeutics; member of the data monitoring committee for Ideaya Biosciences; and consultant for Allergan/Abbvie, Bausch + Lomb, Castle Biosciences, Genentech/Roche, Lupin, Novartis, and Regeneron. He can be followed on Instagram **@retina.ct** and reached at **swalter@retinact.com**.

HOW TO CHOOSE WISELY: PPV, SB, OR BOTH

A closer look at how retina specialists decide the best surgical approach for retinal detachment repair.

BY LINNET RODRIGUEZ, MD

There are three main approaches to repair rhegmatogenous retinal detachments (RRDs): pneumatic retinopexy (PnR), scleral buckle (SB), and pars plana vitrectomy (PPV). Several factors go into deciding whether a patient with primary RRD, who is not a candidate for PnR, would benefit from PPV alone, PPV with SB, or SB alone. This decision varies among physicians, and vitreoretinal fellows have an opportunity to learn various surgical approaches. Here, Wills Eye faculty share how they select the best surgical approach for each patient.

LINNET RODRIGUEZ, MD: IF A PATIENT PRESENTS WITH A PRIMARY RRD AND IS NOT A CANDIDATE FOR PNR, HOW DO YOU DECIDE TO REPAIR WITH PPV, PPV WITH SB, OR SB?

Omesh P. Gupta, MD: The ideal patients for PPV are pseudophakic with a posterior vitreous detachment (PVD) and minimal superior and almost no inferior pathology. These patients benefit from vitrectomy since their RDs can have very small breaks that may be difficult to visualize during examination. Other candidates for PPV are phakic patients with superior detachments and no inferior pathology.

PPV with SB is typically reserved for RDs with multiple breaks, large RDs involving two or more quadrants, RDs that have been present for more than 2 to 3 weeks, vitreous hemorrhage (VH) that precludes sufficient scleral depression, primary proliferative vitreoretinopathy (PVR), RDs with giant retinal tears, RDs with associated choroidal detachment, and/or extensive inferior pathology. This combination approach should also be considered when the fellow eye has had a poor outcome from RD repair or there is a strong family history of retinal tear or detachment.

Finally, SBs are usually ideal for young phakic patients with no cataract. Patients with small peripheral breaks with minimal vitreous traction and exclusively anterior pathology and patients of any age with no PVD are favorable candidates as well. Surgeons should consider this procedure in high-risk eyes to minimize the risk of postoperative PVR.

Sonia Mehta, MD: I decide the surgical approach on an individual basis. If the patient is young and phakic with no PVD, I will likely use SB; if the patient is pseudophakic and has superior pathology with a PVD, then I usually prefer PPV.

If the patient is pseudophakic and has inferior or extensive pathology (eg, 360° lattice) with a PVD, I might consider PPV with SB. However, there are always exceptions, which is why my approach is personalized to the patient and their eye. For example, if a young phakic patient with Marfan syndrome has a very thin or no sclera, I would favor PPV over SB.

Jason Hsu, MD: In patients younger than age 50, a primary SB is preferred, especially if there is no evidence of a PVD. Separating the hyaloid in these patients can be very difficult. In addition, the risk of cataract development is higher.

PPV alone is more beneficial in pseudophakic patients who are 65 years of age or older. In these patients, a good shave of the vitreous base can be achieved without drastic changes in refractive error, which can occur with SB placement. Even if multiple breaks or lattice are present, circumferential endolaser can be performed. This procedure is also beneficial for localized RDs or RDs with one or two breaks. If there are multiple breaks or other peripheral pathology, combining SB and PPV may be a better option.

For patients between the ages of 50 and 65, SB with or without PPV depends on the lens. If the patient is phakic, consider SB. If the RD is more complex with multiple breaks in different quadrants and/or VH is present, then PPV with SB is more beneficial. For pseudophakic patients in this age group, also consider PPV with SB.

A combined procedure should also be considered for RD due to giant retinal tears. These patients have an abnormal vitreous base and would benefit from circumferential laser regardless of the lens status. If grade C or worse PVR is

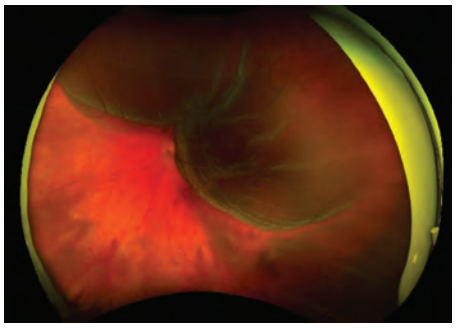


Figure 1. A 50-year-old woman presented with 1 day of decreased vision in the left eye. She was phakic with a PVD and a macula-off RD from the 10 to 5:30 clock hours with two large retinal tears at the 11 and 2:30 clock hours. How would you treat this patient?
Dr. Gupta: PPV with SB
Dr. Mehta: PPV
Dr. Garg: PPV with SB
Dr. Yonekawa: PPV
Dr. Regillo: PPV

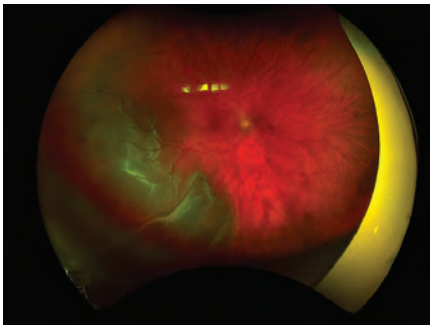


Figure 2. A 58-year-old man presented with 3 days of decreased vision in the right eye. The patient was pseudophakic with a PVD and a macula-on RD from the 6 to 11 clock hours with lattice and retinal tears at the 8 and 9 clock hours. What would be your surgical approach?
Dr. Gupta: PPV
Dr. Mehta: PPV
Dr. Garg: PPV with SB
Dr. Yonekawa: PPV
Dr. Regillo: PPV

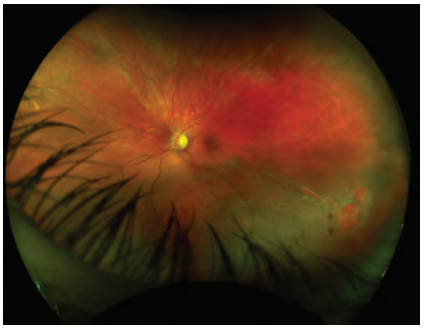


Figure 3. A 25-year-old woman presented with new floaters in the left eye. She was phakic with no PVD and had a macula-off RD from the 3 to 8 clock hours with multiple holes. Which surgical technique would you choose for this patient?
Dr. Gupta: SB
Dr. Mehta: SB
Dr. Garg: SB
Dr. Yonekawa: SB
Dr. Regillo: SB

present, then PPV is preferred. I generally place a buckle in these situations even if I am doing a retinectomy. Supporting the peripheral retina and the edges of the retinectomy is beneficial. I would not place a buckle for a funnel RD where a retinectomy alone would probably be performed.

Sunir J. Garg, MD: Patients 40 years of age or younger, or those without a PVD, often do best with SB alone. Unnecessarily manipulating the young vitreous can precipitate additional tears. I also find SB alone to be the best choice for retinal dialysis. In these cases, I place a small segmental sponge.

PPV alone is a great option for eyes that have a PVD and are pseudophakic. An older patient who already has a moderate cataract without other substantial vitreoretinal pathology would also be a good candidate.

I prefer combined PPV and SB for eyes with tears in multiple locations, abnormal/broad vitreous base, extensive lattice degeneration, a suboptimal RD outcome in the fellow eye, trauma, family history of RD, and/or patients at risk of PVR with the presence of VH or substantial smoking history.

Yoshihiro Yonekawa, MD: Many studies have shown that PPV alone provides excellent surgical outcomes. But the best single-surgery success rates are in pseudophakic eyes with PVDs.

When it comes to combined procedures, you will never regret adding a buckle to a vitrectomy, but you will often regret not adding one if a primary vitrectomy succumbs to PVR. I prefer placing an encircling SB in eyes at higher risk for recurrent RD. Of course, this is if the clinical picture forces me to do a vitrectomy. Many complex pathologies can be fixed with SB alone, which is preferred if possible.

In terms of SB alone, pediatric patients are always good candidates, as separating the hyaloid is nearly impossible. In addition, they have difficulty positioning and can get PVR after a failed PPV. Young adults almost always get primary buckles with me, as does any adult with no PVD. If the break is posterior, you can do a radial buckle. In some scenarios, you may do primary buckling even if you would normally opt for a primary PPV or PPV with SB. One such scenario is in patients with self-injurious behavior.

Carl D. Regillo, MD: For me, if it is PPV, it is almost always PPV only. Rarely do I add SB. The buckle adds very little, and you can still get good results without routinely doing PPV with SB. Most RDs can be repaired with PPV alone. They usually occur in patients 50 years or older with some preexisting cataract and flap tears, indicating a complete or partial PVD. The preference now is shifting toward PPV because you can eliminate induced myopia and other problems related to buckles. You can also clear the media at the same time. Adding SB to PPV may boost the success rate if there is extensive peripheral pathology or high-risk features for PVR.

Patients getting SB only are those younger than 50 years of age, as they typically do not have a PVD. They generally should not get PPV unless the media is not clear.

ILLUSTRATIVE CASES

I asked the interviewees to review three cases and decide if they would choose PPV, PPV with SB, or SB (Figures 1-3). ■

LINNET RODRIGUEZ, MD
- Vitreoretinal Surgery Fellow, Wills Eye Hospital Retina Service, Mid Atlantic Retina, and Sidney Kimmel Medical College, Thomas Jefferson University, Philadelphia
- linrodriguez@midatlanticretina.com
- Financial disclosure: None

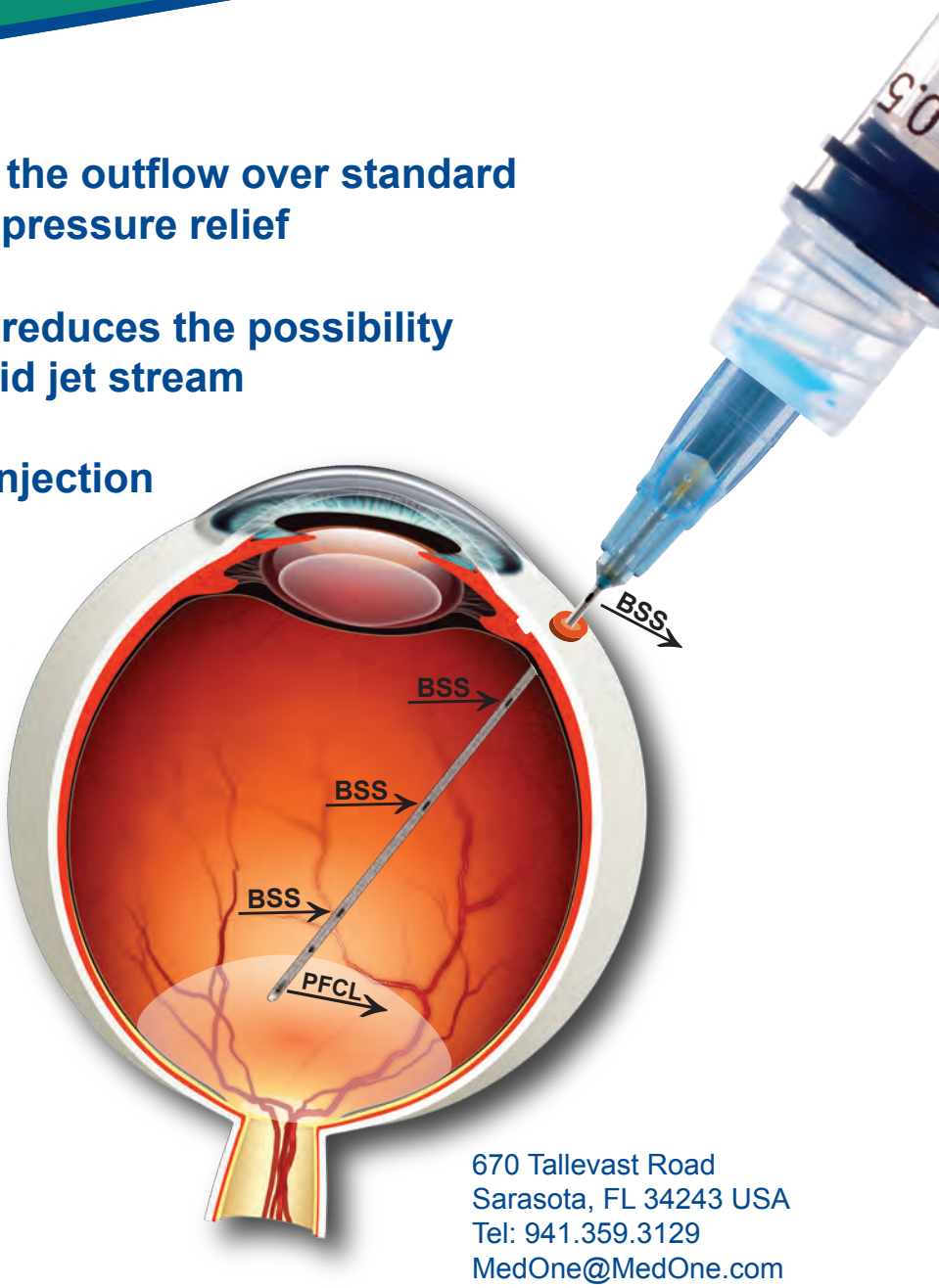
Works Best Under Pressure!

DualBore SideFlō® Cannulas

Optimized for simultaneous relief of pressure during injection of surgical liquids such as perfluorocarbon or staining dye in small gauge surgery.

- **Multiple egress vents double the outflow over standard DualBore cannulas for faster pressure relief**
- **Innovative side-port delivery reduces the possibility of retinal injury caused by fluid jet stream**
- **Maintains stable IOP during injection**
- **Available in 23g, 25g & 27g**

Patent #9937300



MedOne®

www.medone.com

670 Tallevast Road
Sarasota, FL 34243 USA
Tel: 941.359.3129
MedOne@MedOne.com

NEW CONCEPTS IN PROLIFERATIVE VITREORETINOPATHY

A look at high-risk cohorts, surgical management, and intravitreal therapy.

By M. Ali Khan, MD, FACS, FASRS

Proliferative vitreoretinopathy (PVR) remains an unmet clinical need in the practice of surgical retina, with ongoing research seeking to better describe, manage, and prevent this challenging disease process.[1] Several such projects were recently published or presented at the 2023 American Society of Retinal Specialists (ASRS) Annual Meeting, adding practical considerations to the current body of literature. In this article, I summarize the recent work that may aid the retina specialist when encountering PVR during repair of rhegmatogenous retinal detachment (RRD).

HIGH-RISK RETINAL DETACHMENT

When encountering a primary RRD, several risk factors for PVR have been previously described, including vitreous hemorrhage, preoperative PVR, large or chronic detachments, large or multiple retinal breaks, choroidal detachment, intraocular inflammation, and extensive cryotherapy (Figure 1).[2] However, limited studies exist that evaluate the role of these high-risk features on RRD repair outcomes and whether such risk factors truly influence single-surgery anatomic success (SSAS) in primary RRD.

Salabati et al recently published a study of 389 eyes that evaluated SSAS rates for primary RRD repair in eyes with high-risk features for PVR.[3] Eyes were deemed high-risk if they had at least one of the following risk factors: preoperative PVR grade A or B, vitreous hemorrhage, RRD involving 50% or more of the retinal area, presence of three or more retinal breaks, history of prior cryotherapy, presence of choroidal detachment, and/or duration of RRD greater than 2 weeks. Choice of surgical technique was pars plana vitrectomy (PPV) in 67.9% of eyes and combined PPV with scleral buckling (SB) in 32.1% of eyes. Overall, the SSAS rate was 71.5% at 3 months after surgery. When comparing surgical techniques, the SSAS rate was significantly higher in eyes treated with PPV/SB compared with PPV alone (80.8% vs 67%, $P = .006$). This higher SSAS was noted even in eyes treated with PPV/SB that were more likely to be macula-off and have a greater extent of RRD compared with eyes in the PPV only group (Figure 2).[3]

The authors completed a multivariate analysis to assess the effect of the various risk factors on SSAS. However, no individual risk factor was significantly associated with the rate. Notably, use of PPV/SB was the only feature associated with SSAS (odds ratio [OR] = 2.04, $P = .019$).

The relatively lower SSAS rate of 71.5% observed in eyes

AT A GLANCE

- Vitrectomy with scleral buckling in eyes with primary rhegmatogenous retinal detachment (RRD) and high-risk features may be advised.
- Extended internal limiting membrane peeling in eyes with proliferative vitreoretinopathy (PVR) grade C may be recommended for anatomic and visual acuity considerations.
- In the GUARD trial of methotrexate for the prevention of PVR after RRD repair, 44% more redetachments occurred in the historical control group compared with the intervention arm.

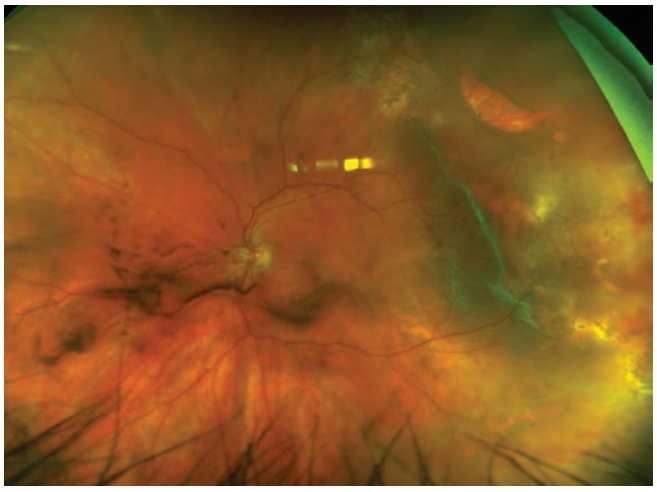


Figure 1. In this patient who presented with a high-risk RRD, vitreous hemorrhage and multiple breaks are present. The larger break superotemporally has rolled edges, consistent with PVR grade B.

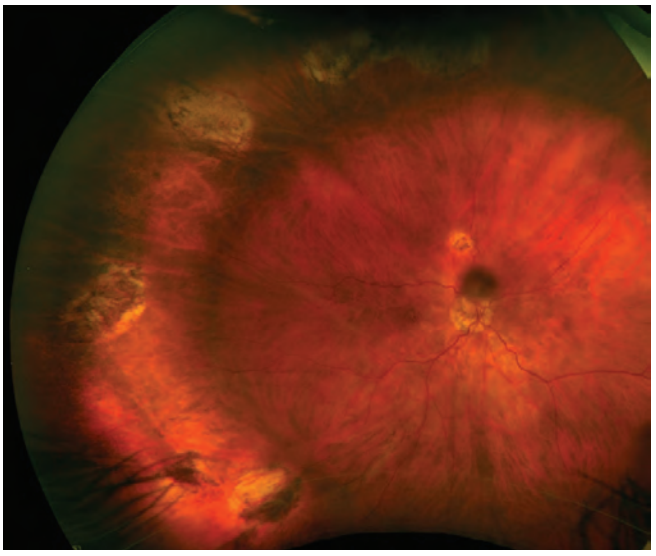


Figure 2. A high-risk RD was repaired with PPV and SB. The initial detachment was macula-off with 8 clock hours of detachment. Note the multiple breaks treated with laser retinopexy temporally.

with RRD and high-risk features, compared with the 88% to 90% rate reported in other large series of primary RRD,[4-6] suggests these risk factors remain clinically relevant. Given the significantly higher SSAS rate with PPV/SB observed in this study, use of PPV/SB in eyes with primary RRD and high-risk features may be advised. Additional study of this high-risk cohort is of interest and may be a study population worth including in future clinical trials for PVR.

EXTENDED ILM PEELING

Internal limiting membrane (ILM) peeling has been suggested during repair of RD with or without PVR.[7] Previous data yielded lower rates of epiretinal membrane formation and recurrent RD incidence with ILM peeling, but results have conflicted between studies and RD populations.

Recently, Yonekawa et al presented data regarding the anatomic and visual benefits of extended ILM peeling for patients with PVR grade C RDs.[8] The authors describe extended ILM peeling as the peeling of ILM not only within the macula, but also beyond the vascular arcades and to the furthest reasonable extent that is surgically available, often under perfluorocarbon liquid.

The retrospective study analyzed 307 eyes of 307 patients from five institutions. The minimum follow-up was 6 months, and 157 eyes treated with extended ILM peeling were compared with 150 eyes without ILM peeling. At 6 months, the reattachment rate under fluid was higher (61% vs 45%, $P = .005$), and the number of redetachments was fewer (0.39 vs 0.59, $P = .010$) in the extended peeling group. Visual acuity and visual acuity improvement were also better in the ILM peeling group ($P < .001$ and $P = .043$, respectively).[8]

Based on this study, extended ILM peeling during RRD repair in eyes with PVR grade C may be recommended for both anatomic and visual acuity considerations. Data from a prospective clinical trial would be helpful to confirm the benefits of extended ILM peeling in PVR-related surgery.

INTRAVITREAL METHOTREXATE

Results of the GUARD trial, a phase 3 prospective clinical trial investigating repeated intravitreal injections of 0.8% methotrexate (ADX-2191, Aldeyra Therapeutics) in PVR RRD, have been highly anticipated by the retina community. Per study protocol, 13 injections of methotrexate were administered over 4 months. The intervention cohort was compared with historical controls, with the primary endpoint being the incidence of recurrent RD requiring reoperation within 6 months.[9]

Results of the study were presented at the 2023 ASRS Annual Meeting.[9] The intervention and historical control arms were similar regarding phakic status and history of open-globe repair. The rate of recurrent RD was 24% in the intervention arm and 39% in historical controls at 6 months ($P = .024$). The primary endpoint was achieved, with the intervention cohort having significantly fewer overall recurrent RDs compared with historical controls (18.8% vs 38.7%, OR = 0.49, $P = .001$) through week 24. The researchers noted that 44% more detachments occurred in the historical control group compared with the intervention arm. Additional outcomes, such as epiretinal membrane formation, hypotony, and adverse events, occurred less often in the intervention arm, although the study was not powered to detect differences for these secondary outcomes.[9]

Data from the GUARD trial were encouraging, with the primary endpoint met. Additional data may further establish intravitreal methotrexate in the treatment of PVR RRD.

(Continued on page 36)

MANAGING VITREOUS FLOATERS

The latest advances in imaging and surgery can help patients with vision-degrading myodesopsia.

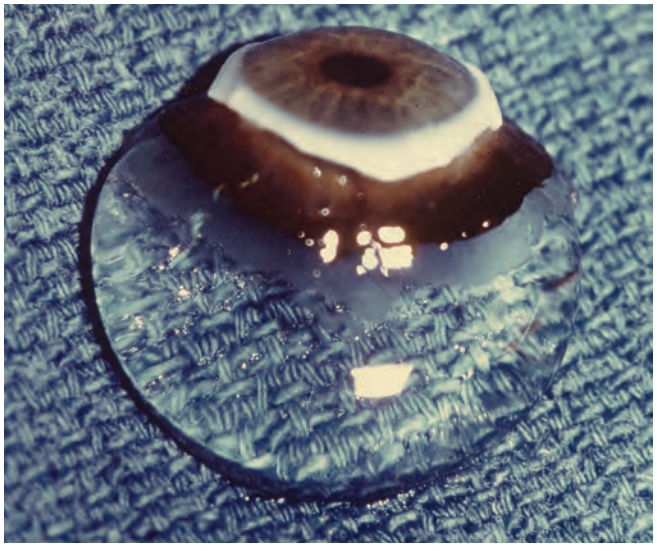
By J. Sebag, MD, FACS, FRCOphth, FARVO

Vitreous floaters are a common symptom, estimated in one survey to affect two out of every three individuals, with one in three reporting visual impairment.[1] When vitreous floaters measurably degrade vision, the diagnosis of vision-degrading myodesopsia (VDM) can be established based on objective, quantitative criteria.[2] The psychological features of depression and perceived stress associated with VDM have been extensively documented.[3-5] Studies have further determined that patients with VDM would be willing to exchange 1 year of each remaining decade of life just to be rid of their floaters.[6] This article explains the pathophysiology of VDM and the emerging treatment approaches.

THE AGING PROCESS

Vitreous is a clear gel in youth but undergoes significant structural changes with aging and myopia.[7] The gel state and transparency of normal vitreous result from an intricate interaction between collagen and hyaluronan, which are initially homogeneously distributed throughout the vitreous body (Figure 1).[8] Vitreous opacification results from fibrous liquefaction, a progressive process that begins in youth and advances more rapidly in myopic eyes, leading to myopic vitreopathy (Figure 2, Video 1).[7,9,10] Fibrous liquefaction features dissociation of hydrophilic hyaluronan molecules from collagen, resulting in the formation of liquid vitreous and crosslinking/aggregation of vitreous collagen into structures that interfere with light passing through the center of the eye, casting perceptible shadows. When fibrous liquefaction of the vitreous body occurs in tandem with dehiscence of vitreoretinal adhesion, the result is a posterior vitreous detachment (PVD), the most common cause of vitreous floaters and VDM.[2,11,12]

Even in the absence of the pathologic effects of anomalous PVD, the separation of the posterior vitreous cortex from the inner limiting membrane (ILM) can significantly disturb vision, due to light scattering. This is caused by the high density of collagen fibrils in the outer vitreous and/or folding



Specimen courtesy of the New England Eye Bank

Figure 1. Postmortem dissection of the sclera, choroid, and retina off the vitreous body, which remained attached to the anterior segment of a 9-month-old child. Although the fresh, unfixed specimen is composed of 98% water and situated on a surgical towel in room air, its solid gel consistency is maintained by the collagen/hyaluronan matrix. ***Reprinted with permission from Sebag J. Vitreous–in Health & Disease. Springer; 2014.***

AT A GLANCE

- Studies show that patients with vision-degrading myodesopsia (VDM) would be willing to exchange 1 year of each remaining decade of life just to be rid of their floaters.
- Vitrectomy is a safe and effective treatment for VDM and can normalize contrast sensitivity within 1 week of surgery.
- Researchers are investigating the use of nanoparticles to enhance laser ablation of vitreous opacities.

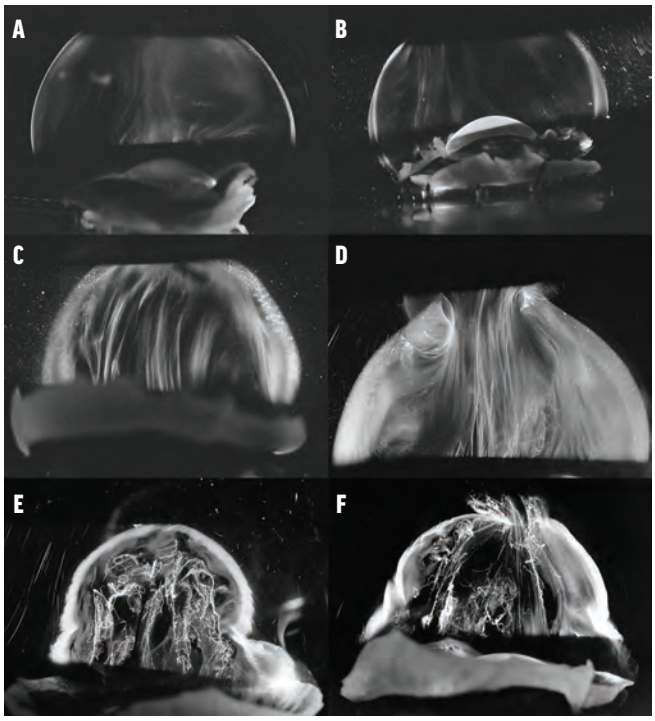


Figure 2. Postmortem darkfield slit microscopy of whole human vitreous with the sclera, choroid, and retina dissected off the vitreous body. The vitreous bodies of an 11-year-old (A) and a 14-year-old (B) feature a homogeneous structure with no significant light scattering, except at the periphery where the vitreous cortex is comprised of a dense matrix of collagen fibrils (see Figure 3). The vitreous structures of a 56-year-old (C) and a 59-year-old (D) feature macroscopic fibrils in the central vitreous body with an anteroposterior orientation. In the eyes of an 88-year-old (E, F), central vitreous fibers are thickened and tortuous. Adjacent to the large fibers are areas of liquid vitreous, at times forming pockets called lacunae. *Reprinted with permission from Sebag J. Vitreous–in Health & Disease. Springer; 2014.*

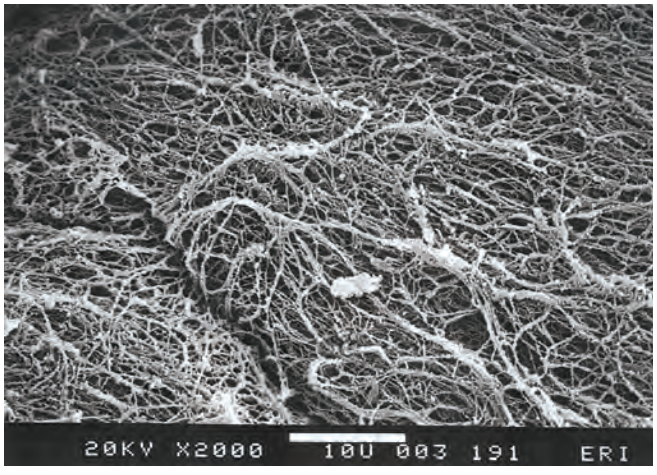


Figure 3. Scanning electron microscopy of the posterior aspect of the posterior vitreous cortex demonstrates dense packing of collagen fibrils (white bar = 10 µm). *Reprinted with permission from Sebag J. Vitreous–in Health & Disease. Springer; 2014.*

of the outer vitreous, which is forced into a smaller surface area after separation from the ILM (Figure 3, Video 2). Opacities in the central vitreous and the outer shell of the vitreous body result in floaters and, in advanced cases, VDM.

WATCH IT NOW

Video courtesy of Carl Glittenberg, MD, and Susanne Binder, MD

Video 1. Myopic Vitreopathy.

VISUAL SIGNIFICANCE

Recent investigations have determined that floaters can have a measurable effect on vision. While visual acuity is unaffected, studies have detected profound degradation in contrast sensitivity; one study found contrast sensitivity declined by 91% compared with age-matched controls.[12] Investigations have correlated this degradation in contrast sensitivity with PVD, vitreous density by ultrasonography, and quality of life as measured by the National Eye Institute Visual Function Questionnaire.[10,13,14] With the advent of quantitative ultrasonography to objectively assess vitreous structure and by measuring contrast sensitivity to evaluate visual function, clinicians are now able to quantitatively determine VDM severity to help guide management.

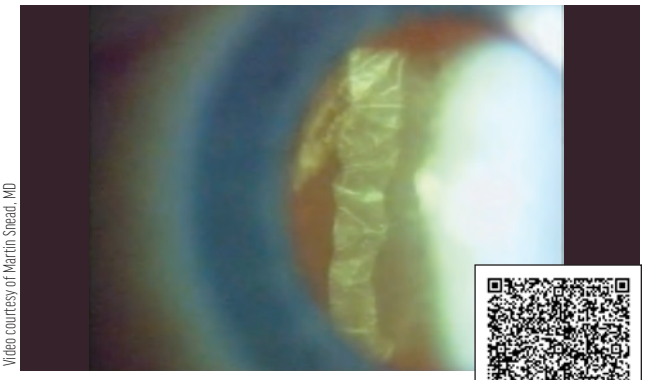
TREATMENT ADVANCES

Although Nd:YAG laser vitreolysis has been widely employed to treat vitreous opacities, no definitive studies prove its efficacy.[12,15-19] Thus, the United Kingdom National Institute for Health and Care Excellence (NICE) concluded that evidence on the safety and efficacy of Nd:YAG laser vitreolysis in the treatment of vitreous floaters is inadequate in quality and quantity. NICE officially recommended that Nd:YAG laser vitreolysis should only be used in the context of research and be done by retina specialists.[20]

In contrast, vitrectomy is a safe and effective treatment for VDM.[12,21-23] In one study of 139 consecutive cases, contrast sensitivity normalized within 1 week of surgery and remained normal for years thereafter.[23] Moreover, vitrectomy for VDM was found to be more cost-effective than cataract surgery, amblyopia therapy, and retinal detachment (RD) repair.[24]

To mitigate complications such as cataract and RD, limited vitrectomy was developed to preserve 3 mm to 4 mm of retrolental gel vitreous and avoid surgical PVD induction. In a series of 195 cases, the incidence of retinal tears and RD was markedly reduced to 1.5% compared with traditional vitrectomy with surgical PVD induction, which has

WATCH IT NOW



Video courtesy of Martin Snead, MD

Video 2. Posterior Vitreous Folds After PVD.

a reported incidence of 30% for retinal tears and 6.8% to 10.9% for RD.[23,25-27] Furthermore, the historically high incidence of cataract surgery following vitrectomy for floaters was reduced to 18% (mean follow-up of 20 months) in one study and 16.9% (mean follow-up of 32 months) in a larger study of limited vitrectomy for VDM.[23,28] In these studies, cataract surgery was required in patients with a mean age of 64 ± 7 years. Importantly, when cataract surgery was performed, there were no complications related to the previous limited vitrectomy, perhaps due to the preservation of intact anterior gel vitreous.

PHARMACEUTICAL INTERVENTION

Despite the demonstrated safety and efficacy of limited vitrectomy for VDM for vitreous floaters, advanced therapeutics may be able to address this issue in the future. Pharmacologic vitreolysis has been approved for treating vitreomacular traction but has not been tested in VDM.[29-31]

One interesting approach is the use of nanoparticles to enhance laser ablation of vitreous opacities. Designed with gold cores coated with hyaluronic acid, these nanoparticles have an affinity for vitreous collagen. Once bound to collagenous opacities and the detached posterior cortex, they absorb laser energy at levels 1,000 times lower than that which is currently employed for Nd:YAG laser vitreolysis and produce nanobubbles that ablate vitreous opacities. In vitro experimentation followed by in vivo investigations in rabbits have demonstrated efficacy and safety.[32,33]

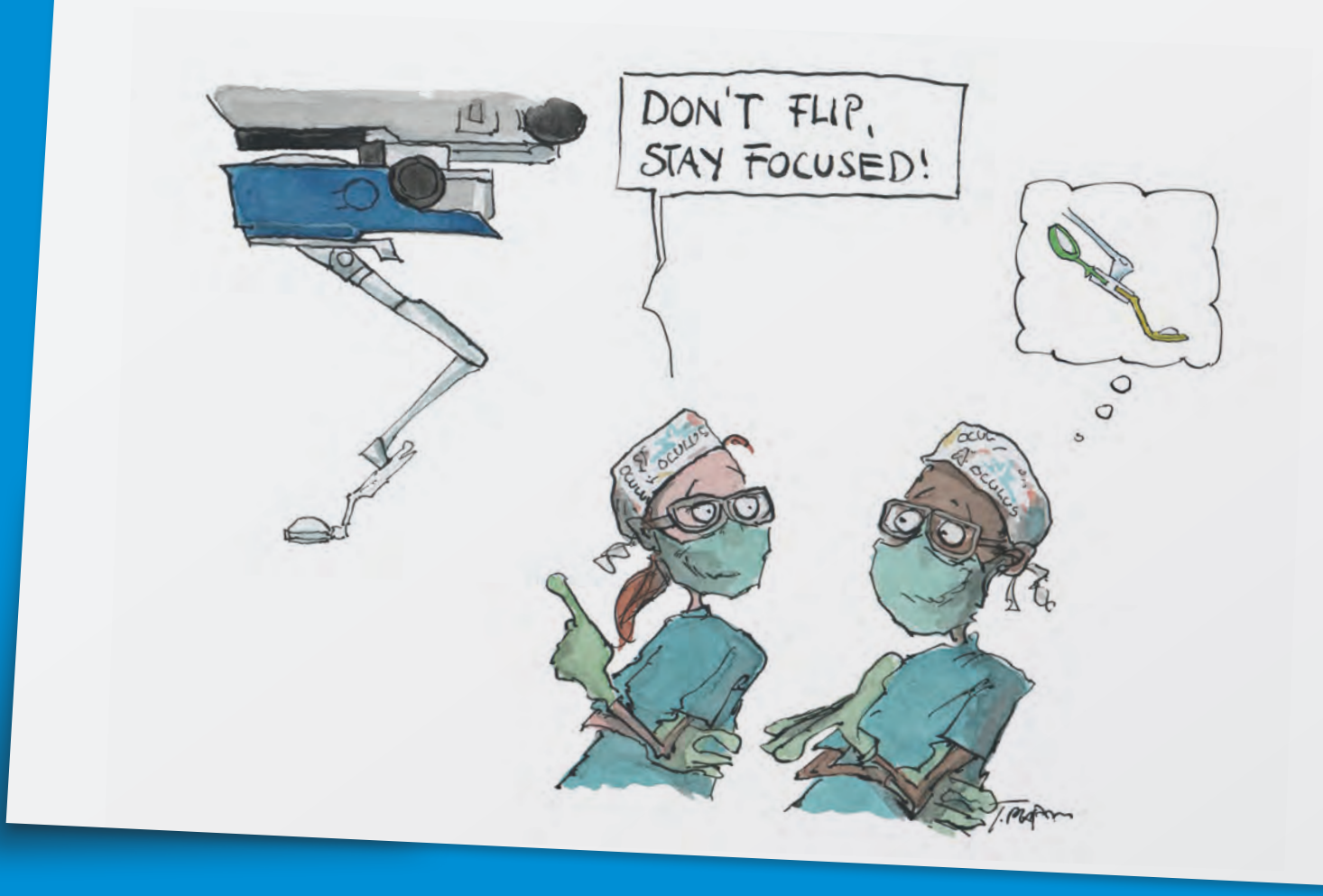
CLINICAL IMPLICATIONS

Our past inability to properly evaluate the structural changes within the vitreous body and their effect on visual function has hampered our willingness to consider vitreous floaters as a disease. While most patients consider floaters a nuisance, some patients may have VDM. We must treat such patients with the same respect and consideration we afford to patients with other vitreoretinal diseases. In addition, we must commit ourselves to the development of novel diagnostic tools and therapeutics to address VDM and improve the quality of life for millions of patients worldwide. ■

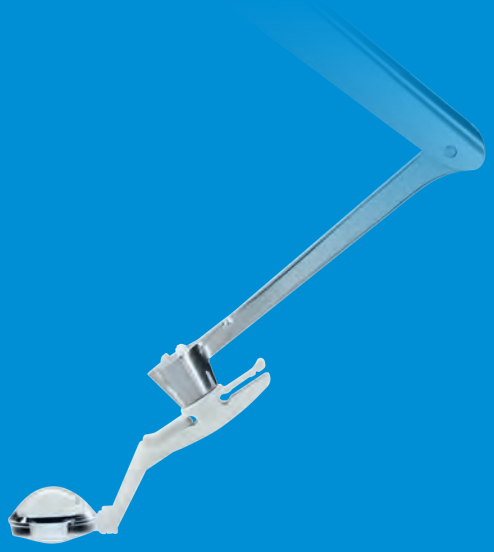
Acknowledgments: Research discussed in this article was supported by the VMR Research Foundation. Alfredo A. Sadun, MD, PhD, FARVO, graciously reviewed this article.

1. Webb BF, Webb JR, Schroeder MC, North CS. Prevalence of vitreous floaters in a community sample of smartphone users. *Int J Ophthalmol*. 2013;6(3):402-405.
2. Sebag J. Vitreous and vision degrading myodesopsia. *Progr Ret Eye Res*. 2020;79:100847.
3. Spielberger CD, Gorsuch RL, Lushene R, et al. Manual for the State-Trait Anxiety Inventory. Consulting Psychologists Press; 1983.
4. Cipolletta S, Beccarello A, Galan A. A psychological perspective of eye floaters. *Qual Health Res*. 2012;22(11):1547-1558.
5. Kim YK, Moon SY, Yim KM, et al. Psychological distress in patients with symptomatic vitreous floaters. *J Ophthalmol*. 2017;1915176.
6. Wagle AM, Lim WY, Yap TP, et al. Utility values associated with vitreous floaters. *Am J Ophthalmol*. 2011;152(1):60-65.
7. Sebag J. The Vitreous - Structure, Function, and Pathobiology. Springer-Verlag; 1989.
8. Chew L, Sebag J. Vitreous. In: Adler's Physiology of the Eye. 12th Ed [in press]. Elsevier; 2023.
9. Nguyen N, Sebag J. Myopic vitreopathy – significance in anomalous PVD and vitreoretinal disorders. In: Myopia & Related Diseases. Midena, ed. *Ophthalmol Comm Soc*; 2005:137-145.
10. Nguyen JH, Nguyen-Cuu J, Mamou J, Routledge B, Yee KMP, Sebag J. Vitreous structure and visual function in myopic vitreopathy causing vision-degrading myodesopsia. *Am J Ophthalmol*. 2021;224:246-253.
11. Sebag J, Yee KMP, Huang L, Wa C, Sadun AA. Vitrectomy for floaters – prospective efficacy analyses and retrospective safety profile. *Retina*. 2014;34(6):1062-1068.
12. Sebag J. Methodological and efficacy issues in a randomized clinical trial investigating vitreous floater treatment. *JAMA Ophthalmol*. 2018;136(4):448.
13. Garcia G, Khoshnevis M, Yee KM, Nguyen-Cuu J, Nguyen JH, Sebag J. Degradation of contrast sensitivity following posterior vitreous detachment. *Am J Ophthalmol*. 2016;172:7-12.
14. Mamou J, Wa CA, Yee KM, et al. Ultrasound-based quantification of vitreous floaters correlates with contrast sensitivity and quality of life. *Invest Ophthalmol Vis Sci*. 2015;56:1611-1617.
15. Nguyen JH, Nguyen-Cuu J, Yu F, et al. Assessment of vitreous structure and visual function after neodymium:yttrium-aluminum-garnet laser vitreolysis. *Ophthalmology*. 2019;126(11):1517-1526.
16. Ivanova T, Jalil A, Antoniou Y, et al. Vitrectomy for primary symptomatic vitreous opacities: an evidence-based review. *Eye*. 2016;30:645-655.
17. Milston R, Madigan M, Sebag J. Vitreous floaters - etiology, diagnostics, and management. *Surv Ophthalmol*. 2016;61(2):211-227.
18. Kokavec J, Wu Z, Sherwin JC, et al. Nd:YAG laser vitreolysis versus pars plana vitrectomy for vitreous floaters. *Cochrane Database Syst Rev*. 2017;6(6):CD011676.
19. Lim JI. YAG laser vitreolysis–is it as clear as it seems? *JAMA Ophthalmol*. 2017;135(9):924-925.
20. NICE. YAG laser vitreolysis for symptomatic vitreous floaters. October 26, 2022. Accessed March 20, 2023. bit.ly/30YraWI
21. Delaney YM, Oyinloye A, Benjamin L. Nd:YAG vitreolysis and pars plana vitrectomy: surgical treatment for vitreous floaters. *Eye*. 2002;16(1):21-26.
22. Mason III JO, Neimkin MG, Mason IV JO, et al. Safety, efficacy, and quality of life following sutureless vitrectomy for symptomatic vitreous floaters. *Retina*. 2014;34(6):1055-1061.
23. Sebag J, Yee KMP, Nguyen JH, Nguyen-Cuu J. Long-term safety and efficacy of vitrectomy for vision degrading myodesopsia from vitreous floaters. *Ophthalmol Retina*. 2018;2(9):881-887.
24. Rostami B, Nguyen-Cuu J, Brown G, Brown M, Sadun A, Sebag J. Cost-effectiveness of limited vitrectomy for vision degrading myodesopsia. *Am J Ophthalmol*. 2019;204:1-6.
25. Tan HS, Mura M, Lesnik Oberstein SY, Bijl HM. Safety of vitrectomy for floaters. *Am J Ophthalmol*. 2011;151(6):995-998.
26. Schulz-Key S, Carlsson JO, Crafoord S. Long-term follow-up of pars plana vitrectomy for vitreous floaters: complications, outcomes, and patient satisfaction. *Acta Ophthalmol*. 2011;89(2):159-165.
27. de Nie KF, Crama N, Tilanus MA, et al. Pars plana vitrectomy for disturbing primary vitreous floaters: clinical outcome and patient satisfaction. *Graefe's Arch Clin Exp Ophthalmol*. 2013;251(5):1373-1382.
28. Yee KM, Tan HS, Lesnick-Oberstein SY, et al. Incidence of cataract surgery after vitrectomy for vitreous opacities. *Ophthalmol Retina*. 2017;1:154-157.
29. Sebag J. Pharmacologic vitreolysis (Guest Editorial). *Retina*. 1998;18:1-3.
30. Sebag J. Pharmacologic vitreolysis – premise and promise of the first decade. *Retina*. 2009;29(7):871-874.
31. Sebag J. Pharmacologic vitreolysis. In: Sebag J, ed. Vitreous–in Health & Disease. Springer; 2014:799-816.
32. Sauvage F, Fraire JC, Remaut K, et al. Photoablation of human vitreous opacities by light-induced vapor nanobubbles. *ACS Nano*. 2019;13(7):8401-8416.
33. Sauvage F, Nguyen VP, Li Y, et al. Laser-induced nanobubbles safely ablate vitreous opacities in vivo. *Nat Nanotechnol*. 2022;17(5):552-559.

J. SEBAG, MD, FACS, FRCOphth, FARVO
- Senior Research Scientist, Doheny Eye Institute, Pasadena, California
- Professor of Clinical Ophthalmology, Department of Ophthalmology, Geffen School of Medicine, University of California Los Angeles, Los Angeles
- Founding Director, VMR Institute for Vitreous Macula Retina, Huntington Beach, California
- jsebag@vmrinstitute.com
- Financial disclosure: Past Consultant (Alcon, Bayer, Bausch + Lomb, Genentech/Roche, ThromboGenics); Patents - Minority (Nanobubble Technology, Quantitative Ultrasonography)



OCULUS HD Disposable LenZ – For single-use on the ZEISS RESIGHT®



- **Perfect view in every case**
  Single-use means no scratches or opacities
- **Always sterile**
  Minimizes risk of infection and cross-contamination
- **Always available on the spot**
  Increase your O.R. capacity utilization

www.oculussurgical.com +49 641 2005-298 855-SDI-BIOM (Toll Free, US Only)

OCULUS® SURGICAL

MACULAR HOLE CLOSURE: A NEW CLASSIFICATION

Novel surgical techniques call for a different way to categorize large macular holes.

By Flavio A. Rezende, MD, PhD

Despite the impressive evolution in retinal imaging and instrumentation, most ophthalmologists still use the Gass reappraisal of macular hole classification from 1995.[1] It was based on biomicroscopic features for pathophysiological purposes alone, not surgical prognosis. The first classification for full-thickness macular holes (FTMHs) based on spectral-domain OCT (SD-OCT) was introduced in 2013 by the International Vitreomacular Traction Study Group.[2] Although the main purpose was to define the pathological progression of anomalous posterior vitreous detachment at the vitreomacular interface, the group also classified eyes with FTMHs into three groups: small (< 250 µm), medium (≥ 250-400 µm), and large (> 400 µm). These are based on what they called *minimum hole width* or aperture size, which is measured at the narrowest point of the hole in the mid retina (now termed *minimum linear diameter* [MLD]). More recently, surgical series using internal limiting membrane (ILM) peeling have demonstrated that FTMHs < 400 µm have success rates near 100%, but holes > 400 µm only reach 80% closure rates overall.[3]

THE NEED FOR BETTER CLASSIFICATION

The first attempt to introduce a surgical FTMH classification was made by the Manchester Large Macular Hole Study.[4] The series, which included only eyes undergoing pars plana vitrectomy and wide ILM peeling, confirmed a worse outcome for FTMHs beyond MLD of 650 µm.

Parameters other than MLD, such as base linear diameter (BLD), hole edge height and configuration (lifted edges with a subretinal fluid cuff vs flat), macular hole index (height x BLD), cystoid changes, presence of vitreomacular traction, and presence of epiretinal membrane/epimacular proliferation, have been described as SD-OCT biomarkers that have additional effects on either anatomical and/or functional surgical outcomes.[5,6] Lately, many alternative surgical techniques—such as autologous ILM flaps, perifoveal hydrodissection, human amniotic membrane (hAM) graft, and autologous retinal transplantation (ART)—have been introduced with encouraging results for large FTMHs with worse SD-OCT characteristics or recurrent and recalcitrant holes.[7-10]

THE CLOSE CLASSIFICATION

A group of experienced retina surgeons convened (virtually during the COVID-19 pandemic) to create the CLOSE Study Group.[11] The main goal was to gather cases of FTMHs beyond 400 µm and propose a new classification based on surgical results that included newer techniques. The new CLOSE classification is based on preoperative MLD (determined using dense radial SD-OCT scans) and

AT A GLANCE

- Most clinicians still use the 1995 classification system for full-thickness macular holes (FTMHs), which does not integrate newer treatment approaches.
- The CLOSE Study Group gathered cases of FTMHs beyond 400 µm and proposed a new classification system based on surgical results, including those of newer techniques.
- The new CLOSE classification may help clinicians better care for patients with large FTMHs that until recently were deemed inoperable.

TABLE 1. CLOSE CLASSIFICATION STRATIFYING MACULAR HOLES BEYOND 400 μm	
Classification	**Hole size (μm)**
Small	< 250
Medium	> 250 - ≤ 400
Large	> 400 - ≤ 650
X-large	> 650 - ≤ 800
XX-large	> 800 - ≤ 1,000
Giant	> 1,000

TABLE 2. POSTOPERATIVE FTMH CLOSURE RATES (%)				
Surgical Technique	**Large**	**X-Large**	**XX-Large**	**Giant**
ILM Peeling	96.8	86	80	NA
ILM Flap	100	99.1	93	90
Macular Hydrodissection	NA	88.9	60	87.1
Human Amniotic Membrane	100	100	100	100
Autologous Retinal Transplantation	100	87.8	94.7	87
NA, not enough numbers available				

TABLE 3. MEAN BCVA GAINS BASED ON SURGICAL TECHNIQUE (LOGMAR)				
Surgical Technique	**Large**	**X-Large**	**XX-Large**	**Giant**
ILM Peeling	-0.5293	-0.4248	-0.3858	NA
ILM Flap	-0.3602	-0.3778	-0.2338	-0.2694
Macular Hydrodissection	NA	-0.4748	-0.3441	-0.5664
Human Amniotic Membrane	-0.4902	-0.5177	-0.5342	-0.3497
Autologous Retinal Transplantation	0.2202	-0.3561	-0.4633	-0.4178
NA, not enough numbers available				

postoperative visual acuity recovery and hole closure (type 1) outcomes of more than 1,000 cases (Tables 1-3, Figure 1).

The classification also considers the importance of measuring BLD and hole edge height (Figures 2 and 3). Larger FTMHs and holes that fail to close with the first intervention are more likely to have flatter edges and are less likely to respond to ILM peeling/flap techniques. These flat-edged holes (type 2) were considered successful anatomical results in the past but are now deemed failed holes, and further surgical intervention can provide additional visual gains.

The new classification shows high closure rates and significant visual acuity gains for large macular holes undergoing

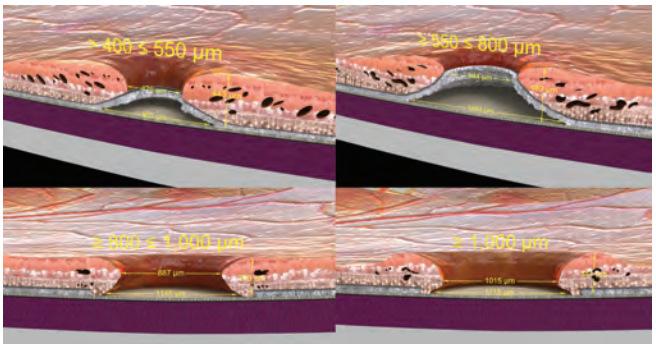


Figure 1. These 3D illustrations of each hole size group show MLD, BLD, and macular hole edge height measurements. As the hole gets larger, the edges become flatter with less cystic cavities (shorter height), and MLD and BLD dimensions become similar.

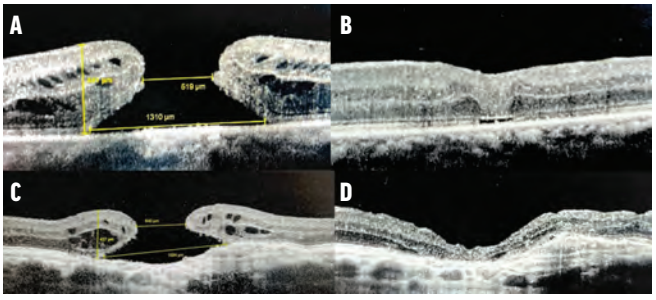


Figure 2. This preoperative large macular hole (MLD: 519 μm) has elevated edges and multiple cystoid spaces (A); 6 months after wide ILM peeling, OCT shows continued improvement of the outer foveal structure after hole closure and 6 lines of visual acuity gain (B). This preoperative X-large FTMH (MLD: 640 μm) also has elevated edges and cystoid spaces (C); the patient was being treated with an anti-VEGF agent for a juxtafoveal neovascular membrane. An inverted ILM flap technique achieved good closure with 4 lines of visual acuity gain (D).

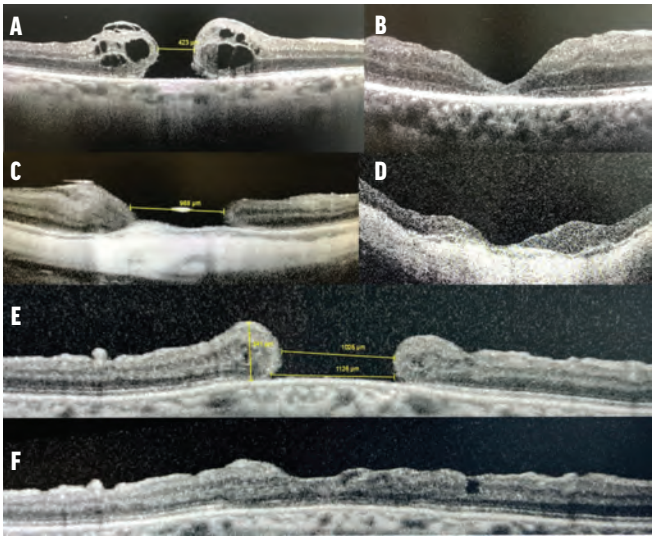


Figure 3. This large FTMH (MLD: 423 μm) did not close after a previous ILM flap procedure but still had elevated edges with cystoid spaces (A). Hole closure was achieved with perifoveal hydrodissection, and VA improved from 20/400 to 20/60 1 year postoperative (B). This XX-large hole (MLD: 933 μm) was under silicone oil tamponade after multiple surgeries (C). Hole closure was achieved with a hAM graft, and VA improved from hand motion to 20/300 (D). This giant hole (MLD: 1,025 μm) with flat dehydrated edges had undergone two previous surgeries (E). After ART, the hole closed with significant VA improvement from counting fingers to 20/80 (F).

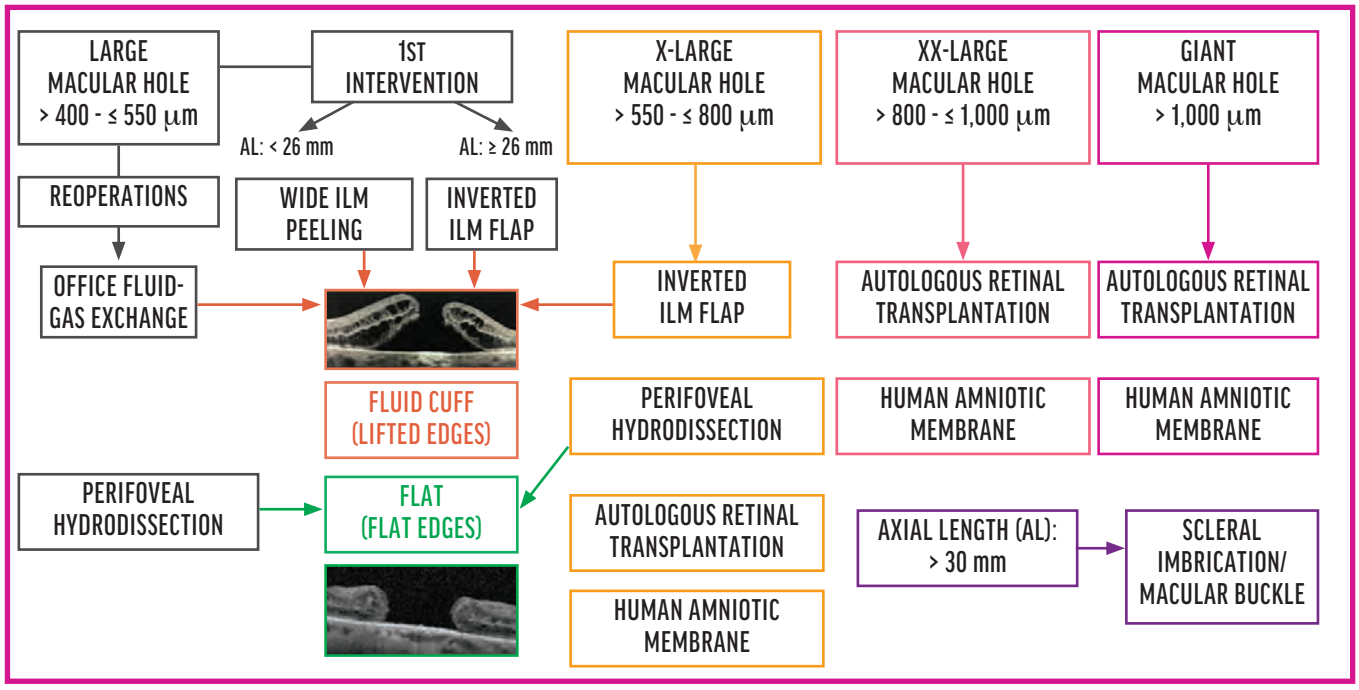


Figure 4. My personal surgical algorithm for MLD > 400 µm for primary or failed macular holes.

ILM peeling. However, the success rates with ILM peeling dropped with the X-large group and were worse for holes beyond 800 µm. ILM flaps performed well even for primary holes that were XX-large and bigger.

Thus, alternative techniques, such as perifoveal hydrodissection, hAM grafts, and ART, should be reserved for eyes that failed the first surgery with ILM peeling or flap techniques or when a patient presents with a FTMH that is larger than 800 µm with flat dehydrated edges.

An important aspect to keep in mind is that surgical goals are slowly changing, and macular hole closure is no longer the only target; instead, the aim is to also reestablish outer foveal integrity (external limiting membrane and ellipsoid zone continuity on SD-OCT). An updated hole closure classification recently published by Rossi et al can also help understand the differences in healing patterns after various surgical techniques.[12]

Macular holes with or without retinal detachment in eyes with high myopia and features of myopic tractional maculopathy are a subset that may benefit from alternative techniques not included in the CLOSE classification, and we refer to the classification proposed by Parolini et al for those.[13]

IMPLEMENTATION

Using this latest information, I created a personal surgical algorithm to address various situations associated with primary or failed macular holes beyond 400 µm (Figure 4). As more retina surgeons and researchers become familiar with the new CLOSE classification, we can start speaking the same language and better care for patients with large FTMHs, which until recently were deemed inoperable, by choosing the best surgical approach for each clinical scenario. ■

1. Gass JDM. Reappraisal of biomicroscopic classification of stages of development of a macular hole. *Am J Ophthalmol*. 1995;119(6):752-759.
2. Duker JS, Kaiser PK, Binder S, et al. The International Vitreomacular Traction Study Group classification of vitreomacular adhesion, traction, and macular hole. *Ophthalmology*. 2013;120(12):2611-2619.
3. Liu L, Enkh-Amgalan I, Wang NK, et al. Results of macular hole surgery. Evaluation based on the International Vitreomacular Traction Study Classification. *Retina*. 2018;38(5):900-906.
4. Ch'ng SW, Patton N, Ahmed M, et al. The Manchester large macular hole study: is it time to reclassify large macular holes? *Am J Ophthalmol*. 2018;195:36-42.
5. Kusuhara S, Escaño MFT, Fujii S, et al. Prediction of postoperative visual outcome based on hole configuration by optical coherence tomography in eyes with idiopathic macular holes. *Am J Ophthalmol*. 2004;138(5):709-716.
6. Ruiz-Moreno JM, Staicu C, Piñero DP, Montero J, Lugo F, Amat P. Optical coherence tomography predictive factors for macular hole surgery outcome. *Br J Ophthalmol*. 2008;92(5):640-644.
7. Michalewska Z, Michalewski J, Adelman RA, Nawrocki J. Inverted internal limiting membrane flap technique for large macular holes. *Ophthalmology*. 2010;117:2018-2025.
8. Meyer CH, Szurman P, Haritoglou C, et al. Application of subretinal fluid to close refractory full thickness macular holes: treatment strategies and primary outcome: APOSTEL study. *Graefe Arch Clin Exp Ophthalmol*. 2020;258:2151-2161.
9. Rizzo S, Caporossi T, Tartaro R, et al. A human amniotic membrane plug to promote retinal breaks repair and recurrent macular hole closure. *Retina*. 2019;39(Suppl 1):S95-S103.
10. Moysidis SN, Koulisis N, Adrean SD, et al. Autologous retinal transplantation for primary and refractory macular holes and macular hole retinal detachments: the Global Consortium. *Ophthalmology*. 2021;128(5):672-685.
11. Rezende FA, Ferreira BG, Rampakakis E, et al. Surgical classification for large macular hole: based on different surgical techniques results: The CLOSE study group. *Int J Retina Vitreous*. 2023;30;9(1):4.
12. Rossi T, Bacherini D, Caporossi T, et al. Macular hole closure patterns: an updated classification. *Graefes Arch Clin Exp Ophthalmol*. 2020;258(12):2629-2638.
13. Parolini B, Arevalo JF, Hassan T, et al. International validation of myopic traction maculopathy staging system. *Ophthalmic Surg Lasers Imaging Retina*. 2023;54(3):153-157.

FLAVIO A. REZENDE, MD, PHD
- Vitreoretinal Specialist, Centre Universitaire d'Ophtalmologie, Maisonneuve-Rosemont Hospital (CUO-HMR). Montreal, Canada
- Associate Professor, Department of Ophthalmology, University of Montreal, Montreal, Canada
- cuohmrchief@gmail.com
- Financial disclosure: None

Macular Hole Classification in Myopia
For more on this classification system, scan the QR code or read *Manage Myopic Traction Maculopathy With Ease* at bit.ly/3QWIZrJ.

RETINA PATTERN SCANNING IN EVERY COLOR

THE MOST COMPREHENSIVE RETINA LASER PORTFOLIO IN OPHTHALMOLOGY

Integre® Pro Scan
Pattern Scanning | Green | Yellow | Red
*Single Spot Available on Integre® Pro

EasyRet®
Pattern Scanning | Single Spot | Subthreshold | Yellow

Vitra® 2
Pattern Scanning | Single Spot | Green

See in color.
Green
Yellow
Red

LUMIBIRD® MEDICAL

FORMERLY ELLEX | QUANTEL MEDICAL
www.lumibirdmedical.com

INTEGRE® PRO SCAN

SURPRISES FROM THE RETINA OR

Even the best-laid plans can go awry—see how these experts handled unexpected intraoperative events.

By Takumi Ando, MD; Haley S. D'Souza, MD, MS; and Matthew R. Starr, MD

Retina surgeons are often tasked with seemingly impossible surgical scenarios, whether it's an ocular trauma case, severe diabetic eye disease, or secondary IOL implantation, to name only a few. Surgeons must be nimble because even if the surgical plan seems straightforward, the case can quickly become a challenge if the unexpected happens.

Retina Today asked experts to share their "oh no" moments in the OR and how they handled the complications with grace.

CASE NO. 1: INTRAOCULAR CONTENTS EXTRUSION

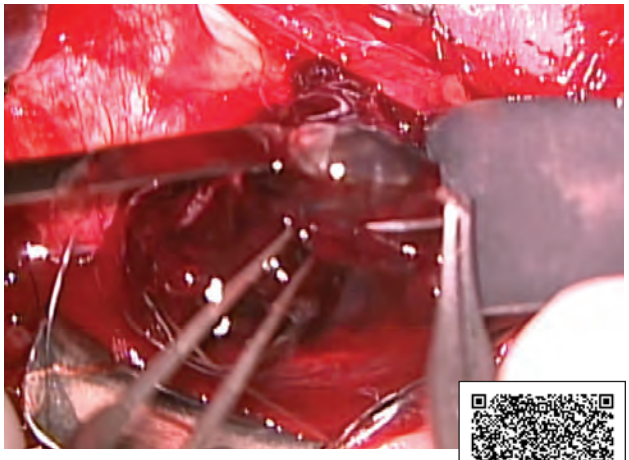
By Takumi Ando, MD

A man in his fifties presented after his right eye had been hit by a piece of wood at work. Slit lamp examination revealed hemorrhagic chemosis and a massive hyphema in the affected eye, and a CT scan showed an irregular globe contour. B-scan ultrasonography documented vitreous hemorrhage and membranes. The patient was diagnosed with an occult globe rupture, and my surgical team immediately performed surgical exploration and planned a one-stage surgery, if possible (Video 1).

During surgical exploration, a deep scleral rupture approximately 10 mm from the corneal limbus was found at the superotemporal quadrant (Figure 1A). Despite an attempt to suture the wound by reducing the aqueous humor as much as possible and avoiding any pressure on the globe, the intraocular contents prolapsed when the first stitch was placed (Figure 1B). Because repositioning the contents was ineffective, the vitreous body was removed, avoiding the retina. The mass was very large, and the wound remained difficult to suture; therefore, the entire contents were removed, causing extensive retinal incarceration and a retinal defect.

The scleral rupture was circumferentially long, extending under the superior rectus muscle. The superior rectus muscle was incised, and additional sutures were placed.

WATCH IT NOW



Video 1. Intraocular Contents Extrusion From a Deep Scleral Rupture.

AT A GLANCE

- During surgical exploration of an open-globe injury, the intraocular contents prolapsed through the deep scleral rupture.
- Postoperative proliferative vitreoretinopathy resulted in total retinal detachment, necessitating another trip to the OR.
- Another case of ocular trauma led to a macula-involving rhegmatogenous retinal detachment and a superior scleral rupture, which required a scleral buckle, vitrectomy, and a second surgery.

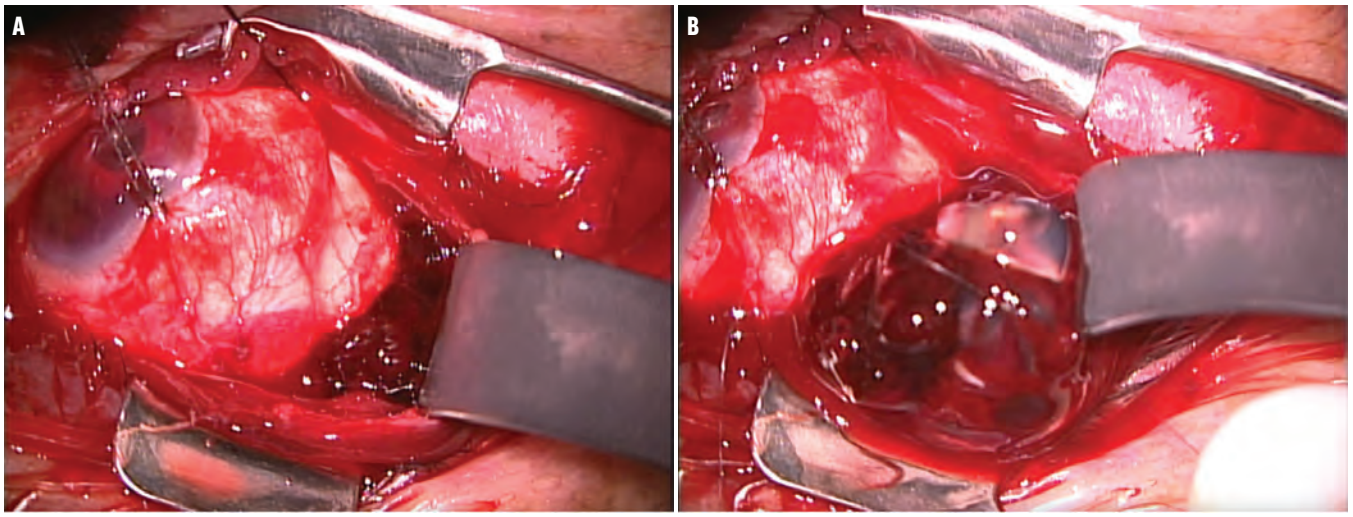


Figure 1. Surgical exploration revealed a deep scleral rupture approximately 10 mm from the corneal limbus (A), through which the intraocular contents prolapsed during surgery (B).

The circumferential length of the scleral wound was approximately 25 mm. Finally, the ruptured wound was discovered to be a very deep and long scleral rupture.

After suturing, the planned lensectomy and vitrectomy was performed. Fluid-air exchange to drain the vitreous hemorrhage revealed that the entire retina was incarcerated into the superior wound. During the retinectomy, perfluorocarbon liquid was injected, but the retinal incarceration remained. We released it again, performed panretinal photocoagulation in all quadrants, and placed silicon oil.

After 4 weeks, the superior retina had been pulled into the superior ruptured wound, resulting in total retinal detachment (RD) caused by proliferative vitreoretinopathy (PVR), necessitating another trip to the OR.

At postoperative week 6, the patient's VA was 20/500 OD. The retina was attached, but the macula had rotated upward. The nasal choroid was torn by proliferative tissues and the sclera was exposed. At 18 months follow-up, VA was counting fingers, IOP was 5 mm Hg, and neither the RD nor the PVR had recurred. Because of hypotony, the silicone oil tamponade remained in the eye.

CASE NO. 2: A HIDDEN SCLERAL RUPTURE


By Haley S. D'Souza, MD, MS, and Matthew R. Starr, MD

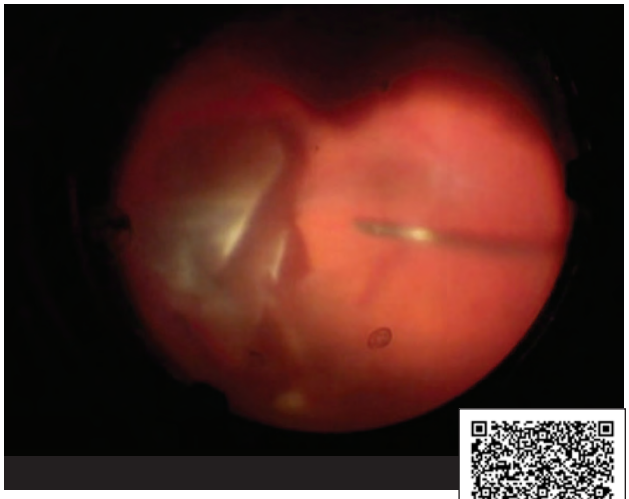
A 59-year-old man presented to the emergency department due to decreased vision in his left eye 2 days after sustaining a fall in which he struck his eye on a door handle. VA was 20/30 OD and hand motion OS. The left pupil was minimally reactive but without an afferent pupillary defect, and IOPs were 16 mm Hg OD and 10 mm Hg OS. Examination of the left eye was remarkable for chemosis with subconjunctival hemorrhage, anterior chamber cell, and a dense vitreous hemorrhage with no view to the posterior pole. B-scan demonstrated a nasal area suspicious for choroidal hemorrhage. The patient was started on prednisolone acetate (Pred Forte, Allergan/Abbvie) six times per day and atropine twice per day. The patient followed up in the retina clinic 2 days later, where B-scan demonstrated an area of vitreoretinal traction concerning for a tear or RD; the decision was made to proceed with early pars plana vitrectomy (Video 2).

The case began with a standard three-port setup. A pre-tested infusion line was inserted and turned on after verification of positioning with the light pipe. Initial visualization revealed an extremely dense vitreous hemorrhage obscuring the view to the posterior pole. A posterior vitreous detachment was carefully induced, and then a core vitrectomy was performed. At this point, we noted a nasal macula-involving rhegmatogenous RD. After prolonged scleral depression to identify the retinal break, we were surprised to find the fluid was guttering from a superior scleral rupture site, not a retinal tear. The decision was then made to proceed with scleral buckling and an open-globe repair.

After a 360° conjunctival peritomy and dissection, the scleral rupture was noted to extend from the 9 to 3 clock hours. We imbricated and disinserted the superior rectus muscle and closed the rupture with interrupted 8-0 nylon sutures. We then tied down the superior rectus muscle in its original position. We individually isolated and cleaned the rectus muscles and found no additional rupture. We placed a 41 band around the eye with a Watzke sleeve in the superonasal quadrant.

We then performed careful vitreous base shaving. The retina was incarcerated into the scleral rupture site superiorly from approximately the 10 to 2 clock hours. We used the cutter to remove the incarcerated retina

WATCH IT NOW



Video 2. Repairing a Hidden Scleral Rupture.

superiorly and relax the retina. We instilled perfluorocarbon liquid to reattach the retina and performed endolaser to the superior retinectomy. We then performed a fluid-air exchange and filled the eye with silicone oil.

The patient tolerated the procedure well, and the retina remained attached. Four months postoperatively, he underwent cataract extraction and removal of the silicone oil. At that time, we found that inferior PVR was resting on and just posterior to the scleral buckle, but the retina remained attached. During the oil removal, the internal limiting membrane was peeled and used as a scaffold to peel the posterior PVR.

Ten months following oil removal, the patient's BCVA was 20/50 OS and the retina remained attached. ■

TAKUMI ANDO, MD
- Vitreoretinal Fellow, Division of Ophthalmology and Visual Science, Graduate School of Medical and Dental Sciences, Niigata University, Japan
- takuan-umauma@med.niigata-u.ac.jp
- Financial disclosure: None

HALEY S. D'SOUZA, MD, MS
- Resident, Mayo Clinic, Rochester, Minnesota
- Financial disclosure: None

MATTHEW R. STARR, MD
- Assistant Professor of Ophthalmology, Mayo Clinic, Rochester, Minnesota
- Editorial Advisory Board Member, *Retina Today*
- mstarr1724@gmail.com
- Financial disclosure: Advisory Board (Alimera, Genentech/Roche); Consultant (Gyroscope Therapeutics, Regenxbio)

(Continued from page 25)

EXTENDED ILM PEELING DURING RRD REPAIR IN EYES WITH PVR GRADE C MAY BE RECOMMENDED FOR BOTH ANATOMIC AND VISUAL ACUITY CONSIDERATIONS.

IN THE OR

Renewed interest in the treatment and prevention of PVR has resulted in several ongoing and recently completed research studies. From these data, several insights and considerations may be immediately relevant, including the use of PPV/SB in primary RRDs with high-risk features for PVR and extended ILM peeling in eyes with established PVR grade C RRDs.[3,8]

Moreover, data from the GUARD trial may support the near-term use of intravitreal methotrexate for the prevention of PVR, with additional data regarding efficacy and guidance for case selection of special interest.

Ongoing and future studies will be helpful to further classify high-risk features and cohorts, identify optimal surgical interventions for this population, and, hopefully, identify and refine adjunct therapeutics for the treatment and prevention of PVR. ■

1. Khan MA, Brady CJ, Kaiser RS. Clinical management of proliferative vitreoretinopathy: an update. *Retina*. 2015;35(2):165-175.
2. Nagasaki H, Shinagawa K, Mochizuki M. Risk factors for proliferative vitreoretinopathy. *Prog Retin Eye Res*. 1998;17(1):77-98.
3. Salabati M, Massenzio E, Kim J, et al. Primary retinal detachment repair in eyes deemed high risk for proliferative vitreoretinopathy: surgical outcomes in 389 eyes [published online ahead of print July 13, 2023]. *Ophthalmol Retina*.
4. Rao RC, Blinder KJ, Smith BT, Shah GK. Internal limiting membrane peeling for primary rhegmatogenous retinal detachment repair. *Ophthalmology*. 2013;120(5):1102-1103.e1-2.
5. Joseph DP, Ryan EH, Ryan CM, et al. Primary retinal detachment outcomes study: pseudophakic retinal detachment outcomes: Primary Retinal Detachment Outcomes Study Report Number 3. *Ophthalmology*. 2020;127(11):1507-1514.
6. Ryan EH, Ryan CM, Forbes NJ, et al. Primary Retinal Detachment Outcomes Study Report Number 2: phakic retinal detachment outcomes. *Ophthalmology*. 2020;127(8):1077-1085.
7. Fallico M, Russo A, Longo A, et al. Internal limiting membrane peeling versus no peeling during primary vitrectomy for rhegmatogenous retinal detachment: a systematic review and meta-analysis. *PloS One*. 2018;13(7):e0201010.
8. Yonekawa Y. Extended internal limiting membrane peeling for grade C proliferative vitreoretinopathy: international multicenter study. Paper presented at ASRS Annual Meeting; July 31, 2023; Seattle, WA.
9. Flaxel C. Phase 3 GUARD trial of ADX-2191 (methrotrexate for intravitreal administration) to prevent proliferative vitreoretinopathy and other postoperative complications. Paper presented at ASRS Annual Meeting; July 21, 2023; Seattle, WA.

M. ALI KHAN, MD, FACS, FASRS
- Vitreoretinal Surgeon, Granite Bay, California
- khanretinamd@gmail.com
- Financial disclosure: Consultant (Apellis, Genentech/Roche); Research Support (Regeneron)

eyetube

THE LATEST FROM EYETUBE

CLINICAL MINUTE RETINA

Ramin Tadayoni, MD, PhD, and guests discuss the latest research and clinical studies in retina.

LATEST VIDEO

Meta-Analysis of Anti-VEGF Agents in Wet AMD Therapy

Ramin Tadayoni, MD, PhD, and Jean-Francois Korobelnik, MD, PhD

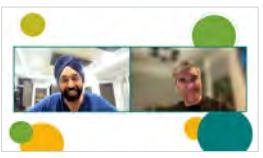
Innovation JOURNAL CLUB

Host I. Paul Singh, MD, interviews prominent ophthalmologists about podium data, peer-reviewed literature, and OUS experience on innovations that may reshape clinical practice.

LATEST VIDEO

Innovations in Geographic Atrophy

I. Paul Singh, MD, and Charles C. Wykoff, MD, PhD, FACS



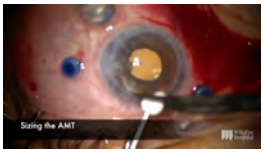
INSIDE THE WILLS OR

Watch as surgeons from Wills Eye Hospital review complex ophthalmic surgery cases.

LATEST VIDEO

Amniotic Membrane for Recalcitrant Macular Hole

Ajay E. Kuriyan, MD, MS



PEDIATRIC VITREORETINAL SURGERY TIPS

The youngest patients require some extra care in the OR. Here's what you need to know.

By Vahid Ownagh, MD; Nita Valikodath, MD, MS; and Lejla Vajzovic, MD, FASRS



There are significant anatomical differences between pediatric and adult eyes that have important implications for pediatric vitreoretinal surgery. For example, posterior segment volume is less than 50% at birth, and axial length is approximately 70% compared with an adult eye.[1] Pars plana width is an important consideration to avoid injury to the lens or retina during trocar placement. The infant lens is thicker and more spherical, and the lens-to-globe ratio is greater in children.[2] The hyaloid is very adherent to the retina in young children, and vitreous removal may be difficult.[3] Here, we highlight a variety of surgical considerations in pediatric cases.

PREOPERATIVE CARE

Obtaining informed consent from the child's legal guardian is a fundamental part of preoperative care. Vitreoretinal surgeons should have a thorough discussion with the legal guardian and caretakers regarding important aspects of perioperative care. Parents should have realistic expectations about the visual prognosis of their child, and they should be educated on the difference between anatomical and functional success. Necessary postoperative care, including compliance with postoperative visits, eye drops, and pain management, should be emphasized.

In clinic, if imaging is not possible or provides inadequate anatomical information, examination under anesthesia (EUA) should be considered prior to any surgery. Surgeons should have a low threshold to perform EUA in the setting of pediatric vitreoretinal disorders. A thorough slit lamp and dilated fundus examination should be performed. OCT and widefield imaging can also be helpful in the preoperative evaluation of pediatric patients. Examination of the fellow eye is critical because bilateral surgery or prophylactic treatment of the other eye may be needed in select cases.

INTRAOPERATIVE CONSIDERATIONS

Scleral Buckles

These remain an essential therapeutic tool in children with retinal detachment (RD). Scleral buckles can be a primary procedure or in combination with vitrectomy, and most rhegmatogenous RDs in children should be approached initially with a scleral buckle (Figure 1), especially in eyes with a clear lens, anterior breaks, and absence of proliferative vitreoretinopathy (PVR).[4] In recent years, scleral buckles have been used less frequently for tractional RDs, such as in the setting of retinopathy of prematurity, given the advances in vitrectomy machines.[1]

After scleral buckling, postoperative considerations in children range from refractive and sensory amblyopia to strabismus and alterations in eye growth. Patients should be routinely followed during the postoperative period by their retina specialist and pediatric ophthalmologist. In younger pediatric patients, scleral buckle revisions are often required to compensate for a growing eye. It is preferable to divide rather than remove buckle elements because the encapsulated explant can provide continued support for the retina and vitreous base.[5]

AT A GLANCE

- Obtaining informed consent from the child's legal guardian is a fundamental part of preoperative care.
- Inducing a posterior vitreous detachment can be one of the most challenging steps during pediatric vitreoretinal surgery.
- In pediatric eyes, less is more, and aggressive surgical manipulation may not be necessary to achieve the planned surgical goals.

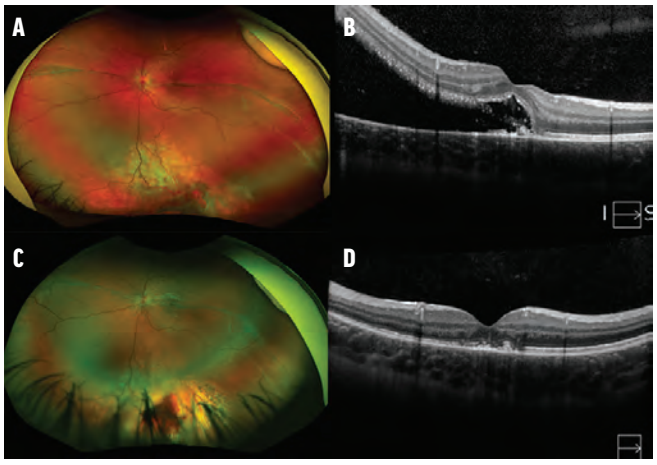


Figure 1. A 5-year-old girl was referred for evaluation of macular fold and noted to have a chronic inferior rhegmatogenous RD with an inferior break and demarcation line through the fovea (A). The patient underwent primary scleral buckle with silicone band and cryotherapy. Preoperative SD-OCT imaging with vertical cut (inferior to superior) demonstrated foveal splitting and a demarcation line (B). Four months after surgery, the peripheral break is surrounded by cryotherapy scars and the retina is attached (C, D).

Surgical Approach

In cases of advanced RD and/or vitreous opacities, lens-sparing vitrectomy may be necessary to release tractional components or clear vitreous opacity. In cases of lenticular opacities or anterior retinal drag, a translimbal approach with combined lensectomy and vitrectomy may be preferable.

Trocar Placement

There are several methods for placing trocars in pediatric eyes. One method adheres to a standard age-adjusted nomogram (Table).[6] Because the pars plana is not fully developed until 8 or 9 months of age, the pars plicata approach with incisions within 0.5 mm to 1 mm posterior to the limbus is preferred in the infant eye.[7] For eyes with unusual anatomy, such as microphthalmos, or eyes with severe anterior segment abnormalities, transscleral illumination is another useful method to determine the location of the pars plana for safe sclerotomy entry.

Trocars and instruments should be inserted perpendicular to the sclera and parallel to the visual axis. Given the increased elasticity and reduced rigidity, entering the pediatric eye is often challenging and may require twisting maneuvers with persistent pressure and counter traction with a second instrument.[1]

Video 1. Inducing a Posterior Vitreous Detachment in a Pediatric Patient.

TABLE. AGE-BASED RECOMMENDATIONS FOR SCLEROTOMY PLACEMENT

Age	Distance From Limbus (mm)
< 1 months	0.75
1 to 3 months	1.0
3 to 8 months	1.5
8 to 12 months	2.0
18 to 24 months	2.5
3 to 6 years	3.0
6 to 12 years	3.5
Adapted from Wright LM et al.[6]	

PVD Induction

In pediatric patients, there is firm adherence of the cortical vitreous to the retina. Therefore, inducing a posterior vitreous detachment (PVD) can be a challenging step during pediatric vitreoretinal surgery. Typically, PVD induction is

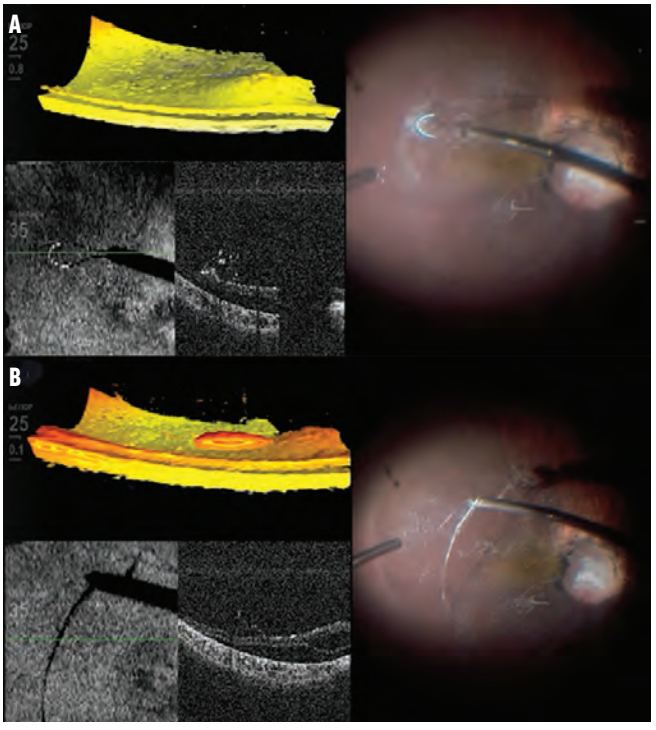


Figure 2. During PVD induction, after highlighting the posterior hyaloid with diluted triamcinolone acetonate, the flex loop is employed to engage and lift the posterior hyaloid with radial movements (A). The hyaloid is seperated from the peripapillary retina with vitreous cutter suction (B).

Video 2. Vitrectomy in a Child with Incontinentia Pigmenti.

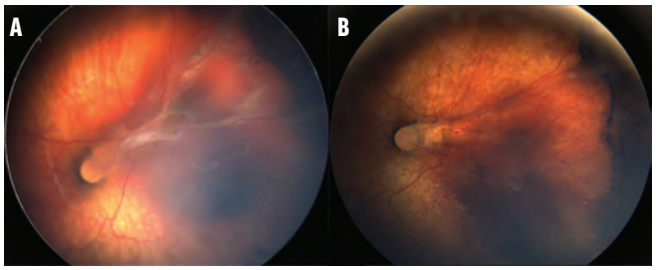


Figure 3. An 11-month-old girl with incontinentia pigmenti and previous history of retinal photocoagulation presented with a temporal ridge and superotemporal tent-like tractional RD in the left eye (A). During the vitrectomy, using the vitreous cutter, vertical scissors, and Maxgrip forceps (Alcon), the posterior hyaloid was carefully peeled and segmented bimanually to avoid the creation of retinal tears. Two months after surgery, the traction was relieved from the optic nerve, and the macula and the retina were relaxed and reattached (B).

indicated for young patients in cases involving traumatic macular hole repair, epiretinal membrane peeling, or RD repair or to address a vitreous opacity, such as vitreous hemorrhage. Failing to induce a PVD in these cases may lead to poor surgical outcomes.[8]

We recommend a stepwise approach by starting the PVD induction with chromovitrectomy with diluted triamcinolone acetonide (Figure 2, Video 1). For particularly adherent vitreous, we use a flexible loop (Alcon) or a bimanual technique using a lighted pick and the vitreous cutter. Once the flex loop touches the retina to engage the posterior hyaloid, the hyaloid is separated from the optic disc and peripapillary retina using gentle radial motions. We aspirate with the cutter over the area near the optic nerve and gently lift the induced edge with the lighted pick from the other end. Perfluorocarbon liquid is helpful for a partially induced PVD, particularly in the setting of macular RD. Perfluorocarbon liquid is gently infused through the opening created in the hyaloid and over the optic nerve to help lift the PVD.

Occasionally, a PVD can be propagated to the periphery, but it is important to avoid causing retinal breaks. A compromise is a judicious core vitrectomy that leaves a layer of cortical vitreous on the retina that is as thin as possible. If complete removal of the vitreous from the periphery is not feasible, a thorough shaving procedure becomes essential.[5]

Lens Management

Recent advances in pediatric vitreoretinal surgery techniques have improved the anatomic and visual outcomes for lens-sparing vitrectomy, and this is the preferred method in most pediatric cases. The main advantage is the preservation of the refractive state of a phakic eye to facilitate visual rehabilitation and development. Lensectomy is recommended for addressing most anterior retinal pathologies or in eyes at high risk for PVR, such as severe globe injury or uveitis.[5] In cases of retinal pathology with advanced PVR, capsular remnants may serve as a scaffold for preretinal proliferation and circumferential vitreoretinal contraction or development of synechiae with distortion of the pupil. Therefore, complete removal of the capsular remnants should be attempted.[9] If lensectomy is planned, some or all the trocars can be placed at the limbus to minimize trocar manipulation of the pars plana. The pediatric crystalline lens is generally soft enough to aspirate with a vitrector.

VITRECTOMY TIPS

In pediatric eyes, less is more (Figures 3 and 4, Video 2). Aggressive surgical manipulation may not be necessary to achieve the planned surgical goals. Iatrogenic breaks often result in severe PVR, causing a catastrophic outcome with inoperable RDs. In eyes with PVR, it is preferable to perform segmentation instead of delamination when removing preretinal membranes due to the firm vitreoretinal attachments in children.[10]

Posterior drainage retinotomies are best avoided, as extensive fibrous proliferation can occur postoperatively, leading to RD.

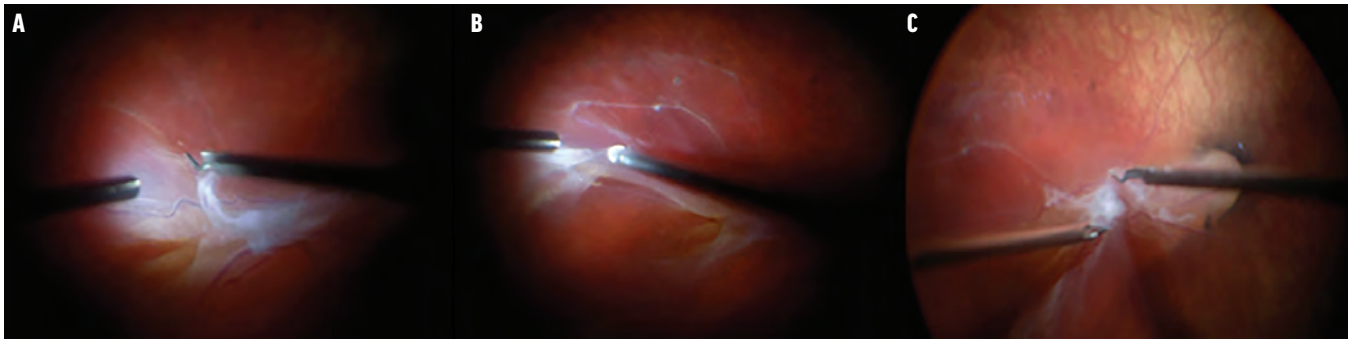


Figure 4. During the lens-sparing pars plana vitrectomy for the patient in Figure 3, vertical scissors (A) and a vitreous cutter (B) were used to carefully segment and delaminate the posterior hyaloid membrane from the underlying detached macula. An additional trocar was inserted to facilitate bimanual dissection of tractional membranes (C).

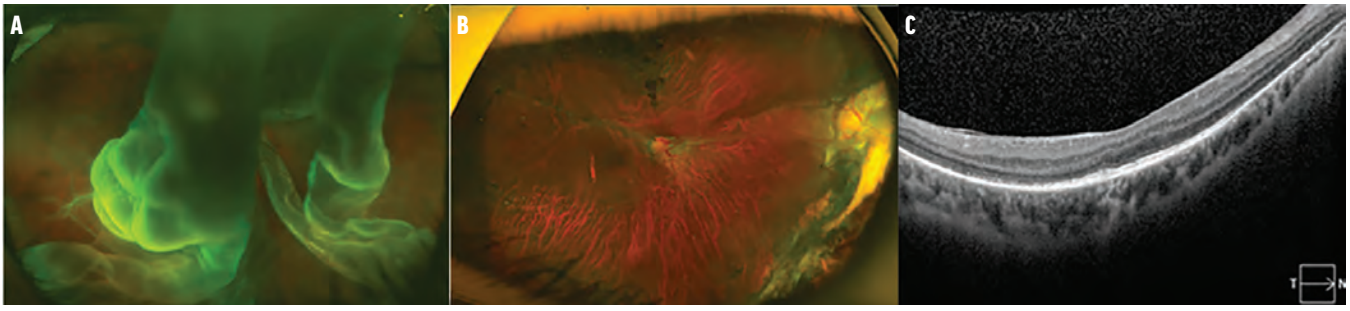


Figure 5. A 12-year-old boy with Stickler syndrome presented with total rhegmatogenous RD of the right eye with two equatorial giant retinal tears (A). The patient underwent 25-gauge pars plana vitrectomy with endolaser and 1,000 cs silicone oil tamponade. Five years after surgery, the retina is attached (B) with excellent macular anatomic reattachment seen on SD-OCT (C).

Choice of Tamponade

Intraocular gas can be challenging to use in pediatric patients, given the difficulties with positioning and IOP monitoring.[11,12] However, gas—especially longer-acting gases—may still be the best tamponade choice, with silicone oil (either 1,000 cs or 5,000 cs) reserved for patients who have inferior pathology or need a longer tamponade (Figure 5). Pediatric patients may maintain intraocular silicone oil for a prolonged time. The tamponade choice and its risks and benefits should be discussed thoroughly with the patient's caregiver.

Closure

Surgeons should suture the sclerotomies at the completion of the surgery to minimize the risk of hypotony, tamponade loss, and infection. Closure of the sclera and conjunctiva may be done with absorbable 8-0 or 9-0 vicryl or plain gut sutures.

POSTOPERATIVE CARE

It is essential to schedule regular postoperative examinations. The primary purpose of postoperative care is to support visual and anatomical rehabilitation and monitor for other conditions, such as cataract, glaucoma, recurrent RD, epiretinal membrane, inflammation, infection, amblyopia, strabismus, diplopia, and ptosis. Refractive issues may need to be addressed with glasses, contact lenses, or patching. Working closely with a pediatric ophthalmologist is crucial to provide comprehensive care. It is important to discuss postoperative positioning, eye drops, and pain management because compliance can be an issue in pediatric patients.

WORTH THE CHALLENGE

Pediatric vitreoretinal surgery can be challenging but extremely rewarding by potentially helping to restore vision and function in a child. Pediatric patients often cannot communicate their thoughts or feelings, and it becomes even more crucial to have a thorough discussion with the patient's caretaker about what to expect during surgery and postoperative instructions. ■

1. Özdek Ş, Berrocal A, Spandau U. Pediatric Vitreoretinal Surgery. Springer International Publishing; 2023.
2. Augusteyn RC. On the growth and internal structure of the human lens. *Exp Eye Res*. 2010;90(6):643-654.
3. Sebag J. Age-related differences in the human vitreoretinal interface. *Arch Ophthalmol*. 1991;109(7):966-971.
4. Wenick AS, Baranano DE. Evaluation and management of pediatric rhegmatogenous retinal detachment. *Saudi J Ophthalmol*. 2012;26(3):255-263.
5. Sadda SVR, Schachat AP, Wilkinson CP, et al. Ryan's Retina. Elsevier Health Sciences; 2022.
6. Wright LM, Harper CA 3rd, Chang EY. Management of infantile and childhood retinopathies: optimized pediatric pars plana vitrectomy sclerotomy nomogram. *Ophthalmol Retina*. 2018;2(12):1227-1234.
7. Hairston RJ, Maguire AM, Vitale S, Green WR. Morphometric analysis of pars plana development in humans. *Retina*. 1997;17(2):135-138.
8. Vajzovic L, Thomas A. Tips for inducing posterior vitreous detachment in young patients. *Retinal Physician*. March 2017. Accessed September 5, 2023. www.retinalphysician.com/newsletter/surgical-maneuvers/march-2017
9. Ranchod TM, Capone A Jr. Tips and tricks in pediatric vitreoretinal surgery. *Int Ophthalmol Clin*. 2011;51(1):173-183.
10. Gan NY, Lam WC. Special considerations for pediatric vitreoretinal surgery. *Taiwan J Ophthalmol*. 2018;8(4):237-242.
11. Berrocal A, Trese M. Pearls for pediatric retina surgery. *Retina Today*. 2023;10(3):34.
12. Fekrat S. The Duke Manual of Vitreoretinal Surgery. Wolters Kluwer; 2020.

VAHID OWNAGH, MD
- Vitreoretinal Research Fellow, Department of Ophthalmology, Duke Eye Center, Duke University, Durham, North Carolina
- Financial disclosure: None

LEJLA VAJZOVIC, MD, FASRS
- Director, Duke Vitreoretinal Fellowship Program, Duke University Eye Center, Durham, North Carolina
- Associate Professor of Ophthalmology with Tenure, Adult and Pediatric Vitreoretinal Surgery and Diseases, Duke University Eye Center, Durham, North Carolina
- Editorial Advisory Board Member, *Retina Today*
- lejla.vajzovic@duke.edu
- Financial disclosure: Consultant (Abbvie/Allergan, Alcon, Alimera Sciences, Apellis, Bausch + Lomb, Beaver-Visitec International, BMC, Clearside Biomedical, Coherus Biosciences, DORC, Genentech/Roche, Guidepoint, Gyroscope, Iveric Bio/Astellas, Janssen, Novartis, Ocugen, Ocular Therapeutix, Oculus Surgical, OcuTerra, Outlook Therapeutics, Regenxbio); Honoraria (Evolve Medical Education, Vindico Medical Education); Investigator (AGTC, Alcon, Aldeyra, Genentech/Roche, Heidelberg, NEI, Novartis, Ocular Therapeutix, Regenxbio); Research Grants (Gyroscope, Heidelberg)

NITA VALIKODATH, MD, MS
- Vitreoretinal Surgeon, Department of Ophthalmology, Kellogg Eye Center, University of Michigan, Ann Arbor, Michigan
- Former Vitreoretinal Fellow, Department of Ophthalmology, Duke Eye Center, Duke University, Durham, North Carolina
- Financial disclosure: None acknowledged

A USEFUL SURGICAL MODALITY FOR MYOPIC TRACTION MACULOPATHY

Consider scleral imbrication with combined vitrectomy and fovea-sparing ILM peeling for this condition.

By Fong May Chew, FRCOphth, MBBS, BSC; David R. Chow, MD, FRCSC; and David Wong, MD, FRCSC



Myopic foveal retinoschisis was first described in 1958 as a posterior retinal detachment without a macular hole.[1] With the advent of OCT, more detailed characteristics have been described.[2] Typical OCT images of this disease show splitting of the inner and outer retina within a posterior staphyloma.

The prevalence of myopic foveoschisis varies from 9% to 34% in myopic eyes.[2] Although myopic foveoschisis remains relatively stable over years for most patients, some can progress to visual loss from progressive traction and schisis, known as myopic traction maculopathy, which can further progress to macular detachment with or without development of a macular hole.

Various surgical approaches have been used for the treatment of the different stages of myopic traction maculopathy. Vitrectomy with internal limiting membrane (ILM) peeling has been the most common choice for managing these patients; however, ILM peeling can be responsible for the creation of a macular hole in 19% to 27% of these patients.[3,4] As a result, fovea-sparing ILM peeling may be able to relieve the traction without the risk of inducing a macular hole.[3]

In the presence of a posterior staphyloma in tractional cases, reapposing the detached macula to the outpouched scleral wall is another complicating factor for which external macular scleral buckling has been used. However, externally applied macular scleral buckles are not commonly available, require a unique set of surgical risks, and come with their own possible postoperative complications.

In these cases, scleral imbrication is an alternative surgical technique that may change the curvature of the macular staphyloma. This approach, first described by Swan in 1959,[5] involves the placement of sutures through the temporal sclera, a technique similar to that which is used with traditional scleral buckling. The placement of these scleral sutures flattens the staphyloma posteriorly and can be an adjunctive step to help relieve traction and allow retinal attachment in challenging myopic traction maculopathy cases.

THE STUDY

We conducted a retrospective, nonrandomized case series of 13 patients who were treated with scleral imbrication combined with vitrectomy and fovea-sparing ILM peeling for myopic traction maculopathy. The primary outcome was the anatomical success rate. The secondary outcomes included

AT A GLANCE

- Various surgical approaches have been used for the treatment of myopic traction maculopathy, the most common being vitrectomy with internal limiting membrane peeling.
- In a study of 13 patients treated with scleral imbrication, the postoperative axial length decreased by a mean of -0.18 ± 0.37 mm.
- The anatomical success rate was good with 71% achieving successful macular reattachment.

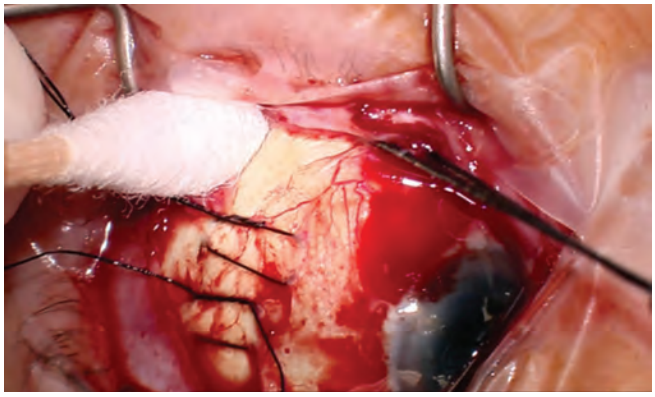


Figure. Two 5-0 partial scleral thickness nylon sutures are placed in the inferotemporal quadrant. The sutures are placed as posteriorly as possible with a bite size of 6 mm in width. The same is repeated in the superotemporal quadrant.

BCVA, axial length change, postoperative refraction, and the shape of the posterior segment as determined by OCT.

The surgical method consisted of scleral imbrication combined with 23-gauge vitrectomy. Imbrication was performed using four 5-0 nylon mattress sutures at 6 mm wide (Figure). Two of the mattress sutures were placed in the superior temporal quadrant, and two were placed in the inferior temporal quadrant. The sutures were placed as posteriorly as possible, and the passage through the sclera was approximately 3 mm to 5 mm.

After the core vitrectomy, the ILM was peeled using ILM forceps, sparing the fovea. The sutures were then tightened once the fluid infusion was switched to air to allow for greater tightening of the mattress sutures. Once the sutures were tied, an indent was noticeable.

The mean preoperative BCVA was 0.97 ± 0.4 logMAR, and the mean postoperative BCVA was 1.16 ± 0.5 logMAR. The mean preoperative axial length was 30.13 ± 1.99 mm, which showed a significant postoperative decrease to 29.38 ± 2.62 mm with a mean decrease in axial length of -0.18 ± 0.37 mm. The postoperative refraction shifted by +0.25 ± 0.79 D. The percentage of successful macular attachment with scleral imbrication/vitrectomy and fovea-sparing ILM peeling was 71.4% with one patient lost to follow-up.

DISCUSSION

Postoperatively, there was a significant decrease in axial length and a significant shift in refraction, but given the small sample size, there was a nonstatistically significant improvement in visual acuity. The anatomical success rate was good with 71% achieving successful macular reattachment. Our longest follow-up period was 4 years for one patient, who did not have a recurrence of myopic traction maculopathy.

This study was limited by its retrospective, noncomparative nature and the number of patients. Other limitations include the short period of follow-up and the nonrandomized design. Further studies with larger sample sizes and longer observation periods are needed to confirm these results and show whether axial length shortening and the subsequent refractive changes diminish over time. Such studies could also reveal whether the imbrication resulted in a slower progression of myopic staphyloma.

THIS APPROACH [...] INVOLVES THE PLACEMENT OF SUTURES THROUGH THE TEMPORAL SCLERA, A TECHNIQUE SIMILAR TO THAT WHICH IS USED WITH TRADITIONAL SCLERAL BUCKLING.

Overall, we found the use of scleral imbrication in combination with vitrectomy and fovea-sparing ILM peeling to be a useful treatment modality for myopic traction maculopathy. ■

1. Phillips CI. Retinal detachment at the posterior pole. *Br J Ophthalmol*. 1958;42(12):749-753.
2. Baba T, Ohno-Matsui K, Futagami S, et al. Prevalence and characteristics of foveal retinal detachment without macular hole in high myopia. *Am J Ophthalmol*. 2003;135(3):338-342.
3. Hirakata A, Hida T. Vitrectomy for myopic posterior retinoschisis or foveal detachment. *Jpn J Ophthalmol*. 2006;50(1):53-61.
4. Sayanagi K, Ikuno Y, Tano Y. Reoperation for persistent myopic foveoschisis after primary vitrectomy. *Am J Ophthalmol*. 2006;141(2):414-417.
5. Swan KC. Scleral imbrication for retinal detachment. *AMA Arch Ophthalmol*. 1959;61(1):110-114.

FONG MAY CHEW, FRCOPHTH, MBBS, BSC
- Consultant Ophthalmologist and Vitreoretinal Surgeon, Sheffield Teaching Hospitals, United Kingdom
- fongmay.chew1@nhs.net
- Financial disclosure: None

DAVID R. CHOW, MD, FRCSC
- Assistant Professor, St. Michael's Hospital, University of Toronto, Toronto Retina Institute, Canada
- davidrchow@me.com
- Financial disclosure: None

DAVID WONG, MD, FRCSC
- Ophthalmologist-in-Chief, St Michael's Hospital, Toronto, Canada
- david.wong@unityhealth.to
- Financial disclosure: None

A VISION FOR SUSTAINABLE CARE IN RETINA

Medical waste in the OR is a serious problem, but there are ways to reduce it.

By Chirantan Mukhopadhyay, MD

Studies have linked environmental pollution climate change to multiple conditions, including infections from viruses and other pathogens[1-4]; worsening allergy season duration and severity[5-7]; damage to nearly every ocular structure[8-11]; and increasing risk of AMD,[12] glaucoma,[13] retinal detachment,[14] and vascular occlusions.[15]

The field of retina, with our high surgical and patient volumes, has many opportunities to reduce medical waste. By understanding how the climate crisis is impacting our patients' ocular and overall health, we can take steps to mitigate the environmental damage our industry causes. I believe we must go even further and join other medical societies in sounding the alarm on this public health emergency.[16,17]

QUANTIFYING OCULAR SURGICAL WASTE

ORs consume three to six times more energy than any other department in the same facility; they also account for 50% of hospital supply costs and 66% of regulated waste.[18] Medical waste from ocular surgery was quantified further by Thiel et al, who showed that a single phacoemulsification performed at Aravind Eye Hospital, India, generated only 3% of the greenhouse gas emissions as did the same surgery performed in the United Kingdom or the United States.[19]

Moreover, the amount of physical waste generated by these surgeries in wealthy countries was about 7 kg versus about a quarter of a kilogram in India.[19,20] Interestingly, the rates of endophthalmitis have been found to be significantly lower at Aravind than in the United States,[21] suggesting that surgeries producing higher amounts of waste do not correlate with improved patient safety.

Another study conducted in Dublin quantified the carbon footprint of intravitreal injections and showed that, if unnecessary materials were eliminated, the net savings across the United Kingdom would be approximately 450,000 kg of CO_2-equivalents per year.

ORS CONSUME THREE-TO-SIX TIMES MORE ENERGY THAN ANY OTHER DEPARTMENT IN THE SAME FACILITY.

What Do Ophthalmologists Think?

When asked, ophthalmologists have recognized the unnecessary level of waste that our sight-saving efforts can produce. A 2020 survey of more than 1,300 ophthalmologists conducted by Chang et al showed that 90% were concerned about global warming and climate change, 93% felt OR waste was excessive, 94% felt we should look for ways to reduce waste, and 78% felt we should seek ways to reuse supplies and instruments.[22,23]

HOW YOU CAN HELP

Fortunately, there are many ways to take action in reducing medical waste and other causes of environmental harm (see *Strategies and Recommendations* for ideas proposed by a group of ophthalmologists). Consider looking into the below resources to get started:

STRATEGIES AND RECOMMENDATIONS

By Albert S. Khouri, MD; Marko Oydanich, MD, MS; and Jasmine Mahajan, BS



No. 1: Analyze the waste. One strategy for reducing OR waste and ophthalmology's carbon footprint is to separate waste from recyclable material.[1]

No. 2: Reconsider regulations. Eye care providers, health care administrators, and product manufacturers can reevaluate the benefits and drawbacks of strict regulations on products for which the risks of contamination are not well studied. The theoretical adverse effects of reusing eye drops, gonioscopy lenses, and tonometer prisms are not equivalent to the measurable financial and environmental burden of the waste produced.[2] Efforts to reduce environmental costs without sacrificing surgical technique and increasing postoperative complications have shown great promise in several countries, creating an opportunity for a shift in others, including the United States.[3]

No. 3: Improve education. Studies have found that trainee surgeons generate almost 25% more waste than experienced surgeons. Efforts to reduce greenhouse gas emissions can be augmented through waste reduction education starting at the trainee level.[4]

No. 4: Conduct research to inform action. There is a dearth of research on the environmental impact of surgical waste in ophthalmology. Studies should be designed to trial different approaches to waste reduction.

This material was adapted from an article that ran in *Glaucoma Today*, a sister publication of *Retina Today*. Scan the QR code to read the article in full.

1. Buchan JC, Thiel CL, Steyn A, et al. Addressing the environmental sustainability of eye health-care delivery: a scoping review. *Lancet Planet Health*. 2022;6(6):e524-e534.
2. Tauber J, Chinwuba I, Kleyn D, Rothschild M, Kahn J, Thiel CL. Quantification of the cost and potential environmental effects of unused pharmaceutical products in cataract surgery. *JAMA Ophthalmol*. 2019;137(10):1156-1163.
3. Namburar S, Pillai M, Varghese G, Thiel C, Robin AL. Waste generated during glaucoma surgery: a comparison of two global facilities. *Am J Ophthalmol Case Rep*. 2018;12:87-90.
4. Khor HG, Cho I, Lee KRCK, Chieng LL. Waste production from phacoemulsification surgery. *J Cataract Refract Surg*. 2020;46(2):215-221.

- Practice Greenhealth[18]
- Healthcare Without Harm[24]
- Medical Consortium on Climate and Health[25]
- EyeSustain[26]
- International Agency for the Prevention of Blindness.[27]

These resources offer a wealth of actionable, evidence-based guidance on how individual ophthalmologists can get involved. In addition, an excellent recent publication by Sherry et al in *Ophthalmology* provides concrete steps that eye care professionals can take to address this problem.[2]

We also have a tremendous ability to educate our colleagues, patients, and the public and advocate for policy changes that can lead to a brighter, more sustainable future for generations to come. ■

1. Khairallah M, Mahendradas P, Curi A, Khochtali S, Cunningham ET Jr. Emerging viral infections causing anterior uveitis. *Ocul Immunol Inflamm*. 2019;27(2):219-228.
2. Merle H, Donnio A, Jean-Charles A, et al. Ocular manifestations of emerging arboviruses: Dengue fever, Chikungunya, Zika virus, West Nile virus, and yellow fever. *J Fr Ophtalmol*. 2018;41(6):e235-e243.
3. Walkden A, Fullwood C, Tan SZ, et al. Association between season, temperature and causative organism in microbial keratitis in the UK. *Cornea*. 2018;37(12):1555-1560.
4. Boss JD, Sosne G, Tewari A. Ocular dirofilariasis: ophthalmic implication of climate change on vector-borne parasites. *Am J Ophthalmol Case Rep*. 2017;7:9-10.
5. Anderegg WRL, Abatzoglou JT, Anderegg LDL, Bielory L, Kinney PL, Ziska L. Anthropogenic climate change is worsening North American pollen seasons. *Proc Natl Acad Sci U S A*. 2021;118(7):e2013284118.
6. Bielory L, Lyons K, Goldberg R. Climate change and allergic disease. *Curr Allergy Asthma Rep*. 2012;12(6):485-494.
7. Echevarría-Lucas L, Senciales-González JM, Medialdea-Hurtado ME, Rodrigo-Comino J. Impact of climate change on eye diseases and associated economical costs. *Int J Environ Res Public Health*. 2021;18(13):7197.
8. Johnson GJ. The environment and the eye. *Eye (Lond)*. 2004;18(12):1235-1250.
9. Cullen AP. Ozone depletion and solar ultraviolet radiation: ocular effects, a United Nations environment programme perspective. *Eye Contact Lens*. 2011;37(4):185-190.
10. Hammond BR, Johnson BA, George ER. Oxidative photodegradation of ocular tissues: Beneficial effects of filtering and exogenous antioxidants. *Exp Eye Res*. 2014;129:135-150.
11. Adar SD, Klein R, Klein BE, et al. Air Pollution and the microvasculature: a cross-sectional assessment of in vivo retinal images in the population-based multi-ethnic study of atherosclerosis (MESA). *PLoS Med*. 2010;7(11):e1000372.
12. Chang K, Hsu P, Lin C, et al. Traffic-related air pollutants increase the risk for age-related macular degeneration. *J Investig Med*. 2019;67:1076-1081.
13. Chua SYL, Khawaja AP, Morgan J, et al. The relationship between ambient atmospheric fine particulate matter (PM2.5) and glaucoma in a large community cohort. *IOVS*. 2019;60:4915-4923.
14. Auger N, Rhéaume MA, Bilodeau-Bertrand M, Tang T, Kosatsky T. Climate and the eye: case-crossover analysis of retinal detachment after exposure to ambient heat. *Environ Res*. 2017;157:103-109.
15. Cheng HC, Pan RH, Yeh HJ, et al. Ambient air pollution and the risk of central retinal artery occlusion. *Ophthalmology*. 2016;123:2603-2609.
16. Atwoli L, Baqui AH, Benfield T, et al. Call for emergency action to limit global temperature increases, restore biodiversity and protect health. *BMJ Open*. 2021;11(9):e056565.
17. Choi-Schagrin W. Medical journals call climate change the 'greatest threat to global public health'. *New York Times*. 2021;9(7). www.nytimes.com/2021/09/07/climate/climate-change-health-threat.html
18. Greening the OR. Practice Greenhealth. Accessed August 30, 2023. bit.ly/45ZPEWN
19. Thiel CL, Schehlein E, Ravilla T, et al. Cataract surgery and environmental sustainability: waste and lifecycle assessment of phacoemulsification at a private healthcare facility. *J Cataract Refract Surg*. 2017;43(11):1391-1398.
20. Venkatesh R, van Landingham SW, Khodifad AM, et al. Carbon footprint and cost-effectiveness of cataract surgery. *Curr Opin Ophthalmol*. 2016;27(1):82-88.
21. Haripriya A, Chang DF, Reena M, Shekhar M. Complication rates of phacoemulsification and manual small-incision cataract surgery at Aravind Eye Hospital. *J Cataract Refract Surg*. 2012;38(8):1360-1369.
22. Chang DF, Thiel CL, Ophthalmic Instrument Cleaning and Sterilization Task Force. Survey of cataract surgeons' and nurses' attitudes toward operating room waste. *J Cataract Refract Surg*. 2020;46(7):933-940.
23. Chang DF. Needless waste and the sustainability of cataract surgery. *Ophthalmology*. 2020;127(12):1600-1602.
24. Healthcare Without Harm. Accessed August 30, 2023. noharm.org
25. The Medical Consortium on Climate & Health. Accessed August 30, 2023. medsocietiesforclimatehealth.org
26. EyeSustain. Accessed August 30, 2023. eyesustain.org
27. Climate Action. The International Agency for the Prevention of Blindness. Accessed August 30, 2023. bit.ly/48s4Uxo
28. Sherry B, Lee S, Brooke S, et al. How ophthalmologists can decarbonize eye care: a review of existing sustainability strategies and steps ophthalmologists can take. *Ophthalmology*. 2023;130(7):702-714.

CHIRANTAN MUKHOPADHYAY, MD
■ Ophthalmologist, NorthShore Medical Group, Skokie, Illinois
■ chirantanmd@gmail.com
■ Financial disclosure: None

YoungMD Connect | RETINA

Unparalleled Access to Thought Leaders in Retina

Calling all trainees and new-to-practice ophthalmologists:

Participate in monthly mentoring sessions & enjoy unequaled access to retina thought leaders and peer mentors.

Scan the QR code for 20% off one-year membership (less than $30).

Discount automatically applied.

MENTORS:

Anton Orlin, MD | Monday, October 16 @ 8:15PM ET

Thomas Albini, MD | Tuesday, December 5 @ 8:15PM ET

PEER MENTORS:

Deepak Sambhara, MD | Monday, November 27 @ 8:15PM ET

YoungMD Connect Members Gain Exclusive Access To:

- ✔ **MENTORING SESSIONS** to build connections with thought leaders.
- ✔ **EDUCATIONAL WORKSHOPS** to complement your clinical training.
- ✔ ***BOOKMARKED* EDITORIAL FORUM** to read the latest articles in eye care.
- ✔ **RESOURCES** to build new skills.
- ✔ **JOB BOARD** to land your first job or make a change.
- ✔ **IN-PERSON EVENTS** to fasttrack your networking opportunities and engage with industry.

YMDC is made possible with industry support from:

VISIONARY: Allergan an AbbVie company | Johnson & Johnson VISION

FOUNDATIONAL: Apellis | Dompé | LUMIBIRD MEDICAL | REGENERON

PARTNER: Alcon | Vision Innovation Partners | STAARSURGICAL

GUIDING: BAUSCH+LOMB | Genentech A Member of the Roche Group | GLAUKOS TRANSFORMING VISION | ZEISS

Brought to you by: bmc vision | RT

OCULAR MANIFESTATIONS OF COBALAMIN C DEFICIENCY

Genetic testing is critical to begin supplementation as early as possible.

BY NIRAJ PATEL, MD; RACHEL SAH, MD; AMY HUTCHINSON, MD; AND SRUTHI AREPALLI, MD

Cobalamin C deficiency is the most common heritable error of vitamin B_{12} metabolism, often leading to severe infantile-onset retinal degeneration.[1] In this autosomal recessive disorder, MMACHC protein dysregulation and subsequent metabolic imbalances contribute to a broad disease phenotype, including rapidly progressive maculopathy that may expand peripherally and optic nerve atrophy.[2]

Given the value of early identification and prompt treatment, newborn screening is commonly recommended. Despite nutritional treatment's effect on systemic disease, ocular disease is notoriously resistant to treatment, and patients almost universally progress to blindness at a young age.[3]

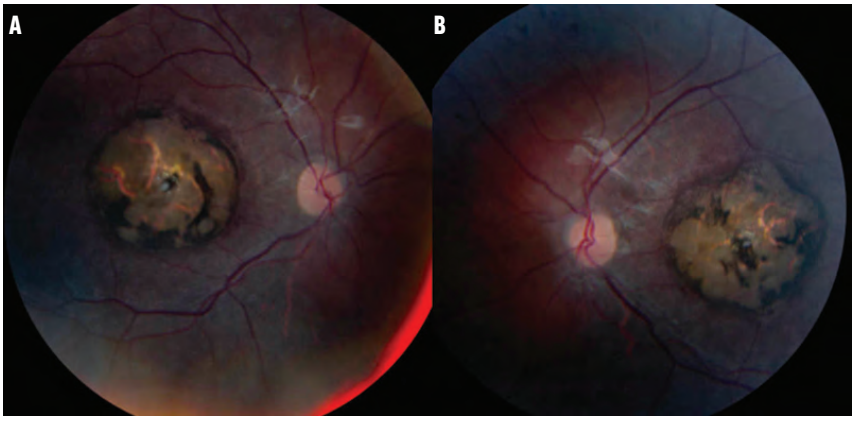


Figure. Fundus photos of the right (A) and left (B) eyes demonstrate findings consistent with a diagnosis of cobalamin C deficiency: mild optic nerve pallor, severe central macular atrophy of the outer retina/retinal pigment epithelium with visible choroidal vasculature, and diffuse peripheral pigmentary abnormalities.

THE CASE

A 3-year-old boy was brought to the Emory Eye Center for a second opinion after not tolerating glasses, despite several attempts at adjusting his prescription. His teachers had commented that his vision did not seem to be affected by wearing glasses. He had previously been diagnosed with myopia and bilateral retinal colobomas, which his parents understood would limit his vision.

On presentation, his visual acuity was central, unsteady, and maintained in each eye. There was no relative afferent pupillary defect, and IOP was 17/16 mm Hg OU. He was orthophoric with intact extraocular muscles and was noted to have nystagmus in each eye. Anterior examination was within normal limits for each eye.

The fundus examination revealed mild bilateral optic nerve pallor, severe central macular atrophy of the outer retina/retinal pigment epithelium with visible choroidal vasculature, and diffuse peripheral pigmentary abnormalities, which are consistent with sequelae of cobalamin C deficiency (Figure). On electroretinogram, the photopic and white scotopic responses were non-recordable, consistent with widespread rod and cone photoreceptor dysfunction.

A genetic evaluation that was undertaken earlier returned as notable for cobalamin C deficiency (an autosomal recessive mutation in the *MMACHC* gene on chromosome 1). This finding resulted in prompt initiation of supplementation and regular follow-up in the genetics clinic to ensure appropriate nutritional titration and to monitor developmental progress.

COBALAMIN C DEFICIENCY IS THE MOST COMMON HERITABLE ERROR OF VITAMIN B12 METABOLISM, OFTEN LEADING TO SEVERE INFANTILE-ONSET RETINAL DEGENERATION.

LOW VISION SUPPORT

Since his diagnosis, the patient continues to follow up routinely for eye examinations. At 11 years of age, he has reported worsening VA of 20/500 OD and 20/640 OS. Fundus examination has shown worsening retinal atrophy.

Globally, he has met developmental milestones without major illnesses or metabolic decompensation. He has done well in school and has explored many hobbies with the aid of low vision resources. ■

1. Lerner-Ellis JP, Tirone JC, Pawelek PD, et al. Identification of the gene responsible for methylmalonic aciduria and homocystinuria, cblC type. *Nat Genet*. 2006;38(1):93-100.
2. Ku CA, Ng JK, Karr DJ, et al. Spectrum of ocular manifestations in cobalamin C and cobalamin A types of methylmalonic acidemia. *Ophthalmic Genet*. 2016;37(4):404-414.
3. Ahrens-Nicklas RC, Whitaker AM, Kaplan P, et al. Efficacy of early treatment in patients with cobalamin C disease identified by newborn screening: a 16-year experience. *Genet Med*. 2017;19(8):926-935.

SRUTHI AREPALLI, MD
- Assistant Professor, Vitreoretinal Surgery and Uveitis, Emory Eye Center, Atlanta
- Mentor, YoungMD Connect
- sruthiarepalli@gmail.com
- Financial disclosure: None

AMY HUTCHINSON, MD
- Professor, Pediatric Ophthalmology, Emory Eye Center, Emory University, Atlanta
- Financial disclosure: None

NIRAJ PATEL, MD
- Ophthalmology Resident, Emory Eye Center, Emory University, Atlanta
- Financial disclosure: None

RACHEL SHAH, MD
- Assistant Professor, Medical Retina and Uveitis, Veterans Affairs Hospital, Atlanta
- Financial disclosure: None

(Continued from page 12)

RISK FACTORS AND IMAGING FEATURES OF VITAMIN A DEFICIENCY RETINOPATHY

Researchers recently found that the presence of nyctalopia and subretinal hyperreflective deposits in patients with a history of gastrointestinal surgery, liver disease, and/or poor diet can be suggestive of vitamin A deficiency, even with supplementation.[1]

The retrospective case series included nine patients, four of whom were taking vitamin A supplements prior to diagnosis. The most common underlying etiologies included history of gastrointestinal surgery (55.6%), liver disease (44.4%), and nutritional depletion due to a poor diet (44.4%). Only one patient had a history of bariatric surgery. All patients had macular subretinal hyperreflective deposits resembling subretinal drusenoid deposits. Six eyes of three patients with longstanding deficiency had defects in the external limiting membrane. Full-field electroretinography demonstrated severe rod dysfunction and mild to moderate cone system dysfunction.[1] Although vitamin A deficiency retinopathy is uncommon, familiarity with its clinical presentation can aid in early intervention to avoid potentially permanent retinal damage, the authors concluded.[1] ■

1. Levine DA, Mathew NE, Jung EH, et al. Characteristics of vitamin a deficiency retinopathy at a tertiary referral center in the United States [published online ahead of print September 4, 2023]. *Ophthalmol Retina*.

Eyewire+ Pharma Update

- Novartis has decided to discontinue development of GT005, a geographic atrophy (GA) gene therapy candidate, after the phase 2 HORIZON clinical trial showed discouraging results.
- The phase 1/2 LIGHTHOUSE trial evaluating subretinal injection of ATSN-201 (Atsena Therapeutics) for the treatment of X-linked retinoschisis has dosed its first patient. ATSN-201 uses a novel spreading capsid to stimulate therapeutic levels of gene expression in photoreceptors of the central retina.
- The FDA did not approve Outlook Therapeutics' biologics license application for ONS-5010 (Lytenava), an investigational formulation of bevacizumab for the treatment of wet AMD, citing chemistry manufacturing and control issues.
- The first patient has been dosed in the phase 1/2 clinical trial evaluating NFS-02 (Neuropath Therapeutics) for the treatment of Leber hereditary optic neuropathy caused by *ND1* gene mutation.
- Astellas Pharma announced 24-month data for avacincaptad pegol (Izervay), showing good safety and efficacy compared with sham in slowing progression of GA. This complement inhibitor was approved for treatment of GA by the FDA in August and is currently under review by the European Medicines Agency.

Want more retina news from *Eyewire+*?

THE BENEFITS OF 360° LASER RETINOPEXY AFTER VITRECTOMY

A few extra minutes of surgical time may be sufficient to prevent vision-threatening postoperative RD.

BY MAROUANE MASLIK, MD; ANAS AGNAOU, MD; IBTISSAM HAJJI, MD, PHD; AND ABDELJALIL MOUTAOUAKIL, MD, PHD

Ideally, rhegmatogenous retinal detachment (RRD) can be repaired with a single surgery; however, despite excellent skills and use of cutting-edge technology, up to 10% of cases require additional intervention.[1] Recurrent RD may be attributable to surgical technique and be affected by the amount of peripheral vitreous that remains after vitrectomy. The presence of a gas bubble in an incompletely vitrectomized eye can induce traction on the peripheral retina, leading to the formation of peripheral breaks and RD.

Due to the vision-threatening nature of this complication, many attempts have been made to prevent postoperative RD, including careful peripheral retinal examination with scleral depression, properly treating retinal breaks at the end of the vitrectomy, and prophylactic scleral buckling or cryopexy.[1,2] However, it would be beneficial if a less invasive management strategy was feasible.

We hypothesize that 360° laser retinopexy anterior to the equator can reduce the incidence of retinal breaks and RD by causing strong chorioretinal adhesion. It may also prevent the progression of an RD, similar to demarcation laser treatment. This procedure can easily be performed during the vitrectomy with an endolaser probe.

METHODS

We retrospectively reviewed patient records to identify those who underwent vitrectomy for RRD by a single surgeon in Mohammed VI University Hospital in Marrakech, Morocco, from January 2020 to December 2021.

The patients were part of a consecutive case series cohort. One group received intraoperative prophylactic 360° laser (n = 142, mean age 52 years), and a control group did not receive this treatment (n = 39, mean age 56.8 years).

Each patient underwent a detailed preoperative evaluation, and a complete ocular examination was performed on postoperative days 1 and 7; at 2, 4, and 8 weeks; and then each month up to 6 months after surgery. BCVA was recorded at each visit and converted to logMAR for statistical analysis.

Exclusion criteria included previous ocular surgery, giant tears, retinal dialysis, trauma, proliferative vitreoretinopathy (grade C or higher), RD with macular hole (high myopia), or round retinal hole with no associated posterior vitreous detachment.

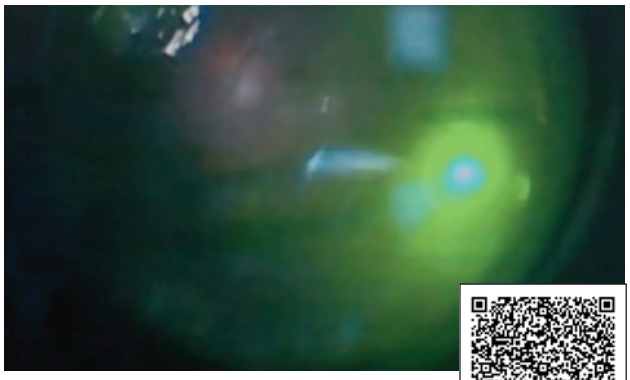
SURGICAL STEPS

1. General anesthesia was given, and cataract surgeries were performed for phakic patients.
2. Sclerotomies were created 3.5 mm from the limbus, and the posterior cortical vitreous was removed up to the vortex vein.
3. 360° scleral depression was performed to trim the vitreous at the base and confirm an absence of iatrogenic retinal breaks, and conventional 23-gauge vitrectomy was performed.
4. If a retinal break was found during the procedure in either group, it was treated with endolaser.
5. After fluid-air or gas exchange, the original retinal break was treated with an endolaser.
6. 360° laser retinopexy was performed by placing three rows of medium-white burns anteriorly from the level of vortex vein, toward and beyond the equator approximately one burn-width apart using the endolaser system (Video).
7. Sclerotomies were sutured with 8-0 vicryl.
8. Patients with superior retinal breaks were positioned upright, whereas those with nasal, temporal, or inferior breaks were positioned on the contralateral cheek.

RESULTS

The 360° laser group showed a significant reduction (12.6%, 13/103 eyes) in RD incidence after vitrectomy up to 6 months postoperatively compared with the control group (28.2%, 11/39 eyes; P = .045). There was

WATCH IT NOW



Video. 360° Laser Retinopexy After PPV.

no significant difference in postoperative logMAR visual acuity (360° laser group: 0.10 ± 0.25; control group: 0.06 ± 0.28; *P* = .193). The proportion of epiretinal membrane (ERM) and development of macular hole, cystoid macular edema, and vitreous hemorrhage were not statistically different between the two groups. Two eyes experienced rupture of the posterior capsule as a complication of cataract surgery but had no other postoperative complications, including RD after surgery.

DISCUSSION

There are two main causes of iatrogenic retinal breaks associated with vitrectomy: 1) insertion of an instrument causes traction on the adjacent vitreous, resulting in an intraoperative retinal tear along the posterior border of the vitreous base, or 2) the vitreous becomes immobilized within the sclerotomy site during withdrawal of an instrument, causing postoperative traction along the posterior border of the vitreous base. Careful peripheral retinal examination with scleral depression should detect breaks induced in this manner.

Intraoperative 360° laser during vitrectomy can treat unseen breaks, prevent the formation of new breaks, and prevent recurrent RD after vitrectomy. This procedure takes only a few minutes to complete and can be performed while observing the peripheral retina during scleral depression. Using a tamponade at the end of the vitrectomy allows for sufficient time for chorioretinal adhesion to develop.[3,4]

Intraoperative 360° laser, as well as cryopexy, may cause the breakdown of the blood-retina barrier with leakage of serum proteins into intraocular fluids.[5] This could be the source of cellular migration and proliferation, resulting in ERM formation. However, in our study, the occurrence of ERM was not significantly different between groups.

The use of cannulated vitrectomy systems may protect the vitreous base by allowing easier entry of instruments, thus causing less frequent herniations of the vitreous into the scleral incision.[6] In this study, 23-gauge vitrectomy was performed, but using smaller-gauge instruments may further decrease trauma in and near the vitreous base adjacent to the sclerotomies. The use of trocars may protect the vitreous base from excessive traction to the adjacent retina.[7,8]

Although the incidence of retinal breaks may decrease with small-gauge vitrectomy, postoperative recurrent RD is still possible; the presence of a gas bubble can induce traction on the peripheral retina, an inflammatory reaction, or vitreoretinal proliferation development, leading to the formation of peripheral breaks and RD.[9]

PREVENT TROUBLE DOWN THE ROAD

Given the vision-threatening nature of postoperative RD, adjunctive treatment with 360° laser retinopexy should be considered. A randomized, prospective clinical trial is necessary to confirm the efficacy of this prophylactic treatment. ■

Acknowledgements: The surgeries in our study were carried out based on the approval of the institutional review board and the established ethical standard. Informed consent was obtained from each patient.

1. Chang TS, McGill E, Hay DA, et al. Prophylactic scleral buckle for prevention of retinal detachment following vitrectomy for macular hole. *Br J Ophthalmol*. 1999;83(8):944-948.
2. Wolfensberger TJ, Aylward GW, Leaver PK. Prophylactic 360° cryotherapy in fellow eyes of patients with spontaneous giant retinal tears. *Ophthalmology*. 2003;110(6):1175-1177.
3. E de Juan Jr, McCuen B, Tiedeman J. Intraocular tamponade and surface tension. *Surv Ophthalmol*. 1985;30(1):47-51.
4. Thompson JT. Kinetics of intraocular gases: disappearance of air, sulfur hexafluoride, and perfluoropropane after pars plana vitrectomy. *Arch Ophthalmol*. 1989;107(5):687-691.
5. Jaccoma EH, Conway BP, Campochiaro PA. Cryotherapy causes extensive breakdown of the blood-retinal barrier. A comparison with argon laser photocoagulation. *Arch Ophthalmol*. 1985;103(11):1728-1730.
6. Territo C, Gieser JP, Wilson CA, Anand R. Influence of the cannulated vitrectomy system on the occurrence of iatrogenic sclerotomy retinal tears. *Retina*. 1997;17(5):430-433.
7. Rizzo S, Belting C, Genovesi-Ebert F, Di Bartolo E. Incidence of retinal detachment after small-incision, sutureless pars plana vitrectomy compared with conventional 20-gauge vitrectomy in macular hole and epiretinal membrane surgery. *Retina*. 2010;30(7):1065-1071.
8. Theocharis IP, Alexandridou A, Gili NJ, Tomic Z. Combined phacoemulsification and pars plana vitrectomy for macular hole treatment. *Acta Ophthalmol Scand*. 2005;83(2):172-175.
9. Sjaarda RN, Glaser BM, Thompson JT, Murphy RP, Hanham A. Distribution of iatrogenic retinal breaks in macular hole surgery. *Ophthalmology*. 1995;102(9):1387-1392.

ANAS AGNAOU, MD
- Ophthalmology Resident, Department of Ophthalmology, Mohammed VI University Hospital, Marrakech, Morocco
- anas.agnaou@gmail.com
- Financial disclosure: None

IBTISSAM HAJJI, MD, PHD
- Professor of Ophthalmology, Department of Ophthalmology, Mohammed VI University Hospital, Marrakech, Morocco
- Financial disclosure: None

MAROUANE MASLIK, MD
- Ophthalmologist, Department of Ophthalmology, Mohammed VI University Hospital, Marrakech, Morocco
- marouane.maslik@gmail.com
- Financial disclosure: None

ABDELJALIL MOUTAOUAKIL, MD, PHD
- Professor of Ophthalmology, Head, Department of Ophthalmology, Mohammed VI University Hospital, Marrakech, Morocco
- Financial disclosure: None

RETINA REIMBURSEMENT 101

A foundational overview from coding and billing specialists.

David Eichenbaum, MD; Ankoor R. Shah, MD; George Williams, MD; and Joy Woodke, COE, OCS, OCSR

Knowing how to navigate reimbursement challenges is an important part of effective patient care. In this YMDC workshop, held in September 2023, retina coding and billing specialists gave residents and fellows a foundational overview of the workings of medical reimbursement.

TAKE CARE OF PATIENTS BUT KNOW THE RULES OF THE GAME

David Eichenbaum, MD

Medical directors will call you periodically to justify your use of a medication. Remember that the insurer's medical director has never been an ophthalmologist and certainly not a retina specialist. Approach these calls with a good attitude and some evidence to support your decision. Just some of the details of the label-enabling study are often sufficient and will ensure a brief conversation.

Never use a stock vial or prefilled syringe of a branded injectable drug without confirmation of third-party payor coverage. This step will keep your employer happy. Use manufacturers' samples when you would like to use a branded drug but are at all unsure of coverage.

Be judicious with your -25 modifiers but charge appropriately for the work you do. Find the balance and be sure to document all of your work. Lastly, never talk about accounts receivable, debts, or charges in the lane with the patient. Other staff members can conduct those conversations. Keep the lane sacred for practicing medicine.

CODING: GETTING PAID FOR YOUR WORK

Ankoor R. Shah, MD

As a newly minted retinal surgeon, I performed one lengthy surgery in which I separated a posterior synechiae, removed not one but two dislocated IOLs, implanted a scleral-fixated IOL, and repaired the retina detachment. Afterward, I billed only for the retinal detachment and realized my lack of coding knowledge prevented me from billing for all the work I had done. Since then, I've stayed involved in surgical coding, and I review my own charts.

Don't reinvent the wheel! Use checklists from national organizations to make sure you are coding correctly for every claim, especially for injections of high-dollar drugs.

Modifier -25 has a lot of importance when billing for retina, so learn to use it appropriately and document your reason for using it for coding exams. Other key modifiers for procedures include -58, -78, and -79.

Finally, learn to use proper verbiage in electronic health records, as you are liable for the defaults it contains. Checking it once early on will save you a headache down the road.

CODING AND BILLING BASICS: WHAT TO KNOW WHEREVER YOU GO

George Williams, MD

No matter what type of work environment you choose, it will be necessary to understand basic coding and billing procedures. For more detailed information, the AAO offers good guidance: https://www.aao.org/practice-management/coding.

It is advisable to develop a comprehensive resource for your practice's local payors and their respective drug coverage. Know who requires step therapy.

Understand the role of the -25 modifier for all minor surgical procedures, not just intravitreal injections. It is not appropriate to use this modifier for every injection.

Learn the coverage for laser procedures. For example, if a patient presents with flashes and floaters and you identify a retinal tear during the comprehensive examination, you can treat the tear with the appropriate code, thus capturing the work.

Know the effects of manufacturer rebates and discounts on Medicare as well as the Medicare-allowable payment for Part B drugs. You will also need to know how to determine the level of evaluation and management (E/M) services.

CONSIDERATIONS WHEN IMPLEMENTING A NEW DRUG

Joy Woodke, COE, OCS, OCSR

Just because a drug is approved by the FDA doesn't mean it is covered by insurance. It is essential to monitor published policies.

For newly approved drugs, begin by reviewing the FDA labeling to determine the indications and dosing. Start with a clean claim that has no coding or formatting errors.

Common reasons why claims for intravitreal injections are denied include coding and the reporting of an off-label indication, unless the specific diagnosis is published in the payor's policy.

Several anti-VEGF drugs are subject to the 28-day rule—if performed sooner, they will be denied. This rule does not apply to geographic atrophy treatment following anti-VEGF injections (but some payors may initially deny for this reason, necessitating an appeal).

Understand the use of the JZ and JW modifiers, as the former was introduced at the beginning of this year with required use July 1, 2023. Residual medication for single-dose vials or prefilled syringes (eg, Vabysmo [Genentech], Eylea [Regeneron], Lucentis [Genentech]) are considered overfill, not measurable, and reported with JZ modifier.

DAVID EICHENBAUM, MD
- Partner and Director of Research, Retina Vitreous Associates of Florida, Saint Petersburg, Florida
- deichenb@yahoo.com
- Financial disclosure: Consultant, investigator, and speaker (Genentech)

ANKOOR R. SHAH, MD
- Retina specialist, Retina Consultants of Texas
- Medical Director of Coding Products, AAOE
- arsmd@retinaconsultantstexas.com
- Financial disclosure: None relevant.

GEORGE WILLIAMS, MD
- Chair, Department of Ophthalmology, and Director of the Beaumont Eye Institute
- Partner, Associated Retinal Consultants
- gwilliams@arcpc.net
- Financial disclosure: None disclosed.

JOY WOODKE, COE, OCS, OCSR
- Director of Coding & Reimbursement, AAO
- jwoodke@aao.org

CHOROIDAL MELANOMA: DOES SKIN TONE MATTER?

The literature shows that Fitzpatrick skin type can affect the prognosis and outcomes of cancers.

BY IRWIN LEVENTER, BA; KEVIN R. CARD, BS; AND CAROL L. SHIELDS, MD

Risk stratification and management of cutaneous melanoma have been rigorously developed for nearly 50 years now.[1] The Fitzpatrick skin type (FST) sorts complexion along a spectrum from I to VI, with FST I representing the lightest skin tone, which consistently burns when exposed to the sun, and FST VI representing the darkest skin tone, which rarely burns with sun exposure.[2] FST was originally developed in a study of skin resilience to ultraviolet light and has since become a useful, at-a-glance means of broadly stratifying cutaneous melanoma risk, with greatest risk in FST I and least in FST VI.[2]

DERMATOLOGY RECAP

In the dermatology literature, FST plays a vital role in the detection and management of cutaneous melanoma and related outcomes. Kulichová et al confirmed the widely recognized fact that patients with FST I and II are at a significantly increased risk for developing cutaneous melanoma in a cohort of 442 patients (odds ratio [OR] = 4.25 and 6.98, $P < .001$).[3]

Mercieca et al further found that skin phototype affected the risk for invasive versus in situ cutaneous melanoma, with individuals with FST I and II having a higher likelihood of developing invasive cutaneous melanoma than FST III and IV ($P = .00027$).[4]

It is evident that a patient's FST is highly relevant for counseling from a dermatology perspective, and using this tool leads to more thorough examination of at-risk patients. Based on these dermatologic observations, our team explored the literature in ophthalmology to better categorize the relationship between FST and uveal melanoma outcomes (Figure).

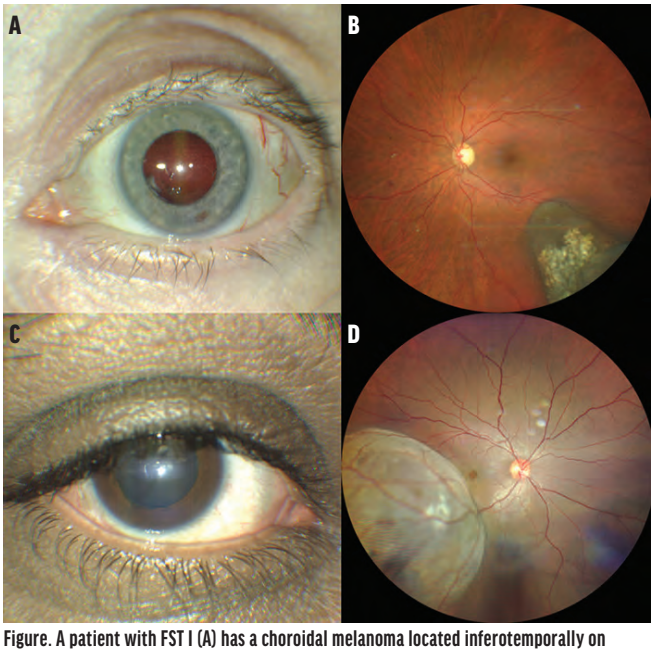


Figure. A patient with FST I (A) has a choroidal melanoma located inferotemporally on fundus photography (B). Another patient with FST V (C) has a choroidal melanoma located inferotemporally on fundus photography (D).

FST AND OCULAR MELANOMA

In the ophthalmology literature, there is little data on this topic, and what does exist has mostly been published within the last 2 years.[5-7] The first report on FST and uveal melanoma was published by Sen et al, evaluating 854 eyes with uveal melanoma for FST-related outcomes. They noted that 90% of tumors had a choroidal location across a spectrum of patient skin tones: FST I (n = 97, 11%), FST II (n = 665, 78%), and FST III-V (n = 92, 11%). They further studied the correlation of FST with The Cancer Genome

STUDY FINDINGS SUGGEST THAT PATIENTS WITH UVEAL MELANOMA AND FST I OR II TEND TO HAVE [...] A GREATER RISK FOR METASTASIS AND DEATH.

Atlas (TCGA) classification. This classification is based on cytogenetic mutations with predictive value for metastasis, including TCGA Group A (disomy 3, no 8q gain), TCGA Group B (disomy 3, partial 8q gain), TCGA Group C (monosomy 3, 8q gain), and TCGA Group D (monosomy 3, multiple 8q gains). They noted that patients with FST I were more likely to have the highest-risk cytogenetic mutations (TCGA group D, OR = 2.34, *P* = .002), while patients with FST III-V were more likely to have lower-risk cytogenetic mutations (TCGA group B, OR = 2.26, *P* = .002).[5] They also noted that there was no difference in melanoma-related metastasis or death within each TCGA group.

The second report on FST and uveal melanoma was by Negretti et al, who further studied the same 854 eyes regarding FST and risk for uveal melanoma-related metastasis and death. They found that patients with FST I (vs FST II vs FST III-V) demonstrated the greatest 10-year incidence of melanoma-related metastasis (25% vs 15% vs 14%, *P* = .02) and death (9% vs 3% vs 4%, *P* = .04).[6] They concluded that FST I patients were at substantially increased risk for melanoma-related metastasis and should be advised to have genetic testing of the tumor.

A third report by Shields et al was on FST related to conjunctival melanoma (n = 540).[8] They looked at patients with FST I (n = 126, 23%), FST II (n = 337, 62%), and FST III-VI (n = 77, 15%). Regarding outcomes, they found that patients with FST I (vs FST II vs FST III-VI) had lower tumor thickness (2.1 mm vs 2.8 mm vs 3.6 mm, *P* = .01) but no difference in 5-year visual acuity loss, tumor recurrence, enucleation, exenteration, metastasis, or death.

Together, these reports define a spectrum of FST as it relates to ocular melanoma. Study findings suggest that patients with uveal melanoma and FST I or II tend to demonstrate more cytogenetic mutations and, thus, have a greater risk for metastasis and death. However, with regard to conjunctival melanoma, those with FST I are more likely to have thinner tumors, and there is no difference in metastasis or death per skin tone.

THE SHORT ANSWER IS YES

Skin tone appears to matter when it comes to the prognosis of ocular melanoma. As with cutaneous melanoma, patients with FST I and II are more vulnerable to developing choroidal and conjunctival melanoma and experience greater risk for metastasis with choroidal melanoma. Thus, a patient's FST is relevant information for the retina specialist, who often is consulted on the nature of a choroidal mass. ■

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

1. Ward WH, Lambreton F, Goel N, et al. Clinical presentation and staging of melanoma. In: Ward WH, Farma JM, eds. Cutaneous Melanoma: Etiology and Therapy. Brisbane, AU: Codon Publications; 2017:79-89.
2. Fitzpatrick TB. The validity and practicality of sun-reactive skin types I through VI. *Arch Dermatol*. 1988;124(6):869-871.
3. Mercieca L, Aquilina S, Calleja N, Boffa MJ. Cutaneous melanoma more likely to be invasive in fairer skin phototypes: a retrospective observational study. *Skinmed*. 2021;19(4):280-283.
4. Kulichová D, Dáňová J, Kunte C, et al. Risk factors for malignant melanoma and preventive methods. *Cutis*. 2014;94(5):241-248.
5. Sen M, Card KR, Caudill GB, et al. Relationship between Fitzpatrick skin type and the cancer genome atlas classification with melanoma-related metastasis and death in 854 patients at a single ocular oncology center. *Ophthalmic Genet*. 2022;43(6):742-755.
6. Negretti GS, Bayasi F, Goldstein S, et al. Association of Fitzpatrick skin type with metastatic risk from uveal melanoma in 854 consecutive patients at a single center. Manuscript submitted for publication.
7. Agrawal KU, Chiang L, Ni R, et al. Correlation of Fitzpatrick skin type and iris color with tumor size in 823 patients with uveal melanoma. Manuscript submitted for publication.
8. Shields CL, Yaghy A, Dalvin LA, et al. Conjunctival melanoma: features and outcomes based on the Fitzpatrick skin type in 540 patients at a single ocular oncology center. *Ophthalmic Plast Reconstr Surg*. 2020;36(5):490-496.

KEVIN R. CARD, BS
- Medical Student, Ocular Oncology Service, Wills Eye Hospital, Thomas Jefferson University, Philadelphia
- kevin@shields.md
- Financial disclosure: None

IRWIN LEVENTER, BA
- Medical Student, Ocular Oncology Service, Wills Eye Hospital, Thomas Jefferson University, Philadelphia
- irwinl@shields.md
- Financial disclosure: None

CAROL L. SHIELDS, MD
- Director, Ocular Oncology Service, Wills Eye Hospital, Thomas Jefferson University, Philadelphia
- Editorial Board Member, *Retina Today*
- carolshields@gmail.com
- Financial disclosure: None

CODING ADVISOR
A Collaboration Between *Retina Today* and AMERICAN ACADEMY™ OF OPHTHALMOLOGY Protecting Sight. Empowering Lives.

HOW TO IMPLEMENT THE –JZ MODIFIER

Reporting zero waste when administering therapeutics is going to look a little different this year. Here's why.

BY JOY WOODKE, COE, OCS, OCSR

Reporting drug usage and waste in the retina clinic has always been trickier than you would expect. Given the sheer volume of therapeutics used to treat everything from diabetic eye disease to AMD—and now geographic atrophy—it's a crucial coding skill to have. Since 2017, to obtain full reimbursement for single-dose containers, vials, and packages for both the injected and discarded amounts of a drug, 1 unit or greater, physicians have reported the –JW modifier, discarded drug not administered.

The Centers for Medicare and Medicaid (CMS) have monitored the use of the –JW modifier and, because of noncompliance, have reported incomplete data on drug wastage. As a result, the CMS created a new modifier, –JZ, zero drug amount discarded/not administered to any patient, that went into effect January 1, 2023.[1] Collectively, the claims data from the –JW and –JZ modifiers will be used to calculate discarded drug refunds for manufacturer rebate requirements.

Physicians shouldn't be too surprised, considering CMS announced this change in their Final Rule in November 2022.[1] The –JZ modifier was effective starting January 1, 2023, but the required use of the –JZ modifier was set for July 1, 2023. This new modifier will be appended to the Healthcare Common Procedure Coding System (HCPCS) code representing the drug used. If not reported when applicable, claims could be subject to audits, and if not used by October 1, 2023, claims may be returned as unable to process.

The –JW and –JZ modifiers are required for single-dose containers, vials, and packages based on the FDA-approved labeling. It is important to confirm if the drug is considered a single dose by reviewing the vial or package labeling.

If the medication is labeled as multidose (ie, when the same vial can be used to treat more than one patient), it is excluded from reporting a –JW or –JZ modifier, and you only need to report the dosage and units used per patient. Ophthalmic examples can include multidose triamcinolone acetonide and fluorouracil. However, because these medications can be distributed as either single or multidose, always confirm the type of vial used. Additionally, the National Drug Code for single or multidose drugs varies.

FREQUENTLY ASKED QUESTIONS

This new modifier will significantly affect how retina specialists report many of their intraocular injections. To help prepare for this transition, let's look at several common questions.

Q: After administering a prefilled syringe of 2 mg aflibercept (Eylea, Regeneron) there is remaining drug in the syringe. Do we report a –JW modifier?

A: The remaining medication in a prefilled syringe is considered overfill and is not reported with a –JW modifier, according to the CMS.[2] Billing for overfill, which is considered medication greater than the amount identified on the package or label, is not appropriate. This applies to

THE -JW AND -JZ MODIFIERS ARE REQUIRED FOR SINGLE-DOSE CONTAINERS, VIALS, AND PACKAGES BASED ON THE FDA-APPROVED LABELING. IT IS IMPORTANT TO CONFIRM IF THE DRUG IS CONSIDERED A SINGLE DOSE BY REVIEWING THE VIAL OR PACKAGE LABELING.

single-dose vials and prefilled syringes of anti-VEGF drugs, such as ranibizumab (Lucentis, Genentech/Roche) and faricimab (Vabysmo, Genentech/Roche). Claims submitted for aflibercept should be reported with HCPCS code J0178–JZ and 2 units.

Q: Do we report the -JZ modifier for Medicare claims only, or is it applicable for all payers?

A: The –JZ modifier should be reported as appropriate for all Medicare Part B claims effective July 1, 2023. Other payers, including Medicare Advantage, commercial, and Medicaid plans, may delay their implementation of this new modifier. Confirm each payer's policy for reporting drug usage and waste.

Q: Are sample drugs reported with -JZ?

A: Drugs that the physician does not purchase and are not payable under Medicare Part B are also excluded from reporting modifiers –JW and –JZ. This includes sample drugs and specialty pharmacy provided medications (also called "white bagged" medication).

Q: Does the -JZ modifier apply to ambulatory surgery center (ASC) billing?

A: Separately billable single-dose drugs submitted as claims to Medicare Part B should report –JZ or –JW as appropriate, unless the drug is excluded (eg, samples, multidose vials).[2]

Q: Is the -JZ modifier used for implants, such as intravitreal dexamethasone (Ozurdex, Allergan/Abbvie), 0.18 mg fluocinolone acetonide intravitreal implant (Yutiq, Alimera Sciences), and 0.19 mg fluocinolone acetonide intravitreal implant (Iluvien, Alimera Sciences)?

A: Included in the CMS guidance is confirmation that the –JW and –JZ modifiers are applicable to all separately payable drugs with a payment indicator (PI) of K2, drugs and biologicals paid separately when provided integral to a surgical procedure on the ASC list; payment based on OPPS rate. Ozurdex, Yutiq, and Iluvien each have an ASC PI of K2 and should be reported with the –JZ modifier, as there is no discarded amount of drug. This is also applicable to the office setting, reporting the –JZ modifier for these drugs.

Q: Would intravenous verteporfin (Visudyne, Bausch + Lomb) be reported with the -JW or -JZ modifier?

A: When an intravenous infusion of verteporfin is performed for photodynamic therapy (PDT), the medication is reported with HCPCS code J3396, injection, verteporfin, 0.1 mg. The single-dose vial contains 15 mg. If, based on the patient's weight, 12 mg of verteporfin was used and 3 mg wasted, report as:

- J3396, 120 units
- J3396–JW, 30 units

Note that, in rare cases when the patient's dosage is 14.98 mg and the wasted drug is 0.02 mg, report J3396 once and append the –JZ modifier, as the discarded drug is less than 1 unit (0.1 mg).

FURTHER READING

For additional resources, visit aao.org/retinapm and access the AAO's –JW and –JZ Fact Sheet and the Table of Common Retina Drugs, which provides specific drug guidance, including when the use of the –JW or –JZ modifier is applicable.[3] ■

1. Medicare and Medicaid Programs; CY 2023 payment policies under the physician fee schedule and other changes to Part B payment and coverage policies; Medicare Shared Savings Program requirements; Implementing requirements for manufacturers of certain single-dose container or single-use package drugs to provide refunds with respect to discarded amounts; and COVID-19 interim Final Rules. Federal Register. November 18, 2022. Accessed August 10, 2023. www.federalregister.gov/documents/2022/11/18/2022-23873/medicare-and-medicaid-programs-cy-2023-payment-policies-under-the-physician-fee-schedule-and-other
2. Medicare program discarded drugs and biologicals – JW modifier and JZ modifier policy frequently asked questions. Centers for Medicare and Medicaid. Accessed August 25, 2023. www.cms.gov/medicare/medicare-fee-for-service-payment/hospitaloutpatientpps/downloads/jw-modifier-faqs.pdf
3. Practice Management for Retina. AAO. Accessed August 25, 2023. www.aao.org/practice-management/coding/retina

JOY WOODKE, COE, OCS, OCSR
- Director of Coding & Reimbursement, American Academy of Ophthalmology, San Francisco
- jwoodke@aao.org
- Financial disclosure: None

RISING STARS IN RETINA

Get to know outstanding retina fellows from the class of 2023.

Chang Sup Lee, MD

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

I first became interested in retina after I shadowed my uncle, who is a vitreoretinal surgeon in South Korea. I was amazed that retina specialists could identify systemic conditions—such as diabetes, hypertension, and prematurity—just by examining the patient's eyes. I was hooked when I observed a vitrectomy, as the surgery was so delicate, and the retina appeared stunning under the microscope.

_RT:_ Who do you look to as mentors in the field?

I would like to thank my mentors at the University of Virginia and West Virginia University for providing dedicated support throughout my medical and ophthalmology training.

During my retina fellowship at the University of Southern California, Andrew Moshfeghi, MD, MBA, and Juan Martinez, MD, encouraged me to become a judicious and meticulous surgeon who is prepared for every scenario. I became a better scleral buckler after I gained experience in different types of buckles with Aaron Nagiel, MD, PhD, and Thomas Chu, MD. I learned the importance of being detail-oriented to capture subtle clues in complex uveitis cases from Brian Toy, MD. During my rotation at Retina-Vitreous Associates, Firas Rahhal, MD, and David Boyer, MD, taught me valuable lessons in managing a retina practice.

_RT:_ What has been one of the most memorable experiences of your fellowship thus far?

I had the most memorable patient encounter at the Los Angeles General Medical Center. He presented to the emergency department with severe bilateral panuveitis without any pertinent medical history. However, a careful systemic examination revealed that he had skin lesions suspicious of syphilis and Kaposi sarcoma. HIV and syphilis testing came back positive. He then received appropriate treatment, which saved his life and vision. This experience was an important reminder that clinicians should evaluate and treat the whole patient, not just their vision.

FIRST CAREER MILESTONE

Dr. Lee is now a vitreoretinal surgeon at Retina Consultants of Orange County.

_RT:_ What are you hoping to accomplish in clinical practice?

I plan to gain the trust of the referring doctors by providing excellent care to our mutual patients and maintaining timely communication. I will look for opportunities to participate in clinical trials, which can offer exposure to the latest therapeutic modalities.

_RT:_ What advice can you offer to residents who are considering retina?

Some residents may have limited exposure to the surgical side of retina, depending on the program. To learn more about vitreoretinal surgery, I recommend using resources such as Eyetube, the Vit-Buckle Academy, Vitreoretinal Surgery Online, and the American Society of Retina Specialists. Interested residents should also be proactive in participating in retina meetings to build professional connections and stay up to date on the latest information. ■

CHANG SUP LEE, MD

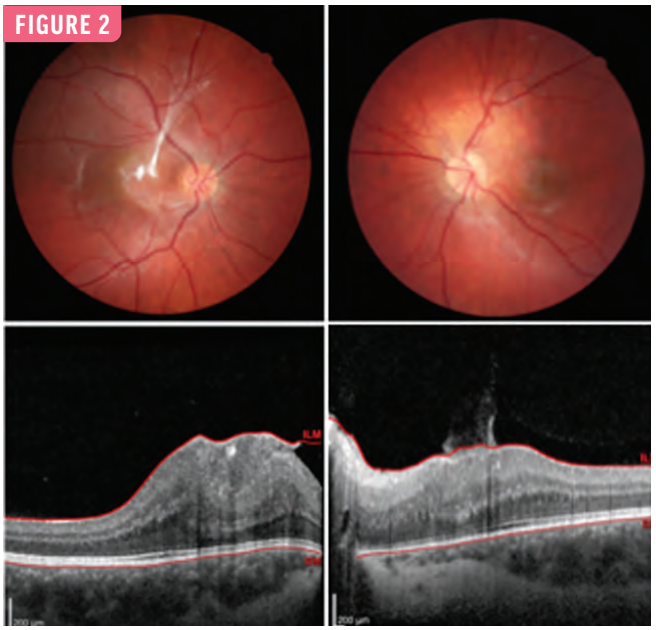
- Former Vitreoretinal Surgery Fellow, University of Southern California, Roski Eye Institute, Los Angeles
- changsupleemd@gmail.com
- Financial disclosure: None

INDEX OF ADVERTISERS

This advertiser index is published as a convenience and not as part of the advertising contract. Although great care will be taken to index correctly, no allowances will be made for errors due to spelling, incorrect page number, or failure to insert.

(Continued from page 58)

FIGURE 2



Photograph by Vivian Mok, COA, Dartmouth Hitchcock Medical Center, Hanover, New Hampshire

ophthalmology and retina. Visual acuity, fundus examination, and OCT results have remained stable for the past 5 years (Figure 2). When the patient is a teenager, a fluorescein angiogram will be pursued to better characterize the lesions. ■

NIKHIL N. BATRA, MD
- Ophthalmologist, Dartmouth Hitchcock Medical Center, Hanover, New Hampshire
- Financial disclosure: None

ANDREW J. CATOMERIS, MD
- Ophthalmology Resident, Dartmouth Hitchcock Medical Center, Hanover, New Hampshire
- andrew.j.catomeris@hitchcock.org
- Financial disclosure: None

MANISH NAGPAL, MS, FRCS, FASRS | SECTION EDITOR
- Senior Consultant, Retina and Vitreous Services, The Retina Foundation, Ahmedabad, India
- drmanishnagpal@yahoo.com
- Financial disclosure: Consultant (Nidek)

ERIN M. SALCONE, MD
- Ophthalmologist, Dartmouth Hitchcock Medical Center, Hanover, New Hampshire
- Financial disclosure: None

If you have an image or images you would like to share, email Dr. Nagpal.
Note: Photos should be 400 dpi or higher and at least 10 inches wide.

COMBINED HAMARTOMA OF THE RETINA AND RPE

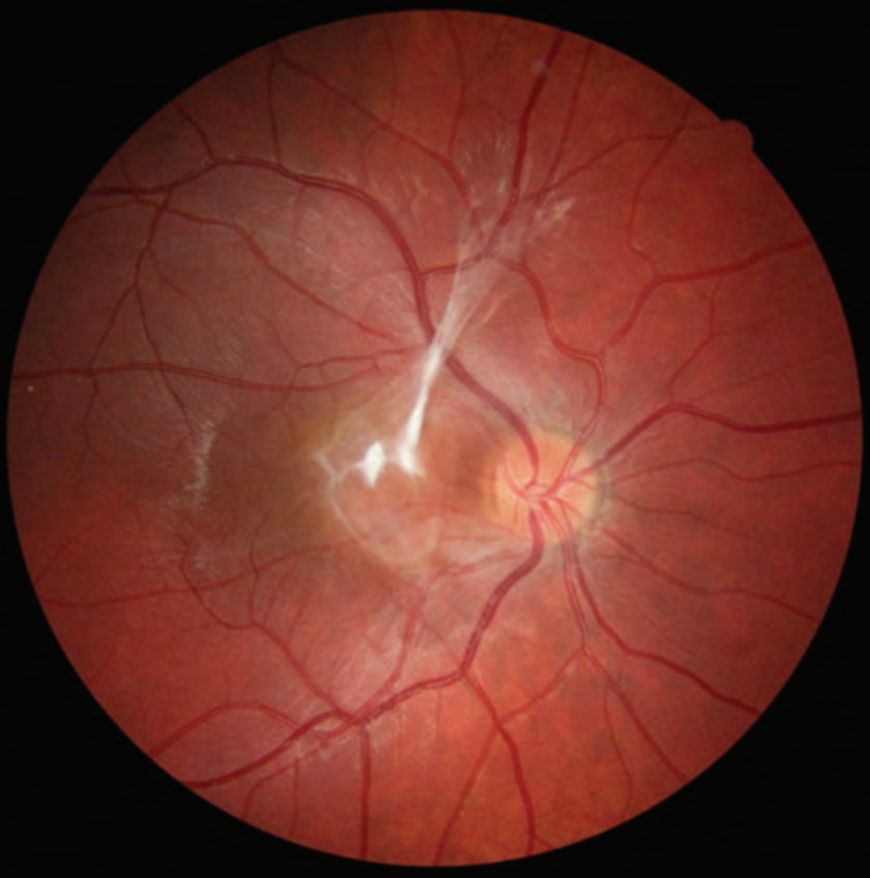


FIGURE 1

Photograph by Vivian Mok, COA, Dartmouth Hitchcock Medical Center, Hanover, New Hampshire

This benign lesion may be the reason for decreased vision in young children.

BY ANDREW J. CATOMERIS, MD; NIKHIL N. BATRA, MD; AND ERIN M. SALCONE, MD

A 6-year-old boy was referred to our clinic for evaluation of his epiretinal membrane. He was born at full-term to a healthy mother with an uncomplicated pregnancy and delivery. He was noted to have difficulty reading in school and to move close to the television for the past year.

FINDINGS AND DIAGNOSIS

On presentation, his uncorrected distance VA was 20/60 OD and 20/25 OS, and his near VA was 20/20 OU. Slit lamp examination of the anterior segment was normal; the posterior pole demonstrated peripapillary thickening of the retina in each eye, with mixed hyper- and hypopigmentation and a prominent white fibrotic epiretinal membrane in his right eye (Figure 1).

Cycloplegic refraction demonstrated low symmetric hyperopia but no indication for glasses. Based on these findings, the patient was diagnosed with hamartoma of the retina and retinal pigment epithelium.

WATCH IT CLOSELY

The patient has been regularly monitored every 6 months, with alternating care provided by pediatric

(Continued on page 57)

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.

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.

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 neovascular AMD, endophthalmitis, and retinal detachments. 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.

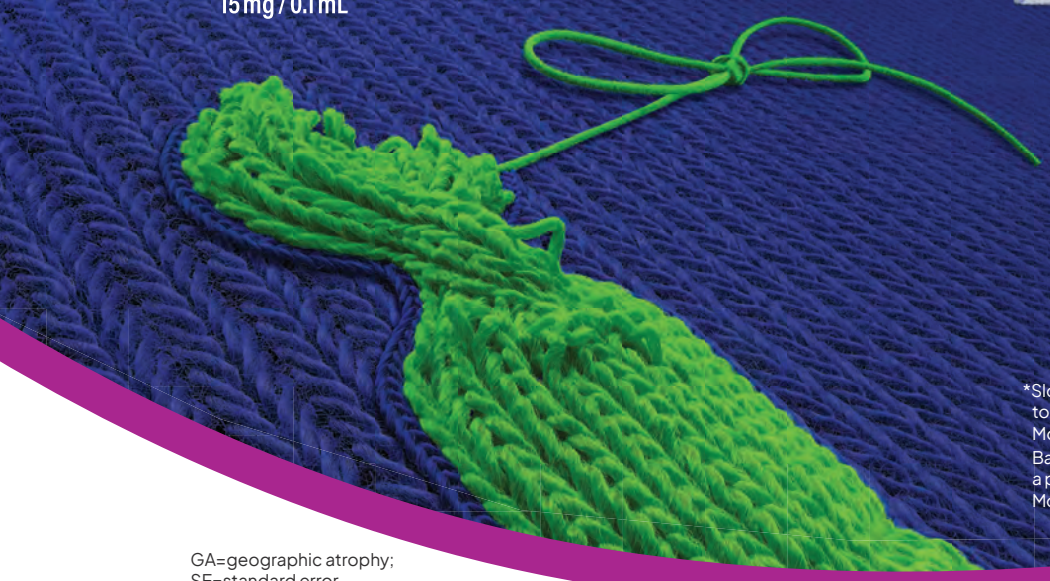
Patients may experience temporary visual disturbances associated either with the intravitreal injection with SYFOVRE or the eye examination. Advise patients not to drive or use machinery until visual function has recovered sufficiently.

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

SYF-PI-17Feb2023-1.0

7/23 US-PEGGA-2200163 v3.0

SYFOVRE®
(pegcetacoplan injection)
15 mg / 0.1 mL



GA unravels so much SAVE RETINAL TISSUE BY SLOWING PROGRESSION[1-3]

SYFOVRE achieved continuous reductions in mean lesion growth rate* vs sham pooled from baseline to Month 24[1,4]

Monthly	Every Other Month (EOM)
OAKS trial (mm^2): (3.11 vs 3.98) **22%**	OAKS trial (mm^2): (3.26 vs 3.98) **18%**
DERBY trial (mm^2): (3.28 vs 4.00) **18%**	DERBY trial (mm^2): (3.31 vs 4.00) **17%**

SE in trials (monthly, EOM, sham pooled): OAKS: 0.15, 0.13, 0.14; DERBY: 0.13, 0.13, 0.17.

*Slope for baseline to Month 24 is an average of slope of baseline to Month 6, Month 6 to Month 12, Month 12 to Month 18, and Month 18 to Month 24.[1]
Based on a mixed effects model for repeated measures assuming a piecewise linear trend in time with knots at Month 6, Month 12, and Month 18.[1]

GA=geographic atrophy;
SE=standard error.

Explore the long-term data

The CMS-assigned permanent J-code for SYFOVRE is J2781—effective 10/1/23[1]

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.
- **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.

Trial Design: SYFOVRE safety and efficacy were assessed in OAKS (N=637) and DERBY (N=621), multi-center, 24-month, 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 EOM, sham monthly, or sham EOM for 24 months. Change from baseline in the total area of GA lesions in the study eye (mm^2) was measured by fundus autofluorescence (FAF).[1,4]

References: 1. SYFOVRE (pegcetacoplan injection) [package insert]. Waltham, MA: Apellis Pharmaceuticals, Inc.; 2023. **2.** Pfau M, von der Emde L, de Sisternes L, et al. Progression of photoreceptor degeneration in geographic atrophy secondary to age-related macular degeneration. *JAMA Ophthalmol*. 2020;138(10):1026-1034. **3.** Bird AC, Phillips RL, Hageman GS. Geographic atrophy: a histopathological assessment. *JAMA Ophthalmol*. 2014;132(3):338-345. **4.** Data on file. Apellis Pharmaceuticals, Inc.

Apellis