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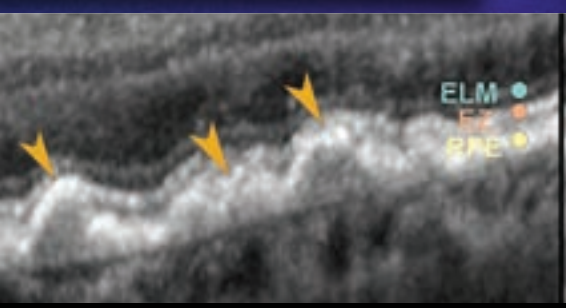
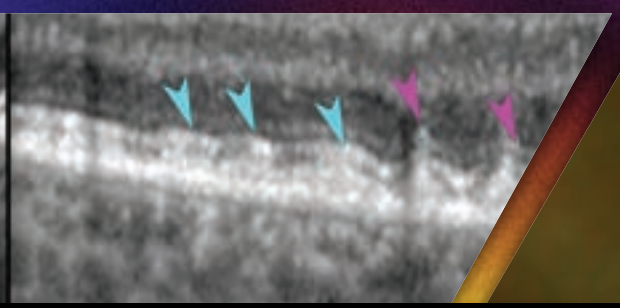
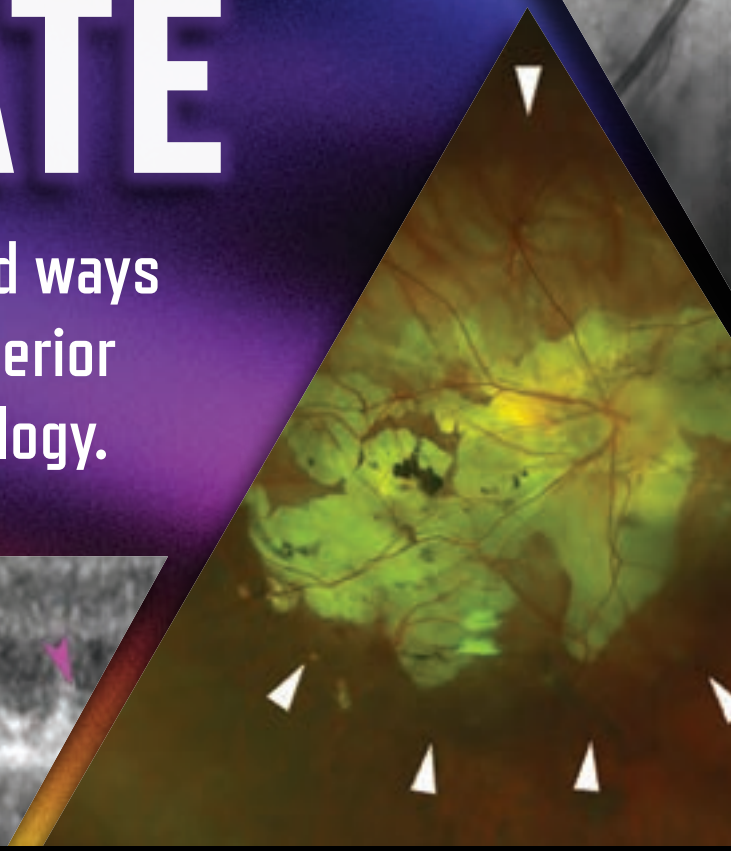
RETINAL IMAGING UPDATE

New and improved ways to capture posterior segment pathology.







AN UPDATE ON OCTA NOMENCLATURE

OCT SPOTLIGHT: CHARACTERIZING GA

MULTIMODAL IMAGING IN PEDIATRICS

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OCT ON THE LOOSE


While traveling back from this year's Aspen Retinal Detachment Society (ARDS) meeting, a colleague shared that their grandmother had, in her lifetime, both traversed the American West in a covered wagon and flown in an airplane. That sort of technological whiplash, which seems wild when put into historical terms, is simply the status quo these days, both in society in general and in the field of retina specifically. Think of our access to movies: We used to "be kind and rewind" our VHS tapes before returning them to Blockbuster, and now the only way to find a movie is through a streaming service.

What precipitated our colleague's comment was our discussion of the ARDS agenda, which was packed with sessions on intraoperative OCT (by Lejla Vajzovic, MD), ultra-widefield navigated peripheral OCT (by Szilárd Kiss, MD), and OCT/OCT angiography (OCTA) in pediatrics (by Audina M. Berrocal, MD). The talk that really caught our attention, however, was by John B. Miller, MD; he took the stage to contend that it might be time to replace fluorescein angiography (FA) with swept-source OCTA when imaging diabetic macular edema (DME).

OCT was first described in the 90s,[1] and it's already integral to our clinical decision making, necessary for clinical trial endpoints, and making its way into our ORs.[2-7] Even some motivated patients are familiar with their own OCTs these days. While most of us aren't quite ready to replace FA with OCTA, Dr. Miller predicts that FA imaging for DME will be a relic within 5 years (check out the Eyetube meeting coverage of Dr. Miller's talk to hear more).

Because OCT is a mainstay in our practices, we focused on OCT in this issue, taking a deep dive into terminology, biomarkers, and more. First up, Marion R. Munk, MD, PhD, and Ferhat Turgut, MD, discuss their new research on standardized nomenclature for OCTA. They explain why it's time to replace terms such as *flow void* and *flux*, adapted from other imaging modalities, with something that better aligns with OCTA's binary principles of presence or absence. We also have disease-specific articles outlining the utility of new OCT biomarkers in DME (eg, disorganization of retinal inner layers) and geographic atrophy (eg, thick basal lamina deposits).

WATCH IT NOW

FA vs OCTA in the Retina Clinic
John B. Miller, MD, and R.V. Paul Chan, MD, MSC, MBA, FACS

OCT isn't just taking over our offices—it's also making its way into patient homes with the FDA clearance of the Scanly Home OCT (Notal Vision) system. For those who are unsure where this new tool fits into retina care, Sri Krishna Mukkamala, MD, has tips for incorporating the novel screening and management tool into your practice.

Of course, OCT isn't the only imaging modality in our clinics, and we have articles that share multimodal imaging pearls for pathologic myopia, macular telangiectasia type 2, and pediatrics.

There are so many ways for us to see the retina beyond what we can visualize through our ophthalmoscopes, and each one provides unique information to help us diagnose, treat, and monitor retina conditions like never before. We can only imagine what the next generation of retina researchers will be able to capture with newer, and more precise, imaging modalities. ■

ALLEN C. HO, MD
CHIEF MEDICAL EDITOR

ROBERT L. AVERY, MD
ASSOCIATE MEDICAL EDITOR

1. Huang D, Swanson EA, Lin CP, et al. Optical coherence tomography. *Science*. 1991;254:1178-1181.
2. Choudhry N. Feasibility and clinical utility of peripheral OCT imaging using a novel integrated SLO ultra-widefield imaging full-field swept-source OCT device. Paper presented at: Macula Society Meeting; February 6-7, 2021.
3. Kaplan RI, Chen M, Gupta M, Rosen RB. Impact of automated OCT in a high-volume eye urgent care setting. *BMJ Open Ophthalmol*. 2019;4:e000187.
4. Volz C, Grassmann F, Greslechner R, et al. Impact of optical coherence tomography (OCT) on decision to continue treatment for neovascular age-related macular degeneration. *Invest Ophthalmol Vis Sci*. 2016;57:3707.
5. Schmetterer L, Scholl H, Garhöfer G, et al. Endpoints for clinical trials in ophthalmology. *Prog Retin Eye Res*. 2023;97:101160.
6. Yordi S, Cakir Y, Kalra G, et al. Ellipsoid zone integrity and visual function in dry age-related macular degeneration. *J Pers Med*. 2024;14(5):543.
7. Ciarmatori N, Pellegrini M, Nasini F, Talli PM, Sarti L, Mura M. The state of intraoperative oct in vitreoretinal surgery: recent advances and future challenges. *Tomography*. 2023;9(5):1649-1659.

On the cover (clockwise from top left): Widefield fundus imaging of a fibrovascular stalk, ultra-widefield OCT of a posterior staphyloma in a highly myopic eye, OCT imaging of disorganization of retinal inner layers in DME, ultra-widefield fundus imaging of a wide macular staphyloma with pigmentary changes, OCT imaging of drusen in geographic atrophy, and loss of temporal perifoveal hypoautofluorescence in early macular telangiectasia type 2.

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(pegcetacoplan injection)
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Save more retinal tissue

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

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

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

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

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

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

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

WARNINGS AND PRECAUTIONS

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

ADVERSE REACTIONS

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

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

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

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

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

Apellis

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

INDICATIONS AND USAGE

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

CONTRAINDICATIONS

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

WARNINGS AND PRECAUTIONS

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

ADVERSE REACTIONS

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

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

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

PM: SYFOVRE monthly; PEOM: SYFOVRE every other month

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

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

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

USE IN SPECIFIC POPULATIONS

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

PATIENT COUNSELING INFORMATION

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

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

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RT NEWS

APRIL 2025

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FIRST TREATMENT FOR MACTEL RECEIVES FDA APPROVAL

The FDA recently approved revakinagene taroretcel-lwey (Encelto, Neurotech Pharmaceuticals) for the treatment of macular telangiectasia type 2 (MacTel). Revakinagene taroretcel-lwey uses an encapsulated cell therapy technology designed to continuously deliver therapeutic doses of ciliary neurotrophic factor to the retina to assist in slowing disease progression.[1]

The therapy's approval was based on results from two phase 3 trials, which demonstrated that the implant significantly slowed the loss of macular photoreceptors in patients with MacTel over 24 months.[1] The trials showed a 56.4% and 29.2% reduction in the rate of disease progression in patients treated with Protocols A and B, respectively.[2]

The encapsulated cell therapy consists of a semipermeable capsule that contains proprietary allogeneic retinal pigment epithelium (RPE) cells that are genetically engineered to produce therapeutic proteins. The capsule is inserted into the vitreous and sutured to the sclera during an outpatient procedure.[2]

In clinical trials, data from 64 patient treated with the device show that the implant produces a steady level of bioactive ciliary neurotrophic factor for at least 14.5 years.[3]

Revakinagene taroretcel-lwey is expected to be available to patients in the United States starting in June.[1]

1. FDA approves Neurotech's Encelto as first and only FDA-approved treatment for MacTel [press release]. Eyewire+. March 6, 2025. Accessed March 12, 2025. eyewire.news/news/fda-approves-neurotechs-encelto-as-first-and-only-fda-approved-treatment-for-mactel
2. Neurotech Pharmaceuticals, Inc. announces positive phase 3 topline results for NT-501 implant in macular telangiectasia type 2 [press release]. Neurotech Pharmaceuticals. November 2, 2022. Accessed March 13, 2025. www.neurotechpharmaceuticals.com/neurotech-pharmaceuticals-announces-positive-phase-3-topline-results-for-nt-501-implant-in-mactel
3. Kauper K, Orecchio L, Nystuen A, et al. Continuous intraocular drug delivery lasting over a decade: ciliary neurotrophic factor (CNTF) secreted from Neurotech's NT-501 implanted in subjects with retinal degenerative disorders. *Invest Ophthalmol Vis Sci*. 2023;64:3680.

AMD INCREASES RISK OF MORTALITY IN CARDIOVASCULAR DISEASE

A study in Australia recently reported that the presence of AMD at any stage in patients with high cardiovascular disease (CVD) risk independently predicted increased all-cause mortality. Any and early AMD also increased the risk of CVD mortality. Although the mechanisms are unclear, this finding sheds light on the potential shared pathways between AMD and CVD.[1]

Of the 1,545 study participants, 107 (6.9%) had any AMD, including early (n = 86) and late (n = 21) AMD. Over 9 years of follow-up, 234 (15.1%) participants died, including 174 (11.3%) participants from fatal CVD events. After controlling for several factors—such as age, sex, body mass index, total cholesterol, smoking status, and history of diabetes, hypertension, myocardial infarction, stroke, and macrovascular coronary artery disease—there was an increased rate of all-cause mortality for those with any (hazard ratio [HR] = 2.37), early (HR = 2.42), and late (HR = 1.08) AMD.[1]

1. Kha R, Burlutsky G, Thiagalingam A, et al. Association between age-related macular degeneration and mortality in a high cardiovascular risk cohort: a prospective cohort study [published online ahead of print February 28, 2025]. *Ophthalmol Retina*.

RPE CELL THERAPY FOR DRY AMD ACHIEVES PROMISING PHASE 1/2A RESULTS

Luxa Biotechnology recently announced clinical data from its phase 1/2a clinical trial (NCT04627428) evaluating RPESC-RPE-4W, a proprietary RPE cell therapy for patients with dry AMD. This comes after the FDA granted Regenerative Medicine Advanced Therapy Designation for RPESC-RPE-4W in the treatment of dry AMD.[1]

Each of the six patients in the first low-dose cohort of the ongoing first-in-human trial received a subretinal injection of 50,000-cell suspension of RPESC-RPE-4W. No serious adverse events related to the therapy were observed. In terms of BCVA, the worse-seeing group experienced an average gain of 21.67 ETDRS letters at 12 months, and the better-seeing group showed a 3.3-letter improvement at 3 months.[1]

The patients with the most severe baseline vision impairment achieved the most significant restoration, the study found. Those who began with better baseline vision saw smaller, yet still clinically relevant, improvements that counteracted the natural decline expected in dry AMD progression.[1] For patients with worse vision who experienced

(Continued on page 10)

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FEATURED ARTICLES

ONLINE FEATURE

DEPARTMENTS

ONLINE EXCLUSIVE

VALEDA®

Light Delivery System

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

It's Time for Patients to See Their Future

MyValeda.com

LumiThera®

Rx Only

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

(Continued from page 7)
significant improvement, the therapy allowed them to read with magnification and possibly drive with daytime driving, according to Jeffrey Stern, MD, Luxa's chief medical officer.[2]

1. Luxa Biotechnology presents data from first-in-human retinal pigment epithelium cell therapy for dry AMD [press release]. Eyewire+. March 10, 2025. Accessed March 12, 2025. bit.ly/4c1knqh
2. Luxa's stem cell therapy for dry AMD shows early promise [press release]. Luxa Biotechnology. March 6, 2025. Accessed March 14, 2025. bit.ly/4c5fbBJ

RESTRICTIONS LOOSENED FOR INTERNATIONAL MEDICAL GRADUATES

Physician shortages are on the rise in the United States, with a disproportionate effect in rural areas. Historically, physicians who trained outside the United States have been required to repeat residency or a similar process in the United States before receiving full licensure. Now, an increasing number of states are making it easier for foreign-trained physicians to practice in the United States, with the intention of increasing the number of physicians in underserved areas. At least nine states have dropped the requirement in the past 2 years, with a dozen more getting in line.[1]

Proponents of the law believe qualified doctors should not have to repeat their training. Opponents are worried about patient safety and doubt this law will address physician shortages due to licensing and employment barriers.[1]

Foreign medical graduates are still required to follow certain guidelines, including working for several years after completing medical school, completing a residency program with similar rigor to that in the United States, and passing the standardized three-part examination required for all physicians to gain licensure in the United States. Those who qualify obtain a restricted license to practice with the ability to receive full licensure over time. Many, but not all, states also require doctors to serve in rural or underserved areas.[1]

1. States loosen restrictions for international medical graduates to address physician shortages [press release]. Eyewire+. March 4, 2025. Accessed March 12, 2025. bit.ly/4iEf96o

PDS SHOWS PROMISE IN NPDR AND DME

Two studies found that the port delivery system (PDS) with ranibizumab (Susvimo, Genentech/Roche) achieved good results for patients with nonproliferative diabetic retinopathy (NPDR), and outcomes in those with diabetic macular edema (DME) were comparable with controls.[1,2]

The Pavilion randomized clinical trial included 174 patients with NPDR who were randomized to the PDS group with refill-exchanges every 36 weeks (n = 106) or the control group (n = 68). At week 52, 80.1% of the PDS group versus 9.0% of the control group had at least a 2-step Diabetic Retinopathy Severity Scale score improvement from baseline. Secondary outcomes included rate of development of center-involved DME, PDR, or anterior segment neovascularization through week 52 (PDS, 7.1%; control, 47.0%) and BCVA change from baseline to week 52 (PDS, +1.4 letters; control, -2.6 letters).[1]

The Pagoda randomized clinical trial included 634 patients with DME who were randomized to the PDS group with refill-exchanges every 24 weeks (n = 381) or the control group that received intravitreal injections of ranibizumab (Lucentis, Genentech/Roche) every 4 weeks (n = 253). The adjusted mean BCVA change from baseline averaged over weeks 60 and 64 was an increase of 9.6 letters for the PDS group and 9.4 letters for the control group, meeting the primary endpoint.[2] ■

1. Pieramici DJ, Awh CC, Chang M, et al. Port delivery system with ranibizumab vs monitoring in nonproliferative diabetic retinopathy without macular edema [published online ahead of print March 6, 2025]. *JAMA Ophthalmol.*
2. Khanani AM, Campochiaro PA, Graff JM, et al. Continuous ranibizumab via port delivery system vs monthly ranibizumab for treatment of diabetic macular edema [published online ahead of print March 6, 2025]. *JAMA Ophthalmol.*

Eyewire+ Pharma Update

- **4D Molecular Therapeutics** began enrollment for its phase 3 4FRONT-1 clinical trial of 4D-150, a potential therapy for wet AMD that uses a single intravitreal injection with a customized vector, R100, to provide sustained delivery of anti-VEGF agents.
- **Adverum Biotechnologies** initiated its phase 3 ARTEMTIS trial of ixoberogene soroparvovec (ixo-vec) gene therapy for the treatment of wet AMD. The trial is evaluating a single injection versus treatment with aflibercept (Eylea, Regeneron) every 8 weeks.
- **Harrow** announced a 5-year agreement with the contract manufacturing organization responsible for producing its 40 mg/mL triamcinolone acetonide (Triesence) to secure the long-term production of the drug and develop a next-generation version.
- **Opthea** announced new data from the phase 2b trial of sozinibercept for the treatment of wet AMD, showing that, in 73% of the study population, sozinibercept combination therapy led to statistically significant additional BCVA gains and better anatomic outcomes compared with ranibizumab monotherapy.
- **Atsena Therapeutics** was granted FDA fast-track designation for ATSN-201, a gene therapy for the treatment of X-linked retinoschisis.
- **Sydnexis'** new drug application for SYD-101, a low-dose atropine drop designed to treat progression of pediatric myopia, was accepted by the FDA, potentially making it the first pharmaceutical therapy for this increasingly prevalent condition.
- **Optos** launched MonacoPro, its next-generation, ultra-widefield retinal imaging device with integrated spectral-domain OCT. The device offers 200° single-shot optomap imaging, an AreaAssist tool for automatically measuring continuous areas of matching color, and access to a large reference database.

Want more retina news from *Eyewire+*?

RT ONE TO Watch

Retina Today

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RENE CHOI, MD, PHD

WHERE IT ALL BEGAN

While growing up in New Jersey, I explored a variety of activities, including soccer, Tae Kwon Do, piano, camping, and robotics. These hobbies helped shape who I am today: a person with a deep curiosity about how things work and a strong appreciation for both teamwork and individual perseverance. I attended Columbia University, where I earned a Bachelor of Science degree in Biomedical Engineering. However, it wasn't until I worked as an emergency medical technician that I truly felt drawn to patient care. Interacting directly with patients and helping them in their time of need opened my eyes to the privilege and responsibility that comes with caring for others.

Dr. Choi's advice: Be honest with yourself about your goals and values. Once you have a clear sense of direction, reach out to your mentors for guidance—they are invaluable resources. And don't forget to give back by supporting the next generation of retina specialists; we all stand on the shoulders of those who came before us.

MY PATH TO RETINA

My journey into the field of retina began as an MD/PhD student when I conducted research on retinal regeneration using a frog model of retinitis pigmentosa. The more I learned, the more captivated I became by the complex yet beautiful role the retina plays in vision.

During residency at the Moran Eye Center, I worked with an outstanding team in the uveitis and retina departments. It was there that I discovered my passion for diagnosing and treating retinal diseases and uveitis. Managing some of the most complex ocular diseases was both challenging and immensely rewarding, and I was humbled by the opportunity to help patients in these critical areas.

SUPPORT ALONG THE WAY

I have been fortunate to receive the support and guidance of many exceptional mentors, for whom I am deeply grateful. At SUNY Upstate Medical University, my mentors included Michael Zuber, PhD; Samuel Spalding, MD; and Anthony Andrews, MD. During my time at the Moran Eye Center, I was mentored by Paul Bernstein, MD, PhD; Albert Vitale, MD; and Mary Elizabeth Hartnett, MD.

At the Casey Eye Institute and Devers Eye Institute, I learned from Thomas Hwang, MD; Andreas Lauer, MD; Christina Flaxel, MD; Steven Bailey, MD; J. Peter Campbell, MD; Paul Yang, MD; Mark Pennesi, MD; Sirichai Pasadhika, MD; Merina Thomas, MD; Brandon Lujan, MD; James Rosenbaum, MD; Phoebe Lin, MD, PhD; Alison Skalet, MD, PhD; and Eric Suhler, MD. These mentors selflessly invested in my training, and I continue to seek their advice on patient care and professional development.

AN EXPERIENCE TO REMEMBER

Early in my career, a patient presented with acute vision loss in her only seeing eye due to a large submacular hemorrhage caused by wet AMD. Her other eye had already been affected by geographic atrophy, and she was terrified of losing the ability to see her grandchildren, read, and garden. I was deeply moved by the connection we formed as I listened to her fears and concerns. She told me that, regardless of the outcome, she was grateful that I listened—because it made her feel truly cared for. That moment reinforced the power of empathy in medicine and reminded me that, while we can't always control outcomes, showing our patients that we genuinely care can make a significant difference in their lives.

I performed a vitrectomy and used subretinal alteplase with intravitreal gas to displace the hemorrhage, ultimately restoring her vision to nearly baseline levels. ■

Rene Choi, MD, PhD, is a vitreoretinal surgeon and uveitis specialist at Texas Retina Associates, where he works alongside 15 colleagues who share his dedication to the field of retina. He is a consultant for Abbvie, Eyepoint Pharmaceuticals, and Genentech/Roche and serves as a subinvestigator and principal investigator on numerous clinical trials. He can be reached at **rchoi@texasretina.com.**

FELLOWS FORUM 2025: 25 YEARS OF EDUCATION

Expert faculty discussed advances in retina surgery and imparted professional development pearls.

BY ADRIAN AU, MD, PHD

The 25th Annual Fellows Forum, held in Chicago, January 24-25, 2025, provided a platform for second-year retina fellows to navigate the transition to independent practice, refine surgical techniques, and tackle the complexities of disease management. This annual meeting also fosters mentorship, collaboration, and professional growth. Hosted by Carl C. Awh, MD, FASRS; David R. Chow, MD, FASRS; and Tarek S. Hassan, MD, FASRS, the forum includes expert faculty who aim to strengthen professional relationships and facilitate meaningful knowledge exchange (Figure 1). Beyond the sessions, the meeting also provides invaluable opportunities for fellows to network with peers, engage with faculty, and build lasting connections.

INNOVATIONS IN RETINA

This year's distinguished guest speaker, Mark S. Humayun, MD, PhD, set the tone with an inspiring address on the future of the field, emphasizing the need for forward-thinking approaches and technological advances. Rather than a traditional lecture, he led a brainstorming session, during which he encouraged the fellows to conceptualize groundbreaking ideas, such as scleral nerve denervation, radio frequency identification-integrated safety systems, and advanced tamponade agents (Figure 2). The interactive session underscored the importance of innovation and creative problem-solving in shaping the field.

The meeting also showcased emerging therapies in retina care. Adrienne W. Scott, MD, explored the newest approaches to wet AMD treatment, such as faricimab (Vabysmo, Genentech/Roche), 8 mg aflibercept (Eylea HD, Regeneron), and the port delivery system with ranibizumab (Susvimo, Genentech). The panelists discussed the complicated decision of when to switch patients to a newer agent. For example, Margaret A. Chang, MD, noted that she used to stick with the same agent for a long time, but now she is quicker to make a change. The group also explored the biosimilar space, with Sunir J. Garg, MD, explaining that step therapy is likely to dictate much of their use.

EXPERT SURGICAL ADVICE

Several talks focused on surgical tips and tricks, starting with a surgical video panel led by Dr. Garg. He showed a scleral buckle revision surgery in the eye of an 11-year-old boy, performed by Emmanuel Y. Chang, MD, PhD, who then discussed the unique challenges of performing vitrectomy in pediatric patients, such as a formed vitreous. The panel agreed that fellows should seek more experience with scleral buckling—an important surgical approach that is falling out of favor. The panel then tackled sickle cell retinopathy (with a case by Dr. Scott), retinoschisis retinal detachment with an outer retinal hole (shared by Aleksandra Ratchitskaya, MD), and a full-thickness macular hole case (provided by Dr. Awh).

Later in the day, Dr. Emmanuel Chang presented on the surgical management of AMD and shared his subretinal tPA tips to address submacular hemorrhages. The panel discussed pearls for subretinal bleb placement, including the need to create a steady drip with the infusion and find the right pressure for the injection. Dr. Garg added that fellows should consider photodynamic therapy for patients with polypoidal choroidal vasculopathy because it might help extend their anti-VEGF treatment intervals.

Dr. Hassan tackled surgical management of diabetic retinopathy, with the panel first agreeing that you should use imaging to get patient buy-in to improve treatment adherence. As for the surgeries themselves, always try to lift the hyaloid and remove as much traction as possible, Dr. Hassan noted. These days, most of the panelists aren't waiting as long before taking these patients to the OR, particularly if the patient has a premacular hemorrhage, according to Dr. Awh. Still, Dr. Chang suggested sending some patients home with information and an amsler grid to help them better understand the condition before rushing to the OR.

SURGICAL CASE INSIGHTS

During the fellow case presentations, attendees had the chance to showcase and analyze their complex surgical cases. In the first case session, Jake Anderson, MD, described

Figure 1. The 2025 Fellows Forum faculty gathered to celebrate Dr. Humayun, this year's distinguished guest speaker.

Figure 2. Dr. Humayun encouraged attendees to brainstorm innovations in a small-group format and then share their ideas with the room.

the viscostretch technique for recurrent macular hole, David Fell, MD, discussed a case of globe perforation with peribulbar block, Vaishnavi Balendiran, MD, shared her experience explanting a capsular tension ring, and Adrienne Coche, MD, walked attendees through her approach to managing surgical visualization difficulties. In the second session, Blake H. Fortes, MD, provided a video on subretinal tPA complications, Peter W. Jones, MD, PhD, discussed the differentials for panuveitis, Mustafa Iftikhar, MD, described the satisfying removal of a transscleral subretinal band, and Akshay R. Mentreddy, DO, shared a wild video of intraocular foreign body removal and amniotic membrane graft placement. Throughout the sessions, the faculty provided expert perspectives on each approach, offering praise for a job well done and tips for optimizing the surgical techniques.

BUSINESS 101

In addition to clinical pearls, Dr. Margaret Chang also provided a robust discussion on the business of retina, during which she walked attendees through a practice's revenue cycle. She focused on the billing and coding steps that are necessary to get paid and touched on the common revenue cycle pitfalls to avoid. Dr. Chang also took a close look at drug inventory management, noting that physicians should try to get a volume discount or bulk rebate; smaller practices looking to mitigate drug cost can consider joining a group purchasing organization, which often provides cheaper drug prices and inventory software but requires a contract (read it carefully!), membership fees, and administration fees.

NAVIGATING CAREER AND PROFESSIONAL DEVELOPMENT

Beyond the surgical and clinical expertise shared during the meeting, the faculty also addressed professional and personal development in the field of retina. Faculty-led discussions covered essential topics such as work-life balance, financial planning, and career advances, highlighting the importance of building strong professional relationships and making strategic financial decisions.

Speakers shared insights on navigating early career challenges and reflected on the lasting effect of fellowship connections. This theme was particularly meaningful as the forum celebrated its 25th anniversary, showcasing the enduring bonds between its hosts—Drs. Awh, Chow, and Hassan—whose relationships extend beyond the meeting and into their personal lives. Fellows were encouraged to continue fostering their own relationships, as the professional and personal connections made during training often play a vital role in their long-term careers.

NETWORKING AND FELLOWSHIP

Between sessions, attendees engaged in lively discussions over meals, exchanged experiences about their training programs, and strengthened friendships that will carry forward into their professional careers. The event was capped off with a fun and engaging trivia competition and a bowling night, providing relaxed and enjoyable ways for fellows to bond outside the conference room. These activities added an element of camaraderie, reinforcing the sense of community that Fellows Forum has fostered over the years.

The 2025 Fellows Forum successfully blended technical expertise with professional mentorship, equipping attendees with essential knowledge and practical insights. By bridging the gap between experienced specialists and early-career retina surgeons, the forum reinforced the importance of mentorship, innovation, and continuous learning in advancing retina care. Just as importantly, it provided a meaningful opportunity for fellows to connect, collaborate, and build lasting friendships, ensuring that the relationships formed during this pivotal time in their careers will continue well into the future. ■

Save the date for the 26th Annual Fellows Forum, scheduled for January 30-31, 2026, in Chicago!

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A PERITOMY-SPARING APPROACH FOR SCLERAL BUCKLE IN PEDIATRIC RRD


This technique helps maintain conjunctival integrity and maximize ocular surface recovery.

BY MIGUEL CRUZ-PIMENTEL, MD, AND RAJEEV H. MUNI, MD, MSC, FRCSC

Pediatric rhegmatogenous retinal detachment (RRD) cases are usually managed with a scleral buckle (SB) procedure that involves a 360° limbal peritomy. Although this technique has been the standard for years, it is invasive and requires significant manipulation of the conjunctiva and considerable dissection of the intermuscular septum and other tissues.[1,2] Yepez et al introduced modifications to the traditional surgical technique in adult patients, eliminating the need for peritomy.[3] While the primary objective is to achieve retinal reattachment, it is equally important to maintain the integrity of the conjunctiva. Here, we detail how we accomplish both in our pediatric patients undergoing an SB.

NEW AND IMPROVED

We recently published our sutureless, peritomy-sparing SB technique for pediatric RRD, ensuring good preservation of the conjunctiva and maximizing recovery of the ocular surface.[4] This approach includes the following surgical steps:

Transconjunctival Isolation of Recti Muscles

First, isolate each muscle by grasping it with 0.12 forceps. Next, pass a 2.0 silk suture needle beneath the belly of the muscle and loop the muscle transconjunctivally (Figure 1). Perform a forced duction test to ensure proper isolation. To isolate the superior rectus muscle, make a radial conjunctival incision in the superior nasal quadrant, and use a Jameson hook to avoid the superior oblique muscle.

Treatment of Retinal Breaks

After isolating the recti muscles, visualize the retinal breaks using indirect ophthalmoscopy. Mark the breaks on the conjunctiva and treat them with cryopexy.

Radial Conjunctival Incisions and Scleral Belt Loops

In all four quadrants, make small radial conjunctival incisions several millimeters posterior to the muscle insertion and create scleral belt loops using a crescent blade (Figure 2).

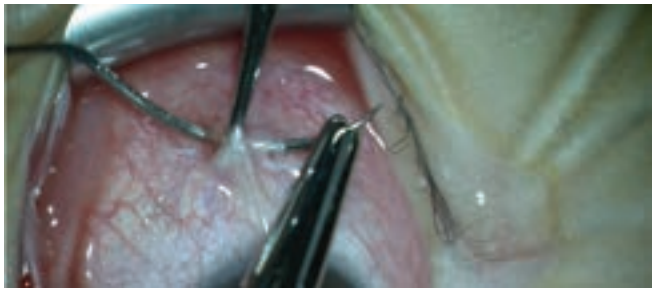

Figure 1. The transconjunctival grasping technique is illustrated with the inferior rectus muscle. A force duction test is conducted on each muscle to confirm adequate localization.

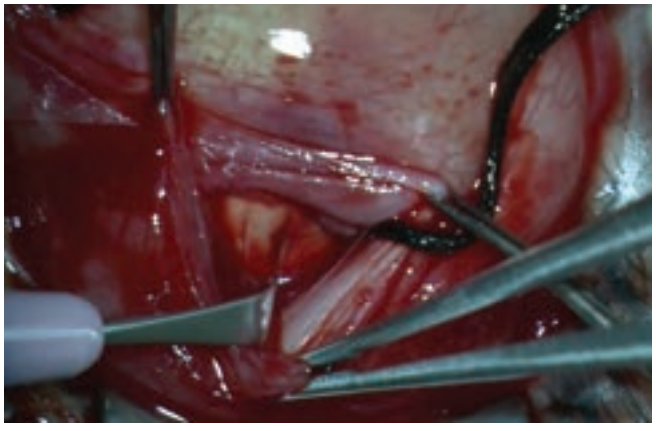

Figure 2. Radial conjunctival incisions and scleral belt loops are done in all four quadrants.

Passing the SB Band

Pass a 41 silicone SB band through the four belt loops and under the four recti muscles. Using a snap or thin, curved forceps helps grasp the band from one radial incision to the other and ensures it is passed fully under the recti muscles (Figure 3). After threading the SB through the belt loops and positioning it under the recti muscles, secure it with a Watzke sleeve in the superior nasal quadrant.

Closure of Radial Incisions

Close the conjunctival incisions with a single absorbable suture or a sutureless technique using a fibrin sealant.

TROUBLESHOOTING

Using anterior segment OCT, researchers reported that children have a significantly thicker anterior conjunctiva compared with adults (280 ± 45 µm vs 239 ± 38 µm), and the difference increases further away from the scleral spur.[5] This is due to a higher number of goblet cells and a higher density of conjunctival lymphoid tissue during childhood.[6,7] Isolating muscles transconjunctivally in patients with a thick Tenon capsule can be challenging. To overcome this, make radial peritomies near the muscle insertion based on the Spiral of Tillaux. Converting to a conventional SB is always an option.

After vitreoretinal procedures, patients have a higher likelihood of experiencing dry eye disease. This is commonly attributed to the surgical trauma inflicted on the conjunctiva, which in turn results in a reduced density of goblet cells. Studies show that vitreoretinal procedures can decrease the distribution of goblet cells by as much as 40% and the density of goblet cells in up to 60% of cases.[8] In a randomized trial in which patients undergoing strabismus surgery were assigned either to a group that received fornix incisions or to a group that received limbal incisions, the latter group had more serious dry eye symptoms and a greater effect on corneal sensitivity and tear film stability.[9]

Using absorbable braided sutures to close conjunctival incisions can cause ocular surface irritation and hyperemia and increase the tear meniscus height.[10,11] A prospective study of strabismus patients undergoing conjunctival closure with fibrin sealant or 8-0 vicryl sutures found that the former group had faster ocular surface rehabilitation.[12]

Pediatric patients who undergo an SB are at risk of developing glaucoma from the SB or subsequent vitreoretinal procedures.[13,14] Studies report that the incidence of glaucoma after an SB can range from 1.4% to 4.4%.[15-18] In children, a history of previous ocular surgery can increase the risk of glaucoma surgery failure.[19] This may be the result of excessive conjunctival fibroblasts and inflammatory cells.[20,21] The limbal peritomy can negatively affect conjunctival health, making it less suitable for glaucoma filtering procedures.

A LITTLE FORETHOUGHT GOES A LONG WAY

It is vital to preserve the conjunctiva of pediatric patients for their long-term ocular health. Although doing so can make RRD surgical repair longer and a little more tedious, we believe the time spent is well worth it. Further data and experience with the technique presented here will help refine the approach to SB surgery in children. ■

1. Nuzzi R, Lavia C, Spinetta R. Paediatric retinal detachment: a review. *Int J Ophthalmol*. 2017;10(10):1592-1603.
2. Starr MR, Boucher N, Sharma C, et al. The state of pediatric retinal detachment surgery in the United States: a nationwide aggregated health record analysis. *Retina*. 2023;43(5):717-722.
3. Yepez JB, Murati FA, Petitto M, De Yepez J, Mura M, Kozak I. Peritomy-sparing scleral buckle. *Am J Ophthalmol Case Rep*. 2019;15:100474.
4. Demian S, Cruz-Pimentel M, Muni RH. Sutureless peritomy sparing scleral buckle in pediatric patients. *Am J Ophthalmol*. 2024;268:e5-e6.

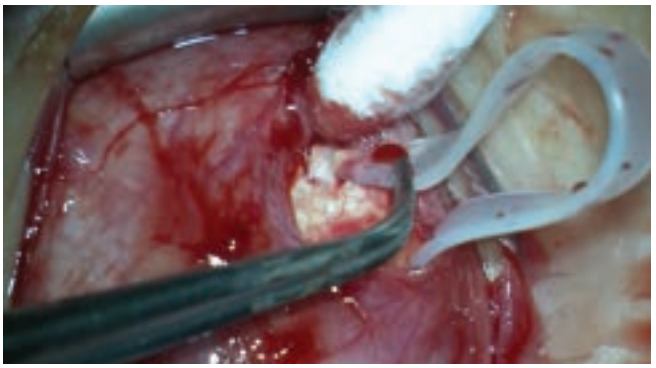

Figure 3. The silicone encircling band is securely threaded through the scleral belt loops and under the recti muscles using radial conjunctival incisions.

5. Read SA, Alonso-Caneiro D, Vincent SJ, et al. Anterior eye tissue morphology: scleral and conjunctival thickness in children and young adults. *Scientific Reports*. 2016;6(1):33796.
6. Kessing SV. Mucous gland system of the conjunctiva. A quantitative normal anatomical study. *Acta Ophthalmol (Copenh)*. 1968:Suppl 95:1+.
7. Österlind G. An investigation into the presence of lymphatic tissue in the human conjunctiva and its biological and clinical importance. H. Ohlssons Boktryckeri; 1944.
8. Mani R, Shobha PS, Thilagavathi S, et al. Altered mucins and aquaporins indicate dry eye outcome in patients undergoing vitreo-retinal surgery. *PLoS One*. 2020;15(5):e0233517.
9. Li Q, Fu T, Yang J, Wang QL, Li ZE. Ocular surface changes after strabismus surgery with different incisions. *Graefes Arch Clin Exp Ophthalmol*. 2015;253(3):431-438.
10. Venkatesh R, Jayadev C, Mangla R, Chitturi SP, Mohan S, Ratra D. Ocular surface changes following vitreoretinal procedures. *Indian J Ophthalmol*. 2023;71(4):1123-1126.
11. Sato T, Koh S, Yasukura Y-i, et al. Surgical factors affecting changes in ocular surface dynamics in the early postoperative period after 25-gauge vitrectomy. *Eye Contact Lens*. 2019;45(4):254-259.
12. Anand K, Goyal G, Goel Y, Bansal Y, Rastogi A, Jaisingh K. Ocular surface response to fibrin sealant versus vicryl suture for conjunctival closure after strabismus surgery: an objective assessment. *Saudi J Ophthalmol*. 2020;34(4):243-246.
13. Pinninti U, Carvounis PE, McPherson AR. Scleral buckle surgery and the development of glaucoma - long term follow up. *Invest Ophthalmol Vis Sci*. 2011;52(14):6154-6154.
14. Kornmann HL, Gedde SJ. Glaucoma management after vitreoretinal surgeries. *Curr Opin Ophthalmol*. 2016;27(2):125-131.
15. Sebestyen JG, Schepens CL, Rosenthal ML. Retinal detachment and glaucoma. I. Tonometric and gonioscopic study of 160 cases. *Arch Ophthalmol*. 1962;67(6):736-745.
16. Hartley RE, Marsh RJ. Anterior chamber depth changes after retinal detachment. *Br J Ophthalmol*. 1973;57(8):546-550.
17. Kreiger AE, Hodgkinson BJ, Frederick AR Jr, Smith TR. The results of retinal detachment surgery. Analysis of 268 operations with a broad scleral buckle. *Arch Ophthalmol*. 1971;86(4):385-394.
18. Perez RN, Phelps CD, Burton TC. Angel-closure glaucoma following scleral buckling operations. *Trans Sect Ophthalmol Am Acad Ophthalmol Otolaryngol*. 1976;81(2):247-252.
19. Miller MH, Rice NS. Trabeculectomy combined with beta irradiation for congenital glaucoma. *Br J Ophthalmol*. 1991;75(10):584-590.
20. Broadway DC, Grierson I, Hitchings RA. Local effects of previous conjunctival incisional surgery and the subsequent outcome of filtration surgery. *Am J Ophthalmol*. 1998;125(6):805-818.
21. Broadway DC, Chang LP. Trabeculectomy, risk factors for failure and the preoperative state of the conjunctiva. *J Glaucoma*. 2001;10(3):237-249.

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WATCH FOR CHOROIDAL DETACHMENTS IN CRYPTOCOCCOSIS

Unusual ocular findings led to the diagnosis of a serious systemic condition.

BY FRIDA VELCANI, BA; SHIVESH SHAH, BA; ALBERT T. VITALE, MD; RACHAEL S. JACOBY, MD; AND NIKHIL N. BATRA, MD, MS

Systemic infection with *Cryptococcus neoformans*, a form of encapsulated yeast, occurs most commonly in immunocompromised individuals and is contracted via inhalation. The primary site of infection is the lungs, although ocular involvement can occur secondary to hematogenous spread or through the leptomeninges. Infection most commonly occurs in patients with human immunodeficiency virus (HIV)/acquired immune deficiency syndrome (AIDS).[1-3] Ocular manifestations may include optic nerve involvement and papilledema.

Here, we report a case of primary bilateral serous choroidal detachments leading to the diagnosis of systemic cryptococcosis and HIV in a previously undiagnosed patient.

CASE REPORT

A 49-year-old White man presented with bilateral vision loss and numbness in his left arm. His ocular history was significant for bilateral cataract extraction at 9 years of age with aphakic correction until he underwent bilateral anterior chamber IOL (ACIOL) placement at 43 years of age. Further details of the cataract extraction were not known.

At presentation, his BCVA was 20/70 OD and 20/100 OS, and his IOP was 17 mm Hg OD and 20 mm Hg OS. The anterior chamber in each eye was deep and quiet, notable only for the ACIOLs. There was no vitritis or vitreous haze in either eye. Fundus examination of each eye showed moderate-sized serous choroidal detachments in the temporal and nasal periphery and multiple choroidal hemorrhages in the nasal periphery (Figure 1). B-scan ultrasonography confirmed the serous nature of the choroidal detachments and revealed a normal axial length in each eye (Figure 2).

The patient reported recent unintentional weight loss of 20 to 30 lbs and serous drainage from a painful tooth abscess. He was immediately hospitalized for evaluation and workup for possible systemic infection or neoplastic process. Multimodal imaging with fluorescein angiography, ICG angiography, and OCT was not obtained at his initial visit due to the urgent need to address his systemic illness.

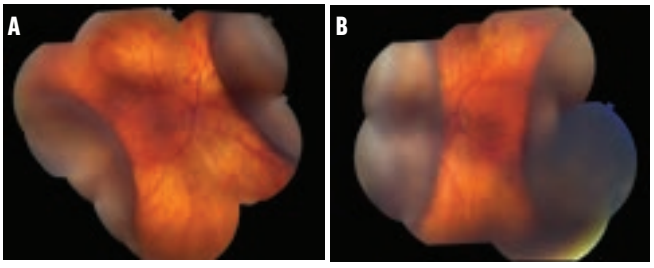

Figure 1. Montage fundus photographs of the right (A) and left (B) eye at presentation showed choroidal detachments and choroidal hemorrhages in the nasal periphery.

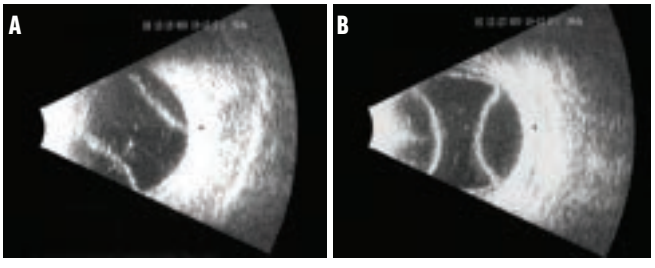

Figure 2. B-scan ultrasound images confirmed the serous nature of the choroidal detachments in the right (A) and left (B) eye.

The patient was subsequently diagnosed with AIDS complicated by cryptococcal infection. His CD4 count was 69, and his HIV viral load was 350,000. Serum *Cryptococcus* antigen was positive, and a CT-guided biopsy of a cavitary lung lesion was positive for *Cryptococcus* by histopathology. Lumbar puncture and cerebrospinal fluid analysis were normal and did not reveal central nervous system (CNS) involvement. The patient was started on topical

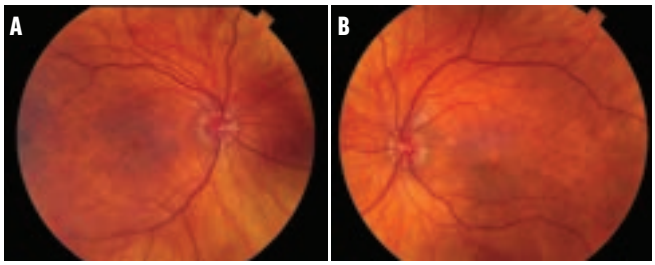

Figure 3. Fundus imaging at the 1-week follow-up visit showed complete resolution of the choroidal detachments in the right (A) and left (B) eye.

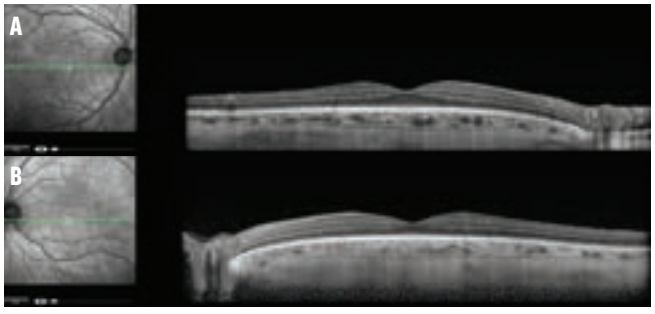

Figure 4. OCT at the 1-week follow-up visit showed normal macular retinal and underlying choroidal architecture in the right (A) and left (B) eye.

1% prednisolone, topical atropine, and systemic induction treatment with intravenous amphotericin and flucytosine.

At his 1-week follow-up at our clinic, his BCVA improved to 20/40 OD and 20/30 OS. Fundus photography showed resolution of the choroidal effusions and choroidal hemorrhages (Figure 3), and OCT was unremarkable (Figure 4).

AN UNUSUAL PRESENTATION

Ocular manifestations of cryptococcosis have been described as a complication of systemic disease. Isolated ocular involvement due to hematogenous spread in the form of multifocal choroiditis or, rarely, endophthalmitis has been reported.[1-3] Papilledema and ophthalmoplegia due to high intracranial pressure from CNS involvement of *cryptococcus* has also been described.[4] In addition, uveal effusion leading to angle-closure glaucoma in phakic patients has been observed in patients with HIV/AIDS.[5]

Our case is unusual because the bilateral serous choroidal detachments were the presenting sign of newly diagnosed HIV/AIDS complicated by systemic *cryptococcal* infection, which, to our knowledge, has not been previously reported. Interestingly, our patient had a history of cataract extraction with ACIOL placement and presented with normal IOPs and deep anterior chambers, despite the moderate-sized serous choroidal detachments in each eye.

The pathogenesis of the choroidal detachments was unclear; however, the fact that his eyes were unicameral may have played a role. The mechanism leading to the serous choroidal detachments was likely multifactorial, involving the hematogenous spread of cryptococcosis and local ocular inflammatory, hemodynamic, and hydrodynamic factors.

KEEP YOUR GUARD UP

Ocular involvement with systemic cryptococcal infection occurs most commonly in the setting of severe immunosuppression. Optic nerve involvement and papilledema due to increased intracranial pressure and, less commonly, multifocal choroiditis are well-described ocular signs of systemic cryptococcosis, particularly among patients with HIV/AIDS. However, this case suggests the presence of bilateral serous choroidal detachments may herald the onset and raise the suspicion of this infection in the appropriate clinical context.

Early recognition of this finding may facilitate prompt diagnosis and treatment with subsequent preservation of visual function and reduced systemic morbidity. ■

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1. Kestelyn P, Taelman H, Bogaerts J, et al. Ophthalmic manifestations of infections with Cryptococcus neoformans in patients with the acquired immunodeficiency syndrome. *Am J Ophthalmol*. 1993;116(6):721-727.
2. Baillif S, Delas J, Asrargis A, Gastaud P. Multimodal imaging of bilateral cryptococcal choroiditis. *Retina*. 2013;33(1):249-251.
3. Chen J, Chai C, Teoh SC. Cryptococcal-related exudative retinal detachment. *Eye*. 2011;25(9):1234-1235.
4. Battu R, Biswas J, Jayakumar N, et al. Papilloedema with peripapillary retinal hemorrhages in an acquired immunodeficiency syndrome (AIDS) patient with cryptococcal meningitis. *Indian J Ophthalmol*. 2000;48(1):47-49.
5. Nash RW, Lindquist TD. Bilateral angle-closure glaucoma associated with uveal effusion: presenting sign of HIV infection. *Surv Ophthalmol*. 1992;36(4):255-258.

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AN UPDATE ON OCT ANGIOGRAPHY NOMENCLATURE


Retina experts have standardized a new reporting terminology for OCTA.

By Marion R. Munk, MD, PhD, and Ferhat Turgut, MD

OCT angiography (OCTA) has become a transformative tool in retinal imaging, offering unparalleled insights into retinal vasculature and disease pathologies. However, the lack of standardized terminology has posed challenges for consistent communication in clinical and research settings. Additionally, many terms commonly used to describe pathological changes on OCTA fail to accurately reflect the underlying physical principles of the technology.

To address these issues, a consensus framework for OCTA nomenclature was developed using a modified Delphi method. This initiative involved retinal imaging specialists with extensive expertise in the field, basic researchers specializing in retinal pathology, and biomechanical engineers actively engaged in the development of OCTA devices and modules. The collaborative initiative included four prominent retina societies: the European Society of Retina Specialists (Euretina), Japanese Retina and Vitreous Society (JRVS), American Society of Retina Specialists (ASRS), and International Retinal Imaging Society (IntRIS).[1,2]

The framework initially focuses on retinal vascular diseases (RVD), and it is currently being expanded to encompass a broader range of retinal and macular diseases.

WHY STANDARDIZED TERMINOLOGY MATTERS

OCTA's rapid adoption has exposed inconsistencies in how findings are described. Terms such as *flow void* and *flux*, adapted from other modalities, do not align with the unique principles of OCTA, which relies on motion contrast rather than direct flow measurement. OCTA's signal detection is inherently binary, identifying the presence or absence of motion contrast, rather than providing a quantitative measure of flow. Using terms such as *flow* implies a level of quantification OCTA does not deliver. Terminology should accurately reflect the underlying principles of a modality. Just as we use *reflectivity* to describe changes on OCT or *fluorescence* to describe findings on fluorescence angiography, OCTA requires terminology that is precise and consistent with its technical basis. Without a standardized nomenclature, comparisons across studies are challenging, and communication among professionals remains ambiguous.

AT A GLANCE

- Experts have developed a consensus framework for OCT angiography (OCTA) nomenclature.
- The structure consists of generic terms (ie, *OCTA signal*), adjective terms (ie, *absence/presence* and *increased/decreased*), and descriptive/etiologic terms (ie, *due to shadowing/decreased perfusion/artifacts*).
- While the proposed terms are tailored to retinal vascular diseases, ongoing efforts aim to extend this nomenclature to other conditions.

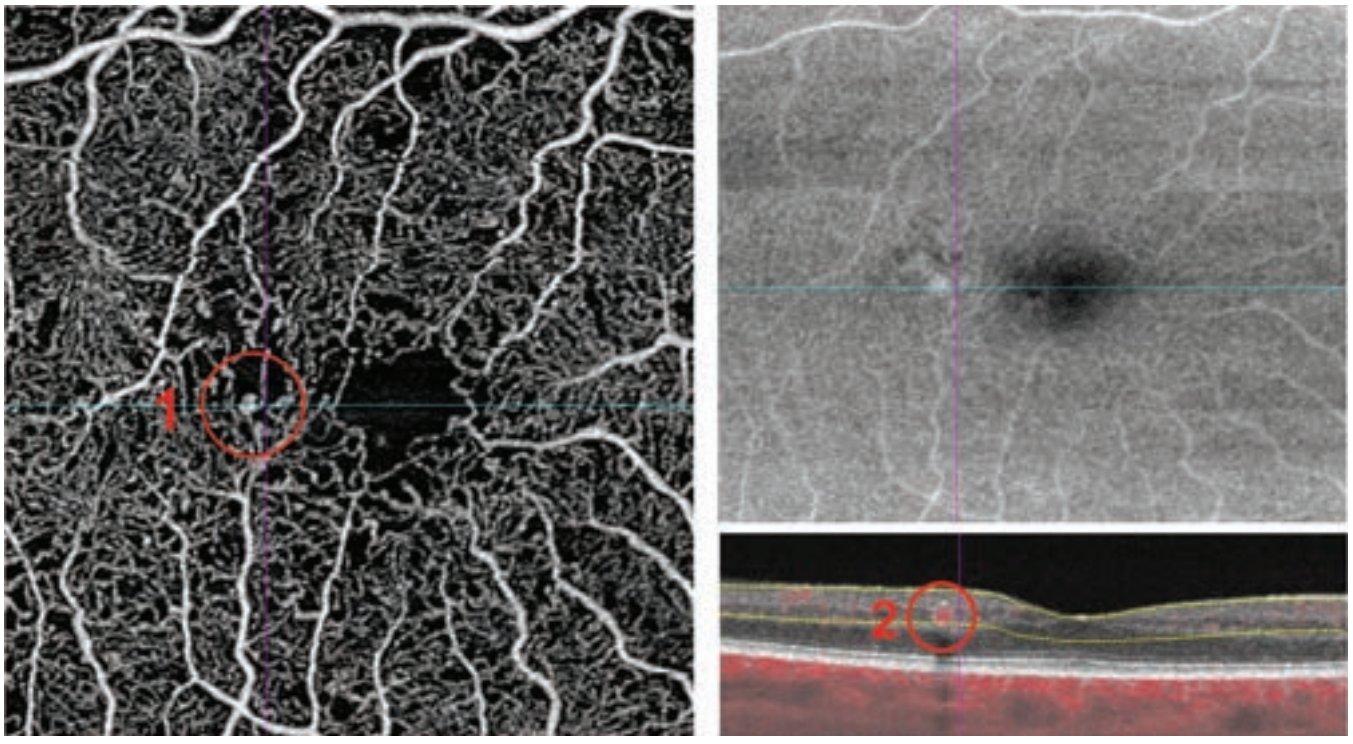

Figure 1. This is the first OCTA image that experts were asked to describe using the proposed nomenclature framework. They were also asked how comfortable they felt using the proposed nomenclature. Descriptions of the marked area (red 1 and 2) include: "The OCTA images reveal a 6 mm x 6 mm macular SCP en face slab with a focal increase in OCTA signal, indicative of a microaneurysm"; "The OCTA B-scan shows an abnormal OCTA signal extension intraretinally, likely at the boundary between the inner nuclear layer and the outer plexiform layer, consistent with a microaneurysm originating from vascular abnormalities"; and "Increased OCTA signal consistent with a microaneurysm."

THE PROCESS OF REACHING CONSENSUS

The initial effort began with a comprehensive survey distributed to Euretina, JRVS, and ASRS members, which did not reach a consensus.[1] Subsequently, a modified Delphi process was conducted, involving experts in the field. Despite this rigorous approach, consensus on OCTA nomenclature remained elusive.[2] What became evident, however, was that achieving consensus required the development of a new framework that accurately reflects the physical principles of OCTA, rather than simply endorsing the terms frequently used in previous literature. Thus, the final effort began with the formation of an executive committee and an expert panel. The executive committee oversaw literature reviews, survey design, and data analysis, while the expert panel, consisting of seven specialists in OCTA technology, retinal diseases, and imaging physics, provided iterative feedback and refinement. A literature review focusing on OCTA and RVD identified 159 relevant terms from 58 studies. This review, together with the initial results of the two prior efforts, formed the basis for the subsequent surveys.[3]

The first survey ranked and selected preferred terms based on expert feedback. In subsequent surveys, these terms were applied to OCTA images to evaluate their accuracy and suitability. After each round, the executive committee and the expert panel refined the framework through discussions, ensuring its applicability to both clinical and research contexts. The iterative surveys adhered to a structured classification system to define levels of consensus:

- **Accepted:** Median ≥ 6, no strict interquartile range (IQR) criteria
- **Considerable Consensus:** Median 6 to 7, IQR ≤ 3
- **Strong Consensus:** Median ≥ 8, IQR ≤ 2
- **Refined Strong Consensus:** Median ≥ 8, IQR ≤ 2, with ≥ 70% responses in the 8 to 10 range

After several rounds of refinement, the final framework was distributed via a survey to IntRIS members. They were asked to apply the framework to describe a series of provided OCTA examples (Figure 1).

KEY FINDINGS

The final framework introduces a three-tiered structure:

1. **Generic Terms:** *OCTA signal* achieved refined strong consensus (median: 8, IQR: 8 to 9, 75.8% agreement). This term provides a versatile and universally applicable descriptor independent of OCTA module and mechanism to generate motion contrast.
2. **Adjective Terms:** Descriptors such as *absence/presence* and *increased/decreased* were preferred for their clarity, achieving refined strong consensus (median: 8, IQR: 8 to 9, 76.6% agreement).

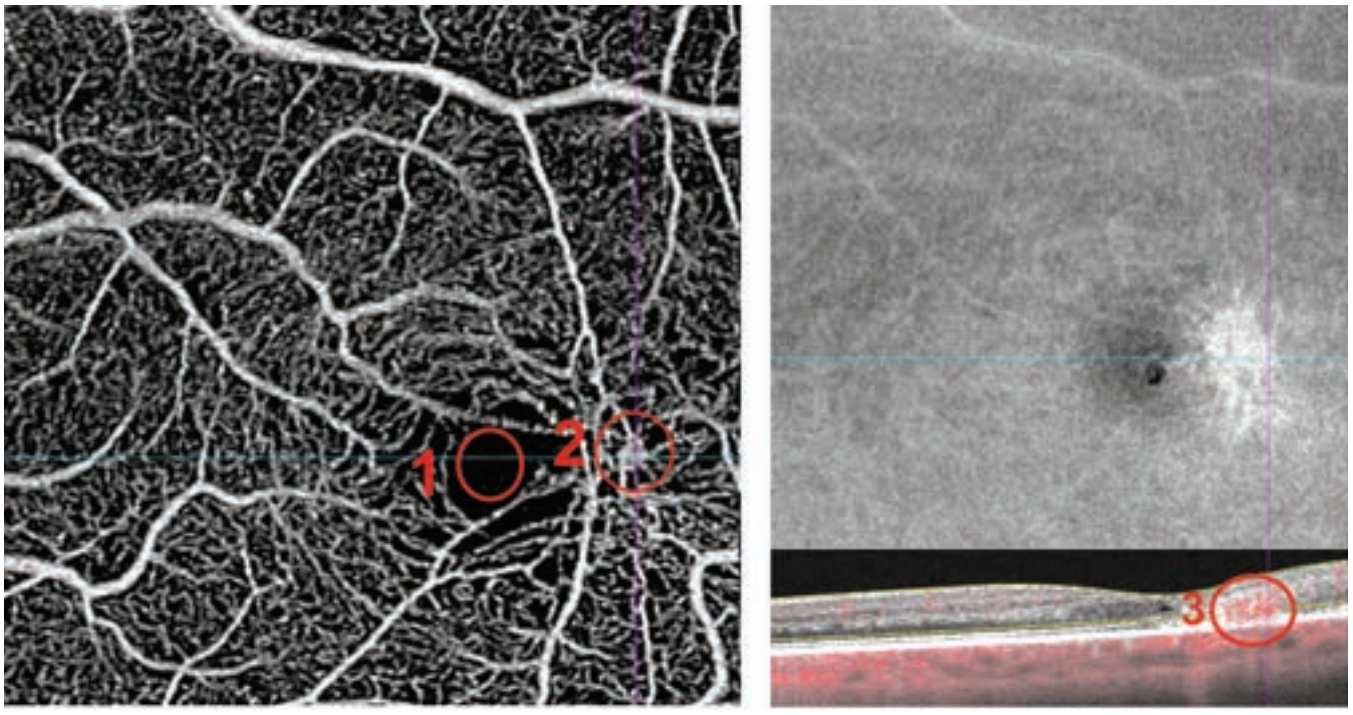

Figure 2. Experts were asked to describe three key changes observed in these OCTA images, applying the standardized terms from the new framework. The first observation (red 1) highlights the 6 mm x 6 mm en face SCP slab displaying a decreased OCTA signal due to nonperfusion at the foveal avascular zone (FAZ). The FAZ boundaries are irregular, with temporal dragging and distortion of the perifoveal capillaries, indicative of vascular disruption. A different feature (red 2) reveals a focal increase in OCTA signal temporal to the FAZ on the SCP en face slab. This finding suggests vascular remodeling or neovascularization, characterized by a cluster of tangled vessels, increased vascular density, and capillary distortion. Finally (red 3), the OCTA B-scan shows a focal area of increased OCTA signal in the outer retina. This signal is localized at the boundary of the MCP and DCP and colocalizes with a hyperreflective lesion at the structural en face scan, suggestive of intraretinal neovascularization and/or chorioretinal anastomosis seen in macular telangiectasia type 2.

3. **Descriptive/Etiologic Terms:** Categories (nonexhaustive) such as *due to shadowing, due to decreased perfusion,* and *due to artifacts* describe the potential underlying origin of the signal and achieved strong consensus (median: 8, IQR: 7 to 9), offering specificity for differentiating signal alterations.

The use of terms within these three categories should be complemented by a detailed description of the scan, including the scan type (eg, en face, OCTA B-scan), scan size (eg, 3 mm x 3 mm, 6 mm x 6 mm), slab (eg, superficial capillary plexus [SCP], deep capillary plexus [DCP], middle capillary plexus [MCP], choriocapillaris, or specific segmentation boundaries used to generate the slab), and any other relevant technical details (eg, swept-source or spectral-domain OCT).The level of detail naturally varies depending on the context but is particularly crucial in scientific settings to ensure clarity, reproducibility, and consistency in reporting (Figure 2).

Utility in Clinical Practice: The framework achieved a median score of 8 (IQR: 7 to 9), with 67.4% of responses in the 8 to 10 range. This underscores its utility in improving interdisciplinary communication and diagnostic accuracy in clinical settings.

Utility in Research: For research applications, the framework was rated highly with a median score of 8.5 (IQR: 8 to 9) and 78% agreement in the top range, emphasizing its value in enhancing reproducibility and facilitating multicenter studies.

(Continued on page 32)

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DRIL: A ROBUST IMAGING BIOMARKER IN DME

Here's why you should be on the lookout for disorganization of retinal inner layers on OCT.

By Andreas Di-Luciano, MD; Manish Nagpal, MD, FRCS, FASRS; Wai-Ching Lam, MD, FRCS; Laurent Velasque, MD; and Eduardo Kenstelman, MD

Diabetic retinopathy (DR) is a major complication of diabetes mellitus, a chronic condition with widespread effect due to its high rates of morbidity and mortality.[1] Diabetic macular edema (DME) is the leading cause of vision loss among individuals with DR, particularly affecting working-age adults.[2] Despite advances in treatments such as intravitreal injections of anti-VEGF agents and corticosteroids, predicting visual outcomes in patients with DME remains challenging. This limitation has spurred research into reliable biomarkers that could better assess treatment efficacy and predict changes in visual acuity.

One promising biomarker is disorganization of retinal inner layers (DRIL), which has shown potential as a noninvasive indicator of visual prognosis in patients with DME. DRIL, observed through spectral-domain OCT (SD-OCT), reveals structural changes in the retina that correlate with decreased visual acuity. Its ease of measurement and noninvasive nature make DRIL a practical tool for tracking DME progression.[2-4]

A PREDICTIVE INDICATOR OF VISUAL ACUITY

After reviewing seven studies that included DRIL as a biomarker, we found that the presence and extent of DRIL consistently correlated with reduced visual acuity in patients with DME.[5] DRIL is defined as the horizontal extent where the boundaries between retinal inner layers (ie, ganglion cell-inner plexiform layer, inner nuclear layer, and outer plexiform layer) become indistinct (Figures 1 and 2).[2] The seven studies showed that an increased extent of DRIL was linked to worse baseline visual acuity and a decline in visual acuity over time. For example, research by Sun et al demonstrated that every 100 µm increase in DRIL corresponded with a reduction of approximately 4.6 ETDRS letters in visual acuity.[2] Similarly, Das et al observed that a greater horizontal DRIL extent significantly predicted poorer visual outcomes over time.[4]

Based on our review, patients with minimal or no DRIL at baseline showed a greater potential for visual acuity improvement, underscoring the importance of detecting DRIL in the early stages of DME. In studies by Radwan et al

AT A GLANCE

- Disorganization of retinal inner layers (DRIL) is defined as the horizontal extent where the boundaries between various retinal inner layers become indistinct.
- In one meta-analysis, the presence and extent of DRIL consistently correlated with reduced visual acuity in patients with diabetic macular edema.
- DRIL is a promising biomarker for clinical practice, especially as a predictor of visual outcomes in diabetic macular edema.

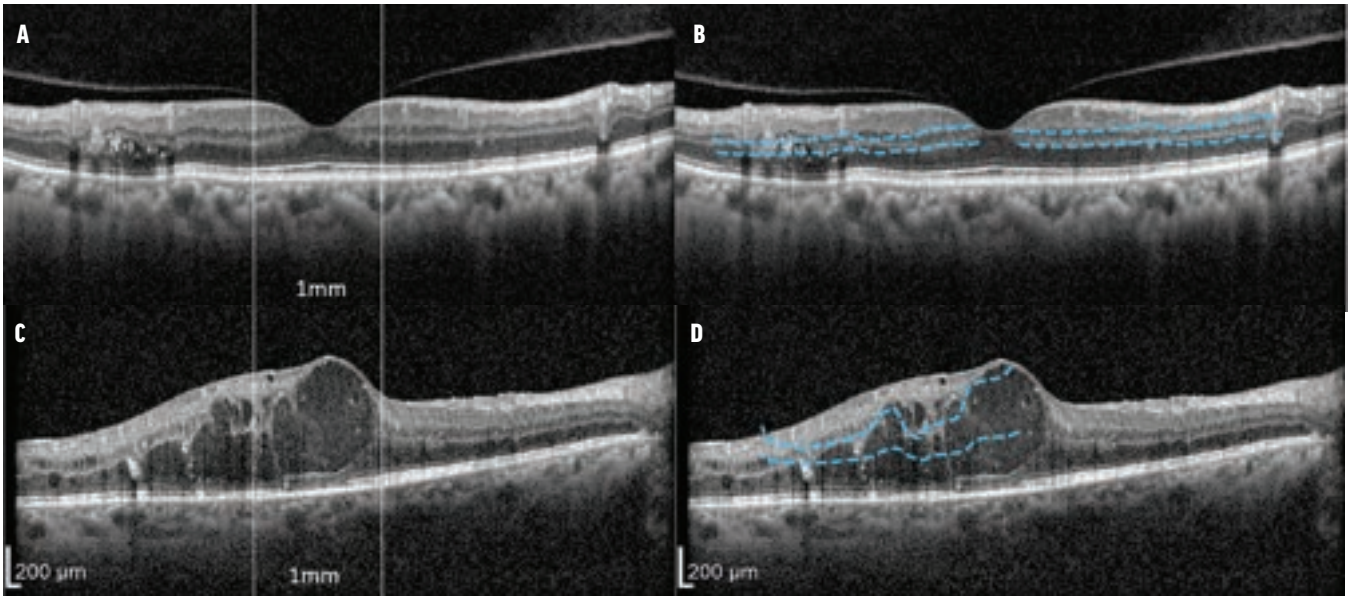

Figure 1. DRIL is evaluated within 1 mm centered on the fovea. In this SD-OCT image of the eye of a 58-year-old man (A), the boundaries of the inner nuclear layer are clearly identified (B, blue lines). Swept-source OCT imaging of the eye of a 61-year-old man (C) shows that the boundaries of the inner nuclear layer cannot be identified clearly (D, blue lines).

and Eraslan et al, patients lacking DRIL at baseline experienced significantly better visual outcomes, while those with existing DRIL saw minimal or no improvement in visual acuity.[6,7] This pattern suggests that DRIL may indicate structural damage to the retina that, once established, could limit the efficacy of DME treatment options.

ASSOCIATION WITH OTHER RETINAL BIOMARKERS

Within these studies, DRIL often appeared alongside other structural and functional abnormalities in the retina. Several studies reported a connection between DRIL and increased retinal thickness, the presence of intraretinal cysts, and reduced vessel density in the superficial capillary plexus (SCP) and deep capillary plexus (DCP).[4] These concomitant factors suggest that DRIL may be part of a broader set of pathological changes in the retinal microstructure. Cennamo et al, for example, found that DRIL was associated with lower vessel density in both the SCP and DCP, suggesting that retinal ischemia and reduced blood flow may contribute to DRIL formation and progression.[8]

Furthermore, DRIL was frequently associated with disruptions in other retinal layers, such as the external limiting membrane (ELM) and ellipsoid zone (EZ). The presence of DRIL alongside ELM and EZ disruptions was found to significantly worsen visual outcomes, as noted by Das et al and Lee et al.[4-9] These disruptions likely reflect damage to essential cellular structures within the retina, including the photoreceptor and bipolar cells, which are critical for transmitting visual information. Consequently, DRIL may serve as an indicator not only of visual acuity loss but also of broader structural deterioration within the retina.

TREATMENT IMPLICATIONS

Our review also examined the effect of DME treatments on DRIL and visual outcomes. Although anti-VEGF injections and corticosteroids have been shown to reduce retinal swelling and, in some cases, improve visual acuity, Sun et al and Zur et al reported their limited effect on reversing DRIL.[4-8] This suggests that once DRIL is established, it may represent irreversible retinal damage, making early detection crucial to managing DME more effectively.

Patients with lower baseline levels of DRIL were more likely to experience visual improvement with treatment; thus, identifying DRIL early could help tailor treatment. Additionally, the presence of DRIL could inform clinicians about the potential limits of visual recovery in patients with advanced DME, supporting realistic patient expectations and guiding decisions on treatment intensity and frequency.

POTENTIAL FOR PERSONALIZED MEDICINE AND AI

As a noninvasive and reproducible SD-OCT measurement, DRIL is a promising biomarker for clinical practice, especially as a predictor of visual outcomes in DME. Given its strong association with poor visual acuity and limited recovery potential, DRIL could become a valuable tool in personalized treatment planning for DR patients. By assessing DRIL early in DME, clinicians could potentially identify patients who are less likely to respond favorably to standard treatments, allowing for more customized and proactive care.[5]

Furthermore, DRIL holds potential for integration into AI and machine learning models that analyze retinal imaging data. DRIL could serve as a key data point for algorithms designed to predict DME progression and treatment

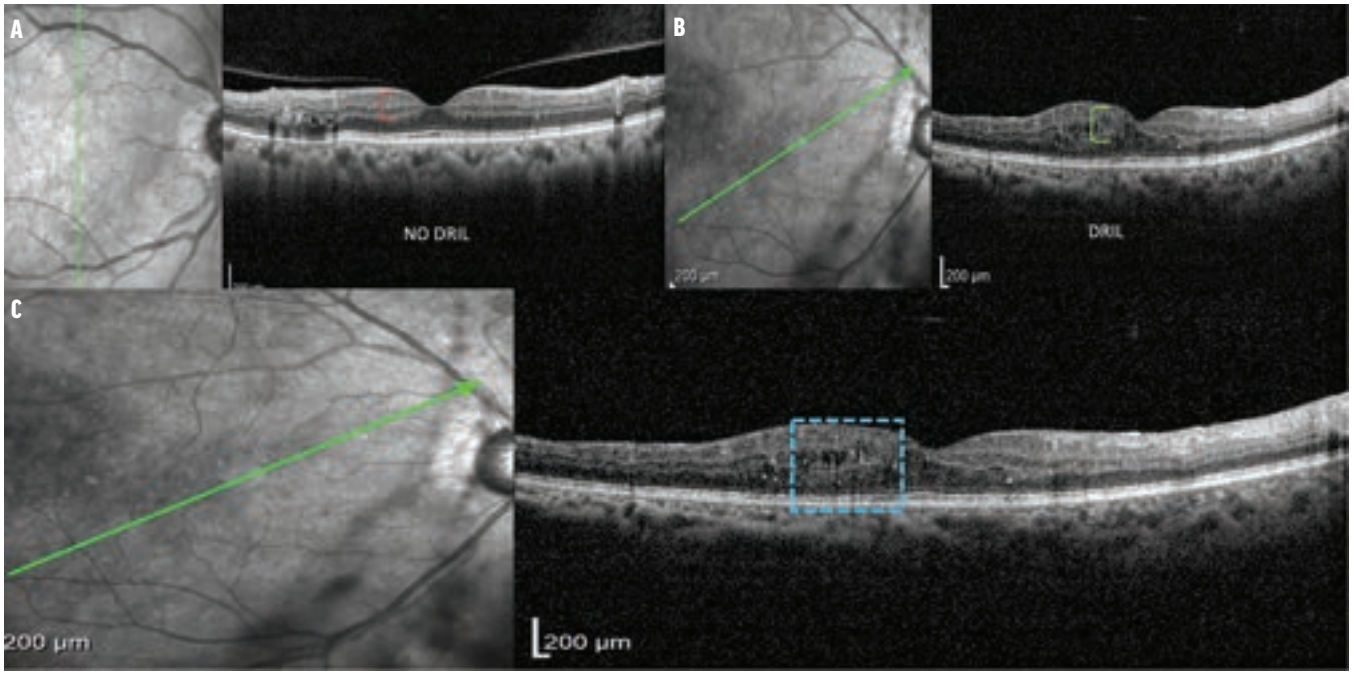

Figure 2. The red bracket in this OCT image shows no DRIL (A). In another OCT, the green bracket (B) and blue rectangle (C) show the lack of definition between the ganglion cell layer, inner plexiform layer, and outer plexiform layer.

response. Standardizing DRIL assessments across OCT devices and enhancing the accuracy of AI-driven interpretations could further improve its clinical utility, reducing variability and improving DME diagnosis and monitoring.[5]

USING DRIL IN YOUR PRACTICE

These findings underscore DRIL's role as a biomarker for assessing visual outcomes in DME patients. Its correlation with poorer baseline visual acuity, limited improvement potential, and association with other retinal pathologies position DRIL as a useful tool for guiding treatment decisions. Early detection and monitoring of DRIL could facilitate more effective, individualized treatment strategies, potentially slowing DME progression.

While further research is needed to clarify the underlying mechanisms of DRIL and standardize its measurement across devices, these findings support DRIL's integration into clinical practice and future AI-driven diagnostic platforms for DR. ■

1. Varma R, Bressler NM, Doan QV, et al. Prevalence of and risk factors for diabetic macular edema in the United States. *JAMA Ophthalmol*. 2014;132(11):1334-1340.
2. Sun JK, Lin MM, Lammer J, et al. Disorganization of the retinal inner layers as a predictor of visual acuity in eyes with center-involved diabetic macular edema. *JAMA Ophthalmol*. 2014;132(11):1309-1316.
3. Soliman AZ, Radwan SH, Prager SG, et al. Spectral domain optical coherence tomography parameters associated with visual acuity in patients with resolved center-involved diabetic macular edema. *Invest Ophthalmol Vis Sci*. 2017; 53(14):1338.
4. Das R, Spence G, Hogg RE, Stevenson M, Chakravarthy U. Disorganization of inner retina and outer retinal morphology in diabetic macular edema. *JAMA Ophthalmol*. 2018;136(2):202-208.
5. Di-Luciano A, Lam WC, Velasque L, et al. Disorganization of the inner retinal layers in diabetic macular edema: systematic review. *Rev Bras Oftalmol*. 2022;81:e0027
6. Radwan SH, Soliman AZ, Tokarev J, Zhang L, van Kuijk FJ, Koozekanani DD. Association of disorganization of retinal inner layers with vision after resolution of center-involved diabetic macular edema. *JAMA Ophthalmol*. 2015;133(7):820-825.
7. Eraslan S, Yıldırım Ö, Dursun Ö, Dinç E, Orekici Temel G. Relationship between final visual acuity and optical coherence tomography findings in patients with diabetic macular edema undergoing anti-VEGF therapy. *Turk J Ophthalmol*. 2020;50(3):163-168.
8 .Cennamo G, Montorio D, Fossataro F, Fossataro C, Tranfa F. Evaluation of vessel density in disorganization of retinal inner layers after resolved diabetic macular edema using optical coherence tomography angiography. *PLoS One*. 2021;16(1):e0244789.
9. Lee H, Kang KE, Chung H, Kim HC. Three-dimensional analysis of morphologic changes and visual outcomes in diabetic macular edema. *Jpn J Ophthalmol*. 2019;63(3):234-242.

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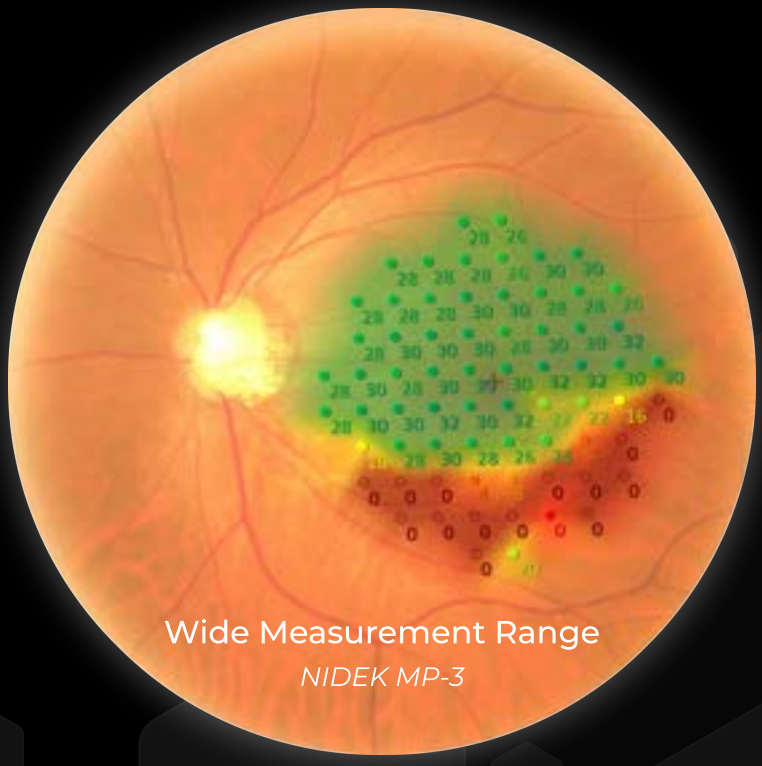

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OCT SPOTLIGHT: CHARACTERIZING GA DEVELOPMENT AND PROGRESSION


New imaging biomarkers are helping clinicians better identify and track geographic atrophy.

By Giuseppe Querques, MD, PhD, and Serena Fragiotta, MD, PhD

Geographic atrophy (GA) is characterized by the complete loss of photoreceptors, retinal pigment epithelium (RPE), and choriocapillaris. This condition profoundly affects the quality of life of patients and their families.[1-3]

Although fundus autofluorescence has historically been regarded as the standard imaging modality for GA assessment and progression, OCT has gained increasing importance.[4-7] OCT surpasses the 2D en face visualization provided by fundus autofluorescence and color fundus photography, offering both 2D and 3D high-resolution imaging. OCT B-scans deliver a cross-sectional view of the retina, enabling precise visualization of the retinal layers and the choroid.[8] This technology allows the identification of early biomarkers of GA development and precursor lesions of atrophy, precise delineation of atrophic lesion borders, assessment of the severity of cellular loss, and detection of nascent neovascular lesions that may further complicate atrophy.[6,9-17]

NOVEL OCT BIOMARKERS

These advantages have expanded the use of OCT for evaluating GA, driving the development of a consensus OCT definition for atrophy. This OCT definition, termed *complete outer retina and RPE atrophy*, characterizes atrophy as a region of photoreceptor degeneration and RPE disruption, accompanied by underlying choroidal hypertransmission measuring at least 250 µm in diameter.[7]

Recent studies have focused on developing predictive models using OCT to estimate GA progression. Several biomarkers have been implicated in GA prediction and prognosis, including reticular pseudodrusen, hyperreflective

AT A GLANCE

- Several biomarkers have been implicated in geographic atrophy (GA) prediction and prognosis, including reticular pseudodrusen, hyperreflective foci, thickness loss of specific retinal bands, drusen volume, and hyporeflective cores within drusen.
- However, current biomarkers do not fully account for the high variability observed in the progression of atrophic lesions.
- The authors have developed a predictive model based on the phenotypic elementary lesions of intermediate AMD associated with GA.

foci, the thickness loss of specific retinal bands (outer nuclear layer, outer retinal bands, RPE plus inner/outer segments of photoreceptors), drusen volume (> 0.03 mm^3), and hyporeflective cores within drusen.[13,18-21] Among factors involved in GA lesion expansion, the choriocapillaris impairment assessed on OCT angiography (OCTA) was demonstrated to be greater at the front of lesion expansion, with a direct correlation between choriocapillaris flow deficits and growth rate.[16,22] Choroidal vascularity index has also demonstrated a strict association with the GA growth rate, further corroborating the undeniable role of choroidal microvasculature.[23]

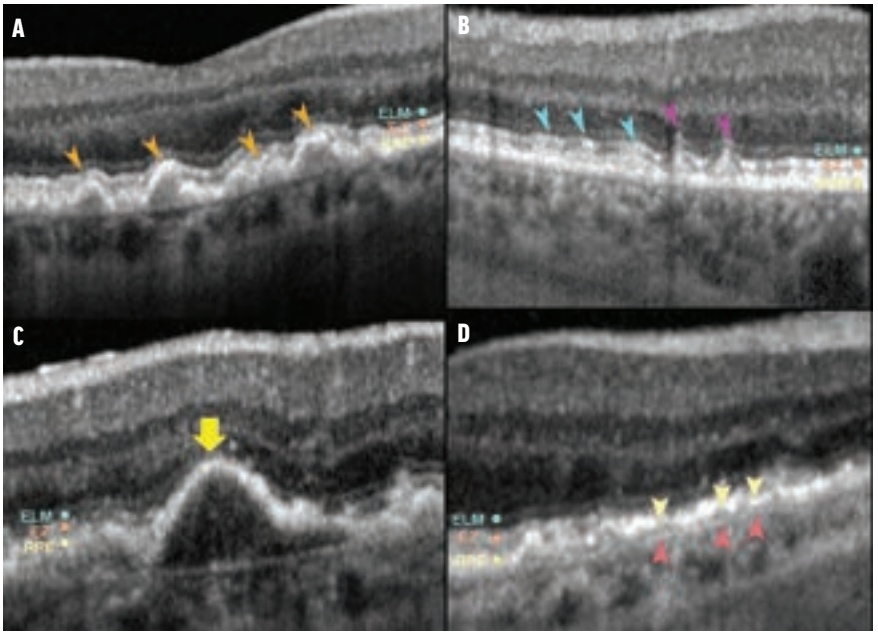

Figure 1. Phenotypic elementary lesions seen in iAMD. Drusen (A, arrowheads) can be appreciated as RPE+basal lamina elevations measuring > 125 µm. Reticular pseudodrusen or subretinal drusenoid deposits appear as subretinal flat hyperreflective deposits (B, blue arrowheads) or conical well-defined deposits (purple arrowheads). Drusenoid pigment epithelium detachment is defined as an RPE mound elevation measuring at least 350 mm in the horizontal diameter (C, arrow). DLS appears as a thin hyporeflective separation between RPE+basal lamina (D, yellow arrowheads) and Bruch membrane (red arrowheads).

DIGGING DEEPER INTO THE OCT

These biomarkers underscore the potential of OCT in identifying early indicators of GA susceptibility and progression. However, they do not fully account for the high variability observed in the progression of atrophic lesions. To address this, our group recently developed a predictive model based on the phenotypic elementary lesions of intermediate AMD (iAMD) associated with GA development and progression (Figure 1). These lesions were represented by drusen, reticular pseudodrusen or subretinal drusenoid deposits, drusenoid pigment epithelium detachment, and the presence of an avascular thin double-layer sign (DLS).[14]

The presence of a thin hyporeflective band between the RPE, its basal lamina, and Bruch membrane, without evidence of a neovascular signal on OCTA, represents the OCT signature for thick basal lamina deposits (BLamD), as recently confirmed by histopathology.[24] However, this signature needs to be distinguished from neovascular DLS, which is characterized by a greater vertical thickness and a multilaminar reflective interior, indicative of neovascular tissue (Figure 2). An accurate distinction between these two entities was performed using OCTA in our series. The identification of a DLS signature for thick BLamD represented the primary baseline predictor of GA progression. Moreover, eyes with DLS presented a faster development of atrophy (1.26 years vs 2.15 years for controls) and larger lesion size at different points compared with controls.[14]

The association between thick BLamD and rapidly evolving GA is further corroborated by previous studies that demonstrate an obvious RPE-basal lamina-Bruch membrane splitting on OCT B-scan in aggressive forms of GA, such as the diffuse-trickling phenotype and extensive macular atrophy with pseudodrusen-like appearance.[25,26] Possible pathogenic explanations for the more aggressive behavior observed in eyes with thick BLamD included the disrupted metabolic support, increased oxidative stress, and chronic inflammation. Specifically, thick and continuous BLamD create a physical separation between the RPE and choriocapillaris, impairing nutrient and oxygen exchange, which results in RPE ischemia and dysfunction.[27] Another possible mechanism resides in the retention of lipoproteins and other macromolecules within the thickened BLamD, leading to a prolonged exposure to these substances, thereby increasing oxidative stress and chronic inflammation.[28]

WATCH FOR A THIN DLS

Thick BLamD, identifiable on OCT as a thin DLS, should be recognized as a critical prognostic predictor in eyes with AMD, leading to earlier development of atrophic lesions and a faster progression rate. Expanding the phenotypic characterization of OCT predictors can help explain the variability in GA progression and support the development of more accurate predictive models and deep-learning algorithms to aid clinical decision making and advance the management of dry AMD. While OCT is increasingly recognized as a critical imaging modality for studying GA, its full potential and implications should be better emphasized, particularly within future clinical trials and GA management. ■

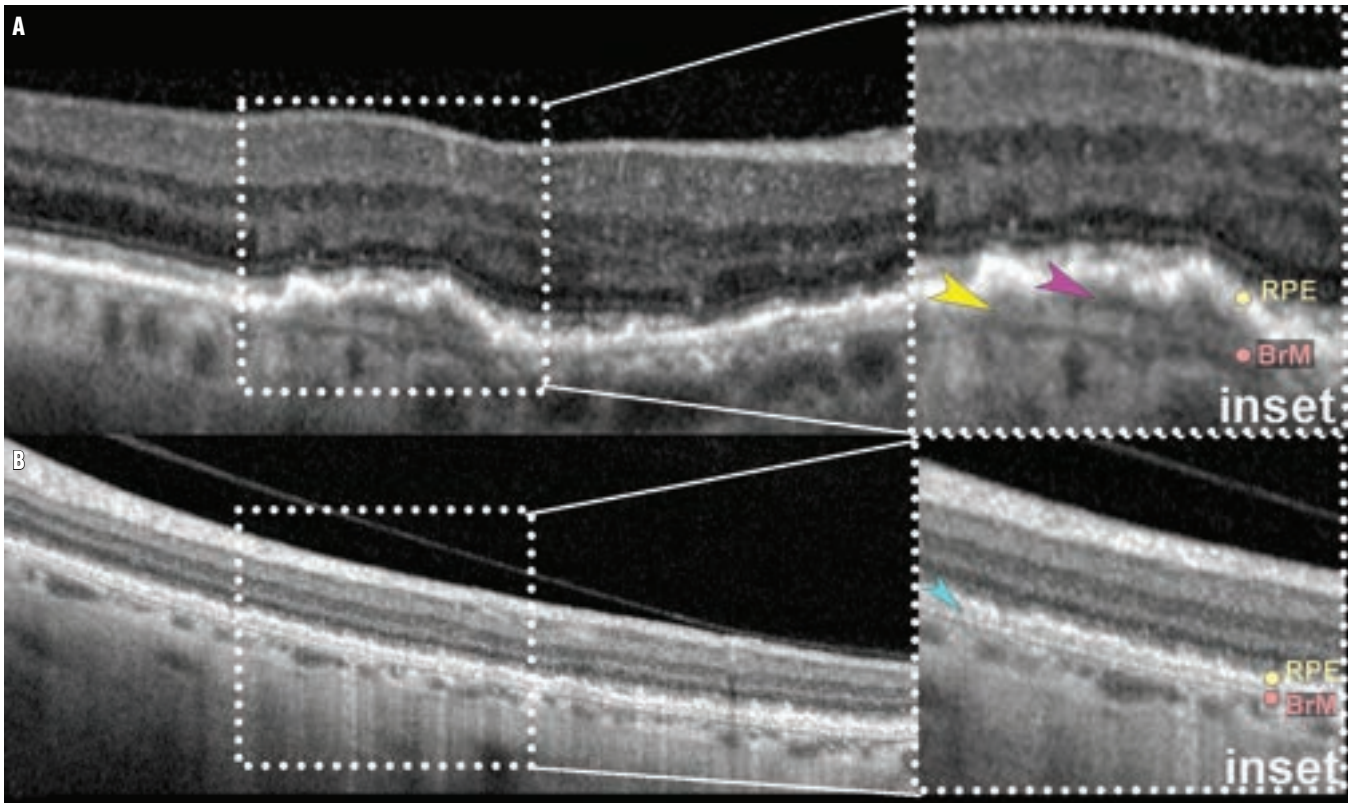

Figure 2. A thick DLS presents an interior multilayered reflectivity (A, hypo: purple arrowhead; midreflective: yellow arrowhead) that can reflect the presence of a neovascular tissue. A thin DLS demonstrates a single hyporeflective band between the RPE and Bruch membrane (B).

1. Sarks JP, Sarks SH, Killingsworth MC. Evolution of geographic atrophy of the retinal pigment epithelium. *Eye (Lond)*. 1988;2(Pt 5):552-577.
2. Li M, Huisingh C, Messinger J, et al. Histology of geographic atrophy secondary to age-related macular degeneration: A Multilayer Approach. *Retina*. 2018;38(10):1937-1953.
3. Querques G, Amblard JC, Andrao A, et al. Expert consensus on geographic atrophy in the EU: a call for urgent policy action. *Ophthalmol Ther*. 2024;13(4):867-881.
4. Holz FG, Bindewald-Wittich A, Fleckenstein M, et al. Progression of geographic atrophy and impact of fundus autofluorescence patterns in age-related macular degeneration. *Am J Ophthalmol*. 2007;143(3):463-472.
5. Holz FG, Sadda SR, Staurenghi G, et al. Imaging protocols in clinical studies in advanced age-related macular degeneration: recommendations from classification of atrophy consensus meetings. *Ophthalmology*. 2017;124(4):464-478.
6. Guymer RH, Rosenfeld PJ, Curcio CA, et al. Incomplete retinal pigment epithelial and outer retinal atrophy in age-related macular degeneration: classification of atrophy meeting report 4. *Ophthalmology*. 2020;127(3):394-409.
7. Sadda SR, Guymer R, Holz FG, et al. Consensus definition for atrophy associated with age-related macular degeneration on OCT: classification of atrophy report 3. *Ophthalmology*. 2018;125(4):537-48.
8. Sadda SR, Chakravarthy U, Birch DG, et al. Clinical endpoints for the study of geographic atrophy secondary to age-related macular degeneration. *Retina*. 2016;36(10):1806-1822.
9. Sacconi R, Sarraf D, Sadda SR, et al. Nascent geographic atrophy as a predictor of type 3 macular neovascularization development. *Ophthalmol Retina*. 2023;7(7):586-592.
10. Schaal KB, Gregori G, Rosenfeld PJ. En face optical coherence tomography imaging for the detection of nascent geographic atrophy. *Am J Ophthalmol*. 2017;174:145-154.
11. Shi Y, Yang J, Feuer W, et al. Persistent hypertransmission defects on en face oct imaging as a stand-alone precursor for the future formation of geographic atrophy. *Ophthalmol Retina*. 2021;5(12):1214-1225.
12. Wu Z, Ayton LN, Luu CD, Guymer RH. Microperimetry of nascent geographic atrophy in age-related macular degeneration. *Invest Ophthalmol Vis Sci*. 2014;56(1):115-121.
13. Schmidt-Erfurth U, Waldstein SM, Klimscha S, et al. Prediction of individual disease conversion in early AMD using artificial intelligence. *Invest Ophthalmol Vis Sci*. 2018;59(8):3199-3208.
14. Fragiotta S, Dysli C, Parravano M, et al. Phenotypic characterization of predictors for development and progression of geographic atrophy using optical coherence tomography. *Retina*. 2024;44(7):1232-1241.
15. Querques G, Capuano V, Frascio P, et al. Wedge-shaped subretinal hyporeflectivity in geographic atrophy. *Retina*. 2015;35(9):1735-1742.
16. Sacconi R, Corbelli E, Borrelli E, et al. Choriocapillaris flow impairment could predict the enlargement of geographic atrophy lesion. *Br J Ophthalmol*. 2021;105(1):97-102.
17. Dolz-Marco R, Balaratnasingam C, Messinger JD, et al. The border of macular atrophy in age-related macular degeneration: a clinicopathologic correlation. *Am J Ophthalmol*. 2018;193:166-177.
18. Nassisi M, Lei J, Abdelfattah NS, et al. OCT risk factors for development of late age-related macular degeneration in the fellow eyes of patients enrolled in the HARBOR study. *Ophthalmology*. 2019;126(12):1667-1674.
19. Lei J, Balasubramanian S, Abdelfattah NS, et al. Proposal of a simple optical coherence tomography-based scoring system for progression of age-related macular degeneration. *Graefes Arch Clin Exp Ophthalmol*. 2017;255(8):1551-1558.
20. Vogl WD, Bogunovic H, Waldstein SM, et al. Spatio-temporal alterations in retinal and choroidal layers in the progression of age-related macular degeneration (AMD) in optical coherence tomography. *Sci Rep*. 2021;11(1):5743.
21. Agrón E, Domalpally A, Cukras CA, et al. Reticular pseudodrusen: the third macular risk feature for progression to late age-related macular degeneration: age-related eye disease study 2 report 30. *Ophthalmology*. 2022;129(10):1107-1119.
22. Nassisi M, Baghdasaryan E, Borrelli E, et al. Choriocapillaris flow impairment surrounding geographic atrophy correlates with disease progression. *PLoS One*. 2019;14(2):e0212563.
23. Sacconi R, Battista M, Borrelli E, et al. Choroidal vascularity index is associated with geographic atrophy progression. *Retina*. 2022;42(2):381-387.
24. Sura AA, Chen L, Messinger JD, et al. Measuring the contributions of basal laminar deposit and bruch's membrane in age-related macular degeneration. *Invest Ophthalmol Vis Sci*. 2020;61(13):19.
25. Fleckenstein M, Schmitz-Valckenberg S, Lindner M, et al. The "diffuse-trickling" fundus autofluorescence phenotype in geographic atrophy. *Invest Ophthalmol Vis Sci*. 2014;55(5):2911-2920.
26. Fragiotta S, Parravano M, Sacconi R, et al. A common finding in foveal-sparing extensive macular atrophy with pseudodrusen implicates basal laminar deposits. *Retina*. 2022;42(7):1319-1329.
27. Sarks S, Cherepanoff S, Killingsworth M, Sarks J. Relationship of basal laminar deposit and membranous debris to the clinical presentation of early age-related macular degeneration. *Invest Ophthalmol Vis Sci*. 2007;48(3):968-977.
28. Curcio CA. Soft drusen in age-related macular degeneration: biology and targeting via the oil spill strategies. *Invest Ophthalmol Vis Sci*. 2018;59(4):AMD160-AMD81.

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DIAGNOSTIC PEARLS FOR MACTEL TYPE 2



Multimodal imaging—and a few adjunct tools—can help catch this rare disease early.

By Elham Sadeghi, MD; Ramesh Venkatesh, MD; and Jay Chhablani, MD

Macular telangiectasia type 2 (MacTel) is typically diagnosed late after patients experience progressive vision loss and may be misdiagnosed as more prevalent conditions such as diabetic macular edema.[1] MacTel is primarily due to Müller cell neurodegeneration, leading to retinal thinning and subsequent vascular changes.[2]

With a novel treatment now available for patients with MacTel, clinicians must be prepared to diagnose these patients as early as possible. Here, we discuss imaging pearls when a patient presents with findings suspicious for MacTel.

THE INITIAL DIAGNOSIS

In the initial stages of MacTel, patients often present with mild or no visual symptoms, and BCVA may remain normal, even as the disease progresses. During disease progression, subtle signs may begin to manifest, such as blurred or distorted central vision, difficulty reading, loss of contrast sensitivity, or paracentral scotoma.[3]

A dilated fundus examination may reveal a normal retina in early states of the disease, but with progression, signs such as a dull or whitening foveal reflex, loss of retinal transparency, faint superficial retinal crystals, and telangiectatic vessels more pronounced temporally than nasally may become evident.[4-6]

OCT often serves as the first diagnostic imaging modality for suspected MacTel cases; a characteristic OCT finding is temporal enlargement and widening of the foveal pit, which leads to asymmetry and thinning on the temporal side of the fovea, resulting in an irregular foveal contour.[6] Additional early signs detectable via OCT include disruptions in the external limiting membrane and ellipsoid zone (EZ), early alterations in the EZ/cone outer segment tips and photoreceptor outer segment reflectivity, hyperreflectivity of the inner retinal layers, superficial hyperreflective retinal dots, and focal outer lamellar defects at the fovea (Figure 1). As MacTel progresses, more pronounced changes can be observed, such as cavity formation, retinal thinning, pigment migration, internal limiting membrane drapes, development of a neovascular membrane, and eventual retinal atrophy.[6-8]

AT A GLANCE

- OCT often serves as the first diagnostic tool for suspected macular telangiectasia (MacTel) type 2 cases; a characteristic finding is temporal enlargement and widening of the foveal pit.
- OCT angiography may help visualize dilated perifoveal retinal vessels, particularly within the deep capillary plexus.
- Other imaging modalities that can assist clinicians in diagnosing early-stage MacTel include confocal blue reflectance imaging, microperimetry, macular pigment optical density mapping, and multifocal electroretinography.

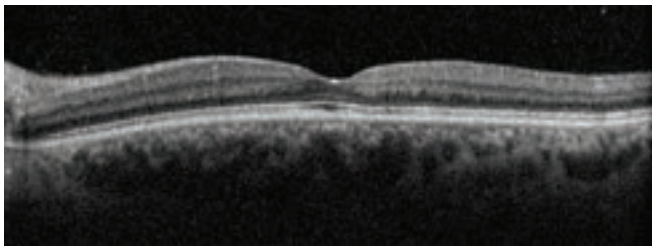

Figure 1. An OCT scan in early MacTel shows a widening of the foveal pit, inner retina layer hyperreflectivity, and minimal EZ/cone outer segment tips alteration.

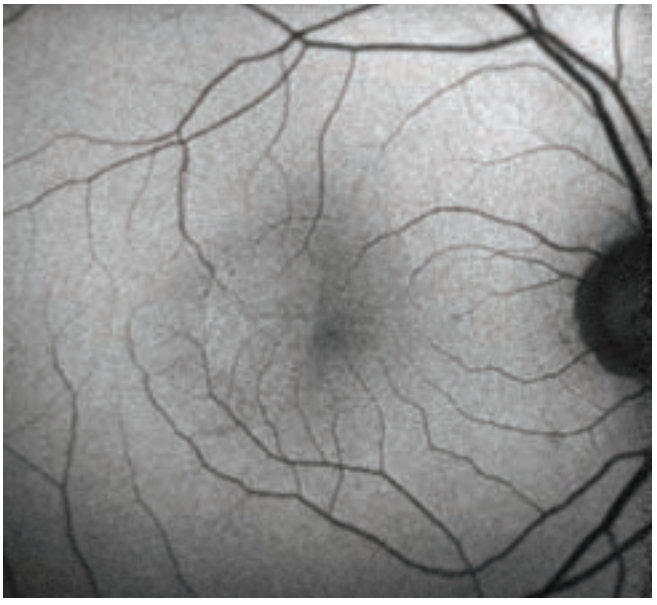

Figure 2. Loss of temporal perifoveal hypoautofluorescence in early MacTel.

Fundus autofluorescence (FAF) can be a valuable tool for revealing a mild loss of hyperautofluorescence in the fovea due to loss of lutein and zeaxanthin (Figure 2). However, light exposure during retinal examinations may cause bleaching of lutein and zeaxanthin in the unaffected retina, leading to a loss of contrast between the normal retina and MacTel lesions, potentially resulting in missed alterations. Therefore, clinicians should consider acquiring an FAF image after a 30-minute recovery.[9]

OCT angiography (OCTA) may help visualize dilated perifoveal retinal vessels, particularly within the deep capillary plexus. It highlights vessel distortion in the foveal avascular zone and the presence of branching vessels, which can be detected in the early stages of the disease.[6] In early-stage MacTel, capillary density may remain normal or decrease in the superficial and deep capillary plexuses, confusing the condition with early diabetic retinopathy.[10,11] Additionally, microcysts are sometimes observed in the ganglion cell and inner nuclear layers, corresponding to the small lacunae in both plexuses.[10] However, in cases of diagnostic uncertainty, fluorescein angiography (FA) can reveal abnormal vessels on the temporal side, displaying early and late perifoveal hyperfluorescence (Figure 3).[6,12]

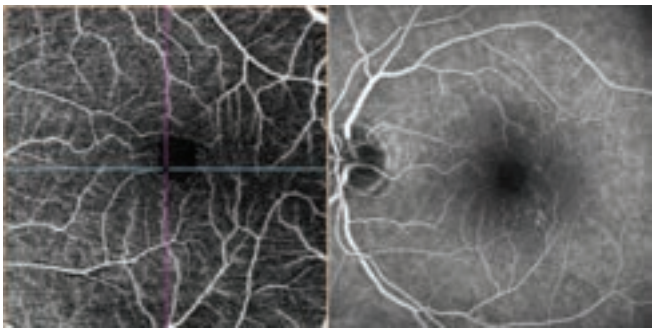

Figure 3. OCTA and FA in early MacTel exhibit faint vascular changes in the temporal side of the fovea and late-phase inferotemporal fluorescein leakage.

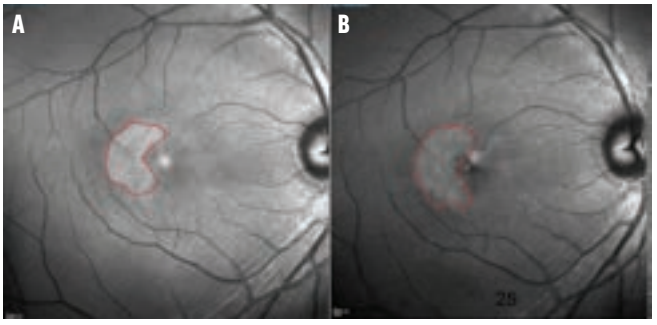

Figure 4. CBR in MacTel shows decreased central hyporeflectance after dark adaptation, as observed immediately after FAF (A) and 30 minutes later (B).

ADJUNCT IMAGING CONSIDERATIONS

Other diagnostic modalities that can assist in diagnosing early-stage MacTel, although not routinely used, include confocal blue reflectance (CBR) imaging, microperimetry, macular pigment optical density (MPOD) mapping, and multifocal electroretinography (mfERG).

CBR shows a well-defined, generally oval parafoveal area of increased reflectance, corresponding to the area of transparency loss. This area is slightly larger than the region of leakage observed in late-phase angiography. Clinicians should perform this imaging after dark adaptation, as the intensity tends to fade with continuous light exposure (Figure 4).[13]

Microperimetry often reveals functional scotomas correlated with areas of EZ loss rather than visual acuity loss. Although a valuable tool, it is subject to lower-session variability and relies on patient compliance.[14] Additionally, MPOD mapping demonstrates decreased macular pigment levels centrally in early stages of MacTel.[15]

The changes in mfERG responses indicate inner retinal layer dysfunction due to abnormal Müller cell function and are correlated with visual acuity. This modality could be used to objectively assess macular function in MacTel.[16-18]

BE SUSPICIOUS

Early-stage diagnosis has become increasingly critical with the advent of MacTel therapy. It should be suspected in asymptomatic or minimally symptomatic patients with unexplained visual problems. Multimodal imaging facilitates

early diagnosis. OCT identifies foveal pit widening, slight temporal foveal thinning, and subtle retinal layer alterations. Loss of hypoautofluorescence on FAF can detect subtle retinal changes. OCTA detects mild perifoveal vessel dilation, and FA effectively identifies vessel changes and leakage. Other modalities such as microperimetry, MPOD mapping, and CBR imaging hold significant potential for the early detection and follow-up of MacTel. ■

1. Macular telangiectasia (MacTel). Macular Society. Accessed March 11, 2025. www.macularsociety.org/macular-disease/macular-conditions/mac-tel
2. Venkatesh R, Mangla R, Handa A, et al. Vitreomacular interface abnormalities in type 2 macular telangiectasia (MacTel). *Graefes Arch Clin Exp Ophthalmol*. 2024;262(5):1455-1463.
3. Heeren TFC, Chew EY, Clemons T, et al. Macular telangiectasia type 2: visual acuity, disease end stage, and the MacTel area: MacTel Project Report Number 8. *Ophthalmology*. 2020;127(11):1539-1548.
4. Sallo FB, Leung I, Zeimer M, et al. Abnormal retinal reflectivity to short-wavelength light in type 2 idiopathic macular telangiectasia. *Retina*. 2018;38:S79-S88.
5. Pauleikhoff D, Pauleikhoff L, Chew EY. Imaging endpoints for clinical trials in MacTel type 2. *Eye*. 2022;36(2):284-293.
6. Venkatesh R, Reddy NG, Mishra P, et al. The preproliferative stage in type 2 macular telangiectasia (MacTel type 2). *Graefes Arch Clin Exp Ophthalmol*. 2022;260(1):121-132.
7. Mirescu AE, Balta F, Barac R, et al. High-resolution imaging in macular telangiectasia type 2: case series and literature review. *Diagnostics*. 2024;14(13):1351.
8. Chew EY, Peto T, Clemons TE, et al. Macular telangiectasia type 2: a classification system using multimodal imaging; MacTel Project Report Number 10. *Ophthalmol Sci*. 2023;3(2):100261.
9. Sharief S, Venkatesh R, Mangla R, Chhablani J. Timing of ocular examination and retinal imaging for the diagnosis of type 2 macular telangiectasia (MacTel). *Euro J Ophthalmol*. 2023;33(6):NP79-NP81.
10. Au S, Su C. Optical coherence tomography angiography for macular telangiectasia type 2. *J Ophthalmol Adv Res*. 2022;3(1):1-10.
11. Mastropasqua R, Toto L, Mastropasqua A, et al. Foveal avascular zone area and parafoveal vessel density measurements in different stages of diabetic retinopathy by optical coherence tomography angiography. *Int J Ophthalmol*. 2017;10(10):1545.
12. Solberg Y, Dysli C, Wolf S, Zinkernagel MS. Fluorescence lifetime patterns in macular telangiectasia type 2. *Retina*. 2020;40(1):99-108.
13. Venkatesh R, Pereira A, Bavaharan B, et al. Relevance of multicolor imaging in type 2 macular telangiectasia. *J Curr Ophthalmol*. 2020;32(4):375-380.
14. Schmitz-Valckenberg S, Ong EL, Rubin GS, et al. Structural and functional changes over time in MacTel patients. *Retina*. 2009;29(9):1314-1320.
15. Srinivasan R, Teussink MM, Sloan KR, Bharat RPK, Narayanan R, Raman R. Distribution of macular pigments in macular telangiectasia type 2 and correlation with optical coherence tomography characteristics and visual acuity. *BMC Ophthalmol*. 2022;22(1):264.
16. Okada M, Robson AG, Egan CA, et al. Electrophysiological characterization of macular telangiectasia type 2 and structure–function correlation. *Retina*. 2018;38:S33-S42.
17. Goel N, Kumari A, Kumar S, Mehta A. Multifocal electroretinography in patients with macular telangiectasia type 2. *Documenta Ophthalmologica*. 2020;141(1):15-21.
18. Ledolter AA, Ristl R, Palmowski-Wolfe AM, et al. Macular telangiectasia type 2: multimodal assessment of retinal function and microstructure. *Acta Ophthalmologica*. 2022;100(6):e1240-e1252.

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(Continued from page 20)

EXPANDING APPLICATIONS

While the proposed terms are tailored to RVD, ongoing efforts aim to extend this nomenclature to other conditions, such as AMD and macular dystrophies, so the framework can be used irrespective of underlying disease. As OCTA technology evolves, new terms may be integrated into the framework to address emerging imaging challenges.

HURDLES TO OVERCOME

Advancing OCTA technology brings new complexities, such as distinguishing between retinal layers like the choriocapillaris and inner choroid. Future refinements will address these challenges, ensuring that the nomenclature remains robust and adaptable to technological innovations.

The new framework provides clinicians with an accurate, flexible, and adaptive system to describe OCTA images using standardized terminology. The consensus nomenclature marks a critical step forward in retinal imaging. By providing a standardized language for describing OCTA findings, it empowers clinicians and researchers to fully leverage this transformative technology, while paving the way for expanded applications in other retinal conditions. ■

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1. Munk MR, Kashani AH, Tadayoni R, et al. Standardization of OCT angiography nomenclature in retinal vascular diseases: first survey results. *Ophthalmol Retina*. 2021;5(10):981-990.
2. Munk MR, Kashani AH, Tadayoni R, et al. Recommendations for OCT angiography reporting in retinal vascular disease: a Delphi approach by international experts. *Ophthalmol Retina*. 2022;6(9):753-61.
3. Munk MR, Turgut F, Faes L, et al; on behalf of the International Retinal Imaging Society Research Group. Standardization of optical coherence tomography angiography nomenclature in retinal vascular diseases: consensus-based recommendations *Ophthalmol Retina*. 2025 Jan 31:S2468-6530(25)00047-8.

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RISING STARS IN RETINA

Retina Today

YoungMD>Connect

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

Jacob S. Heng, MD, PhD

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

I first got interested in retina during my ophthalmology elective in medical school. I learned how to use the direct ophthalmoscope and was instantly captivated by the beauty of the retina. I had also taken a year out of medical school to pursue oncology research because I was interested in targeted therapy. I was awed by how retina specialists were routinely injecting anti-VEGF agents—a form of targeted therapy—directly into the eye and pioneering the first gene therapy trials in the eye, as well as the first human induced pluripotent stem cell trial. From then on, my experiences with the retina and retina specialists further solidified my conviction to become a clinician-scientist in retina.

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

I had the privilege of completing my PhD thesis work with Jeremy Nathans, MD, PhD, who made seminal contributions in retinal biology. Dr. Nathans nurtured me as a scientist and remains one of my esteemed advisors to this day.

During my PhD, James T. Handa, MD, took me under his wing, and I shadowed him in his clinic and OR. It was refreshing to return as a fellow in the Retina division that Dr. Handa leads. During fellowship, Akrit Sodhi, MD, PhD, has mentored me on research projects and as an attending. Peter A. Campochiaro, MD, taught me how to perform my first vitreoretinal surgeries and continues to provide invaluable mentorship. I also have had the privilege of learning from all the exceptional attendings at Wilmer Eye Institute.

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

The most memorable experience of my fellowship thus far was my first scleral buckle. Up to that point, I had only repaired retinal detachments with vitrectomy and gas/oil tamponade. We located and applied cryopexy to the breaks, sutured the buckle, and performed external drainage without any intraocular gas injection. I remember seeing the retina completely flat the next day and thought, "Wow, this works!"

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

I am hoping to establish a career as a clinician-scientist combining clinical practice as a vitreoretinal surgeon with an NIH-funded research laboratory. My practice will likely consist of patients with general medical and/or surgical retinal conditions. My primary research interest is the regulation of the blood-retina barrier, which is relevant to almost all retinal conditions.

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

I highly recommend retina as a specialty; it is an amazing and versatile field with many wonderful people. I also recommend learning all aspects of a comprehensive eye examination, not just a retina examination. Retina specialists see a diverse range of patients who often have multiple eye problems; therefore, being able to perform a comprehensive examination is key to sound management.

If you decide that retina is for you, get involved as early as possible by going to meetings, presenting abstracts, and publishing papers. ■

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IMAGING CONSIDERATIONS IN PATHOLOGIC MYOPIA

How to capture lacquer cracks, macular neovascularization, posterior staphylomas, and more.

By Alexandra Miere, MD, PhD

Pathologic myopia is a leading cause of blindness worldwide and is particularly prevalent in East Asia.[1,2] The global rise in myopia prevalence is expected to subsequently lead to an increase in pathologic myopia cases in the coming years.[3] With the advent of high-resolution imaging techniques, progression of pathologic myopia and subsequent pathological changes (eg, myopic maculopathy) are easily visible, making early intervention possible.

MYOPIC MACULOPATHY DEFINED

Based on long-term data on myopic lesion progression, experts have proposed an international classification of myopic maculopathy.[4] The META-PM Study Group identified four categories, starting with no macular lesions (Category 0) and progressing to a tessellated fundus (Category 1), diffuse chorioretinal atrophy (Category 2), patchy chorioretinal atrophy (Category 3), and, finally, macular atrophy (Category 4). According to this classification, pathologic myopia corresponds to eyes that have lesions in Category 2 or more. Additionally, "plus" lesions correspond to lesions that develop independent of the above progression pattern and consist of lacquer cracks, myopic macular neovascularization (MNV), and Fuchs spots.[4]

Myopic MNV, typically type 2, develops in approximately 10% of eyes with pathologic myopia and is a major cause of visual impairment, while lacquer cracks occur in 4.2% to 15.7% of eyes with pathologic myopia.[4] However, myopic MNVs must be distinguished from simple hemorrhages associated with lacquer cracks, as the treatment and subsequent follow-up differ; while myopic MNVs are treated with anti-VEGF injections, simple hemorrhages on lacquer cracks regress spontaneously and only require monitoring.

AT A GLANCE

- Lacquer cracks facilitate myopic macular neovascularization (MNV) formation through the Bruch membrane opening.
- When myopic MNV occurs, the lesion is visible on conventional invasive imaging, such as fluorescein angiography, and noninvasive imaging techniques, such as OCT and OCT angiography.
- AI has demonstrated strong capabilities in detecting pathologic myopia and identifying myopia-related complications using different imaging modalities.

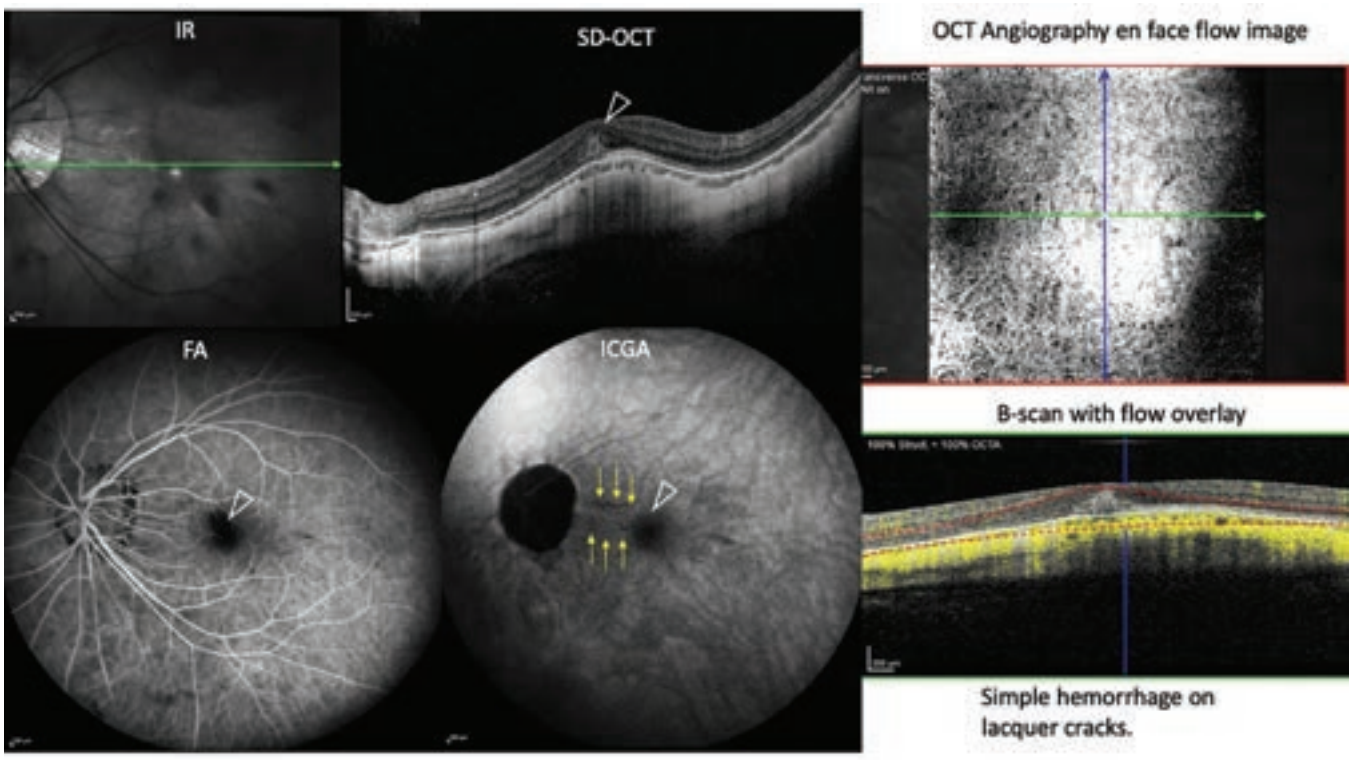

Figure 1. Multimodal imaging of an eye with pathologic myopia and lacquer cracks with a simple hemorrhage. On spectral-domain OCT, the simple hemorrhage complicating lacquer cracks corresponds to an ill-defined subretinal hyperreflectivity (white arrowhead). On FA and ICGA, the simple hemorrhage generates masking (white arrowheads). Note the visualization of lacquer cracks on late ICGA (yellow arrows). OCTA (right panels) confirms the absence of flow, indicating the absence of a neovascular lesion.

IMAGING FINDINGS IN PATHOLOGIC MYOPIA

Lacquer cracks are thought to be breaks within Bruch membrane often accompanied by a simple hemorrhage secondary to traction associated with the increase in axial length of myopic eyes.[5] These lacquer cracks facilitate MNV formation through the Bruch membrane opening, especially when they are newly generated.[6]

In addition to fundus examination and fundus photography, fluorescein angiography (FA) and ICG angiography (ICGA) are useful for detecting lacquer cracks (Figure 1).[4,7] When a simple hemorrhage occurs in conjunction with lacquer cracks, the differential diagnosis of myopic MNV can be difficult. While simple hemorrhage associated with lacquer cracks creates a masking effect on FA, making the distinction from myopic MNVs clear, FA is an invasive examination that's not performed at every visit. On the widely used, noninvasive OCT, the presence of a hyperreflective lesion in the subretinal space in the case of both myopic MNVs and simple hemorrhage on lacquer cracks may be confusing.

OCT angiography (OCTA) is particularly helpful in these cases, allowing clinicians to confirm the absence of flow and, thus, the absence of a neovascular lesion.

When myopic MNV occurs, the lesion is visible on both conventional invasive imaging, such as FA, and noninvasive imaging, such as OCT and OCTA (Figure 2). Of note, the presence of patchy atrophy and lacquer cracks are well-known risk factors for the development of myopic MNV.[4,8]

Although OCTA is helpful in detecting myopic MNV,[9] acquisition can be challenging due to the long axial length and posterior staphyloma, leading to segmentation errors. When FA and OCT imaging are unclear, custom OCTA segmentation, corresponding to the anatomic location of the neovascular lesion, can clarify the presence or absence of myopic MNV (Figure 3).

Another challenge with myopic MNV is the detection of exudation, which is more subtle than in other types of MNV.[10] Clinicians can look for the presence of a gray subretinal hyperreflective exudation and an increase in choroidal thickness (Figure 4). In these cases, a single anti-VEGF injection can address subretinal hyperreflective exudation and decrease the choroidal thickness underneath the myopic MNV.

After studying the morphologic relationship between myopic MNV activity and focal choroidal thickness changes in pathologic myopia during anti-VEGF therapy, researchers found that focal choroidal thickness increased significantly underneath the myopic MNV when exudative signs were present (or preceding exudation in some cases), followed by a significant decrease after anti-VEGF therapy.[11]

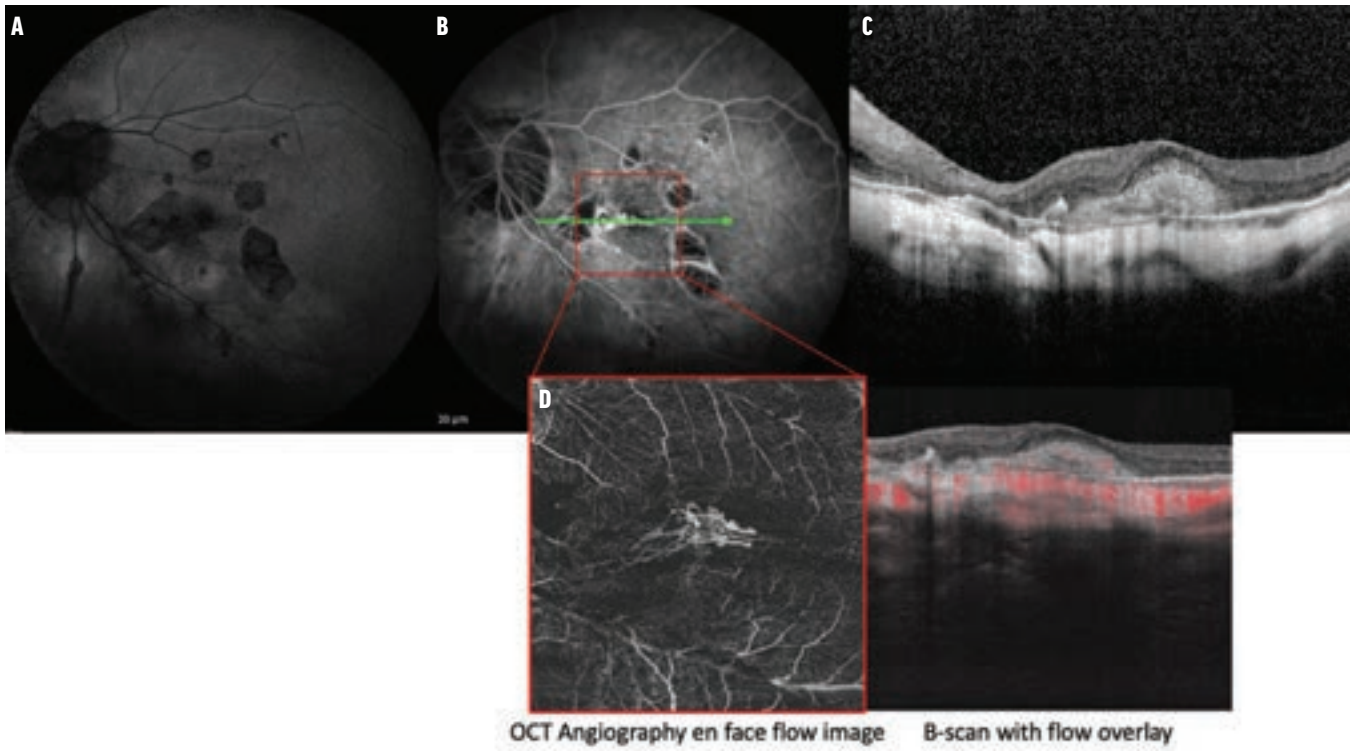

Figure 2. Multimodal imaging reveals myopic MNV at the edge of patchy atrophy, as seen on fundus autofluorescence imaging (A). FA shows leakage (B), and spectral-domain OCT shows a hyperreflective subretinal lesion with fuzzy borders (C). OCTA confirms the presence of a myopic MNV (D).

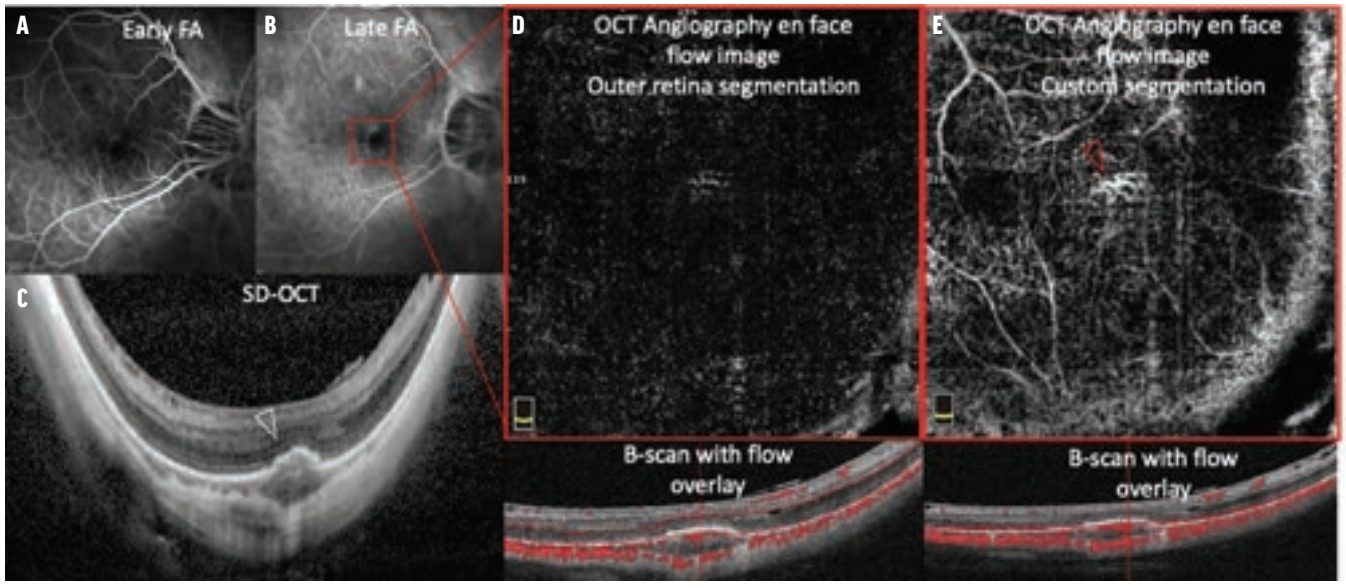

Figure 3. Multimodal imaging of myopic MNV requiring a custom segmentation on OCTA for visualization. FA (A and B) shows a doubtful hyperfluorescence corresponding to the allegedly neovascular lesion seen on spectral-domain OCT (C, white arrowhead) in this highly myopic patient. The 3 mm x 3 mm OCTA with the automatic outer retinal segmentation is not helpful to detect the neovascularization (D). The myopic MNV is easily visible on the custom OCTA segmentation (E, red arrowhead).

CHECK THE PERIPHERY

Beyond the detection of macular lesions in eyes with pathologic myopia, clinicians must remember the large spectrum of peripheral lesions in highly myopic eyes. Ultra-widefield color fundus photography and ultra-widefield OCT have been widely used in recent years for the detailed assessment of posterior staphylomas, a hallmark of pathologic myopia. While the initial 1977 classification of posterior staphylomas identified 10 different types of posterior staphyloma on fundus examination,[12] there was no

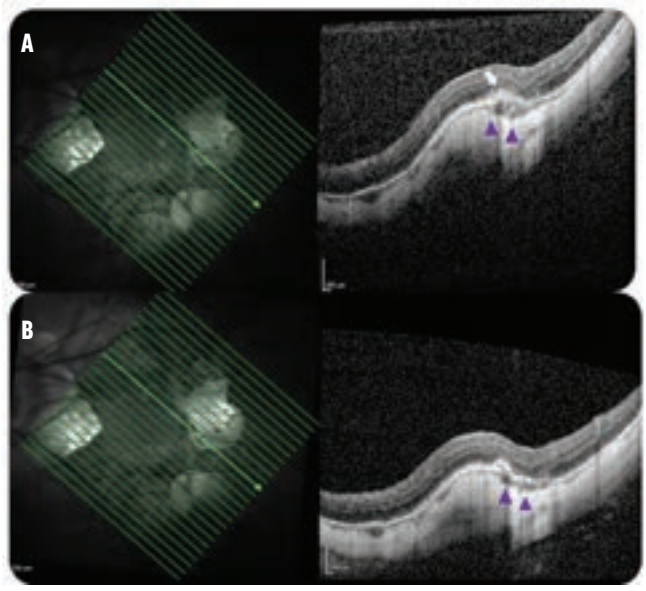

Figure 4. Exudative recurrence, represented by gray subretinal hyperreflective exudation, of a previously treated myopic MNV (A, white arrow) with an increase in choroidal thickness (purple arrowheads). After one anti-VEGF injection (B), OCT shows regression of the subretinal hyperreflective exudation, as well as a decreased choroidal thickness.

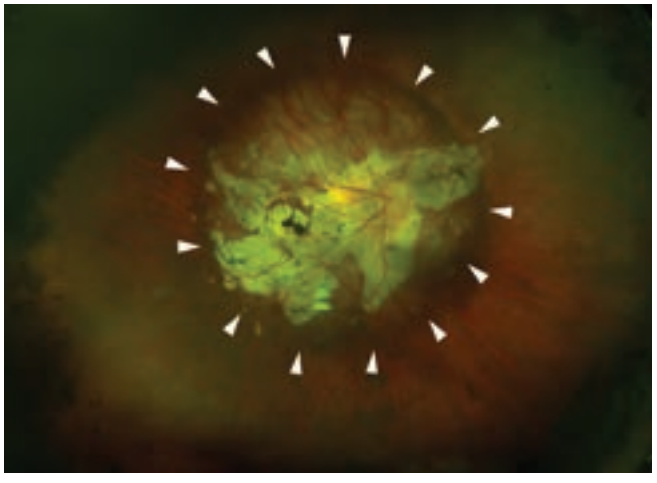

Figure 5. Ultra-widefield color fundus photography shows a wide macular staphyloma with pigmentary changes at the staphyloma edges (arrows) and large areas of patchy atrophy.

universally accepted definition. More recently, Ohno-Matsui et al used ultra-widefield color fundus photography and 3D MRI to visualize the entire extent of posterior staphylomas and critical features of staphyloma edges, such as gradual choroidal thinning from both sides, scleral inward protrusion, and posterior scleral displacement (Figures 5 and 6).[13]

In addition to the features highlighted above, multimodal retinal imaging continues to clarify our understanding of dome-shaped macula and different types of schisis.[14-18]

MORE TO EXPLORE

AI has demonstrated strong capabilities in detecting pathologic myopia and identifying myopia-related

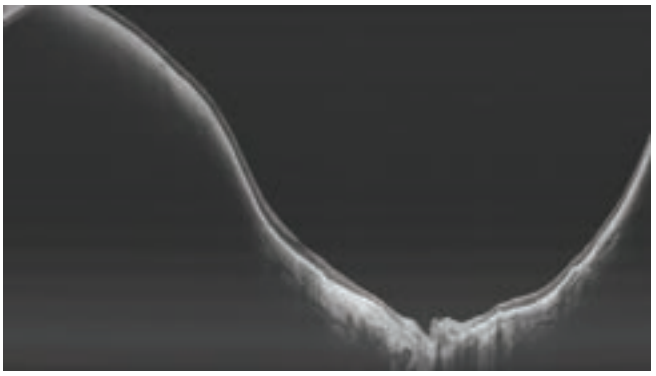

Figure 6. Ultra-widefield OCT of a highly myopic eye reveals a posterior staphyloma. Note the changes at the edge of the staphyloma with a gradual decrease of the choroid and the scleral protrusion.

complications using different imaging modalities.[19,20] These imaging advances, combined with AI analysis, hold the potential to enhance disease monitoring and guide treatment in a world where myopia is a global epidemic.[21] ■

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1. Wong TY, Ferreira A, Hughes R, et al. Epidemiology and disease burden of pathologic myopia and myopic choroidal neovascularization: an evidence based systematic review. *Am J Ophthalmol*. 2014;157:9-25.e12.
2. Wong YL, Saw SM. Epidemiology of pathologic myopia in Asia and worldwide. *Asia Pac J Ophthalmol (Phila)*. 2016;5(6):394-402.
3. Holden BA, Fricke TR, Wilson DA, et al. Global prevalence of myopia and high myopia and temporal trends from 2000 through 2050. *Ophthalmology*. 2016;123(5):1036-1042.
4. Ohno-Matsui K, Kawasaki R, Jonas JB, et al. International photographic classification and grading system for myopic maculopathy. *Am J Ophthalmol*. 2015;159(5):877-883.e7.
5. Klein RM, Curtin BJ. Lacquer crack lesions in pathologic myopia. *Am J Ophthalmol* 1975;79(3):386-392.
6. Xu X, Fang Y, Uramoto K, et al. Clinical features of lacquer cracks in eyes with pathologic myopia. *Retina*. 2019;39(7):1265-1277.
7. Ohno-Matsui K, Morishima N, Ito M, Tokoro T. Indocyanine green angiographic findings of lacquer cracks in pathologic myopia. *Jpn J Ophthalmol*. 1998;42(4):293-299.
8. Ohno-Matsui K, Yoshida T, Futagami S, et al. Patchy atrophy and lacquer cracks predispose to the development of choroidal neovascularisation in pathological myopia. *Br J Ophthalmol*. 2003;87(5):570-573.
9. Bruyère E, Miere A, Cohen SY, et al. Neovascularization secondary to high myopia imaged by optical coherence tomography angiography. *Retina*. 2017;37(11):2095-2101.
10. Bruyère E, Caillaux V, Cohen SY, et al. Spectral-domain optical coherence tomography of subretinal hyperreflective exudation in myopic choroidal neovascularization. *Am J Ophthalmol*. 2015;160(4):749-58.e1.
11. Amoroso F, Miere A, El Matri K, et al. Focal choroidal thickness hemodynamics as a sign of macular neovascularization activity in pathologic myopia. *Retina*. 2022;42(12):2321-2325.
12. Curtin BJ. The posterior staphyloma of pathologic myopia. *Trans Am Ophthalmol Soc*. 1977;75:67-86.
13. Ohno-Matsui K, Alkabes M, Salinas C, et al. Features of posterior staphylomas analyzed in wide-field fundus images in patients with unilateral and bilateral pathologic myopia. *Retina*. 2017;37(3):477-486.
14. Jain M, Gopal L, Padhi TR. Dome-shaped maculopathy: a review. *Eye (Lond)*. 2021;35(9):2458-2467.
15. Lee GW, Kim JH, Kang SW, et al. Structural profile of dome-shaped macula in degenerative myopia and its association with macular disorders. *BMC Ophthalmol*. 2020;20:202.
16. Ohno-Matsui K, Igarashi-Yokoi T, Azuma T, et al. Polarization-sensitive OCT imaging of scleral abnormalities in eyes with high myopia and dome-shaped macula. *JAMA Ophthalmol*. 2024;142(4):310-319.
17. Faghihi H, Hajizadeh F, Riazi-Esfahani M. Optical coherence tomographic findings in highly myopic eyes. *J Ophthalmic Vis Res*. 2010;5(2):110-121.
18. Al-Sheikh M, Govetto A, Phasukkijwatana N, et al. Myopic macular schisis: Insights into distinct morphological subtypes and novel biomechanical hypothesis. *Eur J Ophthalmol*. 2023;33(6):2250-2258.
19. Tang J, Yuan M, Tian K, et al. An artificial-intelligence-based automated grading and lesions segmentation system for myopic maculopathy based on color fundus photographs. *Transl Vis Sci Technol*. 2022;11(6):16.
20. Crincoli E, Ferrara S, Miere A, et al. Correlation between AI-measured lacquer cracks extension and development of myopic choroidal neovascularization. *Eye (Lond)*. 2023;37(14):2963-2968.
21. Ng DSC, Lai TYY. Insights into the global epidemic of high myopia and its implications. *JAMA Ophthalmol*. 2022;140(2):123-124.

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NO supplemental treatment needed to maintain anesthesia*†[1]

NO serious adverse events with an established safety profile[2]

NO patients reported experiencing pain[2]

*In the clinical trial, no patient undergoing routine cataract surgery receiving IHEEZO required supplemental treatment to maintain anesthesia; this was not the case for patients receiving tetracaine. Supplemental treatment was defined as general anesthesia, intraoperative systemic analgesia, or local anesthesia. Though supplemental administration was not required by any patient in the clinical trial, IHEEZO may be reapplied as needed to maintain anesthesia.[1,2]

†Sufficient anesthesia with IHEEZO lasted an average of 21.5 minutes in the clinical trial, while mean total surgical time was 13.9 minutes.[2]

APPROVED USE

IHEEZO is indicated for ocular surface anesthesia.

IMPORTANT SAFETY INFORMATION

IHEEZO is contraindicated in patients with a history of hypersensitivity to any component of this preparation.

IHEEZO should not be injected or intraocularly administered.

Patients should not touch the eye for at least 10 to 20 minutes after using anesthetic as accidental injuries can occur due to insensitivity of the eye.

Prolonged use of a topical ocular anesthetic may produce permanent corneal opacification and ulceration with accompanying visual loss.

Do not touch the dropper tip to any surface as this may contaminate the gel.

IHEEZO is indicated for administration under the direct supervision of a healthcare provider. IHEEZO is not intended for patient self-administration.

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

You are encouraged to report suspected adverse reactions to the FDA. Visit **www.fda.gov/medwatch**, or call **1-800-FDA-1088**.

Please see Brief Summary of Full Prescribing Information for IHEEZO on adjacent page.

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References: 1. Iheezo. Prescribing information. Harrow IP, LLC; 2022. **2.** Data on File. Harrow IP, LLC; 2023.

IHEEZO™

(chloroprocaine HCl ophthalmic gel) 3%

BRIEF SUMMARY OF PRESCRIBING INFORMATION

1 INDICATIONS AND USAGE

IHEEZO™ (chloroprocaine hydrochloride ophthalmic gel) 3% is a preservative-free ester anesthetic indicated for ocular surface anesthesia.

4 CONTRAINDICATIONS

IHEEZO is contraindicated in patients with a history of hypersensitivity to any component of this preparation.

5 WARNINGS AND PRECAUTIONS

5.1 Not for Injection or Intraocular Administration

IHEEZO should not be injected or intraocularly administered.

5.2 Corneal Injury Due to Insensitivity

Patients should not touch the eye for at least 10 to 20 minutes after using anesthetic as accidental injuries can occur due to insensitivity of the eye.

5.3 Corneal Opacification

Prolonged use of a topical ocular anesthetic may produce permanent corneal opacification and ulceration with accompanying visual loss.

5.4 Risk of Contamination

Do not touch the dropper tip to any surface as this may contaminate the gel.

5.5 For Administration by Healthcare Provider

IHEEZO is indicated for administration under the direct supervision of a healthcare provider. IHEEZO is not intended for patient self-administration.

6 ADVERSE REACTIONS

6.1 Clinical Trials Experience

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

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

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

8 USE IN SPECIFIC POPULATIONS

8.1 Pregnancy

Risk Summary

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

8.2 Lactation

Risk Summary

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

8.4 Pediatric Use

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

8.5 Geriatric Use

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

12 CLINICAL PHARMACOLOGY

12.1 Mechanism of Action

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

12.3 Pharmacokinetics

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

Elimination

Metabolism

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

Excretion

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

13 NONCLINICAL TOXICOLOGY

13.1 Carcinogenesis, Mutagenesis, Impairment of Fertility

Carcinogenesis

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

Mutagenesis

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

Impairment of Fertility

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

14 CLINICAL STUDIES

14.1 Study 1 and Study 2

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

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

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

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

Efficacy results of Study 1

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

Efficacy results of Study 2

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

14.2 Study 3

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

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

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

17 PATIENT COUNSELING INFORMATION

Eye Care Precaution

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

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AN ATLAS OF MULTIMODAL IMAGING IN PEDIATRICS

These patients typically undergo examination under anesthesia for the best results.

By Manish Nagpal, MS, FRCS, FASRS; Anjana Mirajkar, MS; Anand Temkar, MS; Ankit Jain, DNB; Atul Reshamwala, MD; and Navneet Mehrotra, MBBS, DNB, FRF

Pediatric ocular examinations can be challenging due to limited patient cooperation. Examination under anesthesia or sedation is often conducted to simplify the process. Retinal imaging also helps clinicians better understand the anatomy, pathophysiology, diagnosis, and management of retinal disorders.

Devices such as the Retcam (Natus) are available to document cases in which a pediatric patient is in a lying down position under anesthesia. Here, we describe pediatric cases that used a standard scanning laser ophthalmoscopy (SLO)-based device, the Mirante (Nidek), as a screening tool for capturing 163° widefield multimodal images in the flying baby position.

CASE 1

A 2-year-old girl presented with dimness of vision with nystagmus in each eye for 9 months. Dilated fundus examination of each eye revealed peripheral pigmentary changes sparing the posterior pole (Figure 1), suggestive of salt and pepper retinopathy. OCT of each eye showed a maintained foveal contour. The patient was advised to undergo screening for toxoplasmosis, rubella cytomegalovirus, herpes simplex, and human immunodeficiency virus and vitamin A supplementation after consulting with her pediatrician.

CASE 2

A 2.5-year-old boy presented with squinting in the left eye since birth. Dilated fundus examination revealed a fibrovascular stalk in the left eye extending from the disc to the posterior capsule of the lens suggestive of persistent hyperplastic primary vitreous (Figure 2). OCT showed an altered foveal contour. Ultrasound of the left eye showed membranous echoes with low to moderate spikes and restricted movements suggestive of persistent hyperplastic

AT A GLANCE

- Pediatric patients undergoing examination under anesthesia can be imaged in the flying baby position.
- Scanning laser ophthalmoscopy can capture peripheral pigmentary changes, fibrovascular stalks, vitreous seeding, peripheral avascularity, and more.
- Ultrasound can be useful for detecting mass-like lesions associated with retinoblastoma and membranous echoes suggestive of persistent hyperplastic primary vitreous.

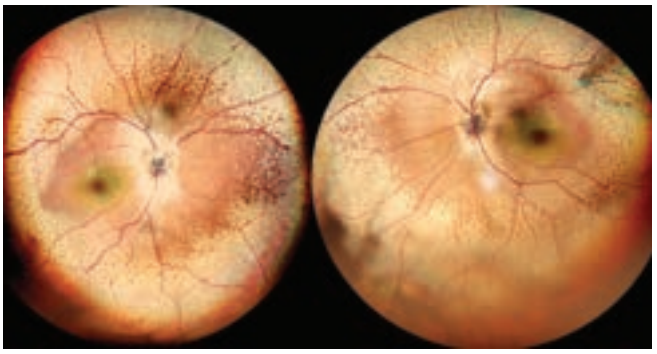

Figure 1. Widefield color imaging of each eye shows peripheral pigmentary changes sparing the posterior pole.

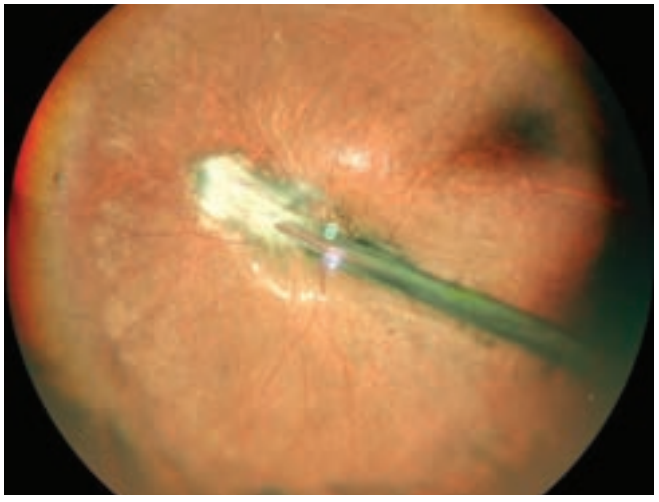

Figure 2. Widefield imaging of the left eye shows a fibrovascular stalk extending from the optic disc to the posterior capsule of the lens.

primary vitreous. The patient was advised to undergo refraction, use low vision aids, and follow up every 6 months.

CASE 3

A 5-year-old boy presented with dimness of vision in the left eye since birth. Dilated fundus examination revealed a large optic disc with glial tissue, straightening of the vessels, and pigmentation, suggestive of morning glory syndrome. OCT showed subretinal fluid suggestive of a retinal detachment associated with morning glory syndrome (Figure 3). No vitreoretinal intervention was recommended, and the patient was scheduled for follow up every 6 months.

CASE 4

A 2.5-year-old girl presented with dim vision and whitish reflex in the right eye for 2 months. Dilated fundus examination of the right eye revealed multiple whitish nodular masses with vitreous seeding, indicative of retinoblastoma (Figure 4). Ultrasound of the right eye revealed hyperechoic homogenous masses with high spikes and restricted movements suggestive of calcification associated with retinoblastoma. The patient underwent enucleation of the right eye.

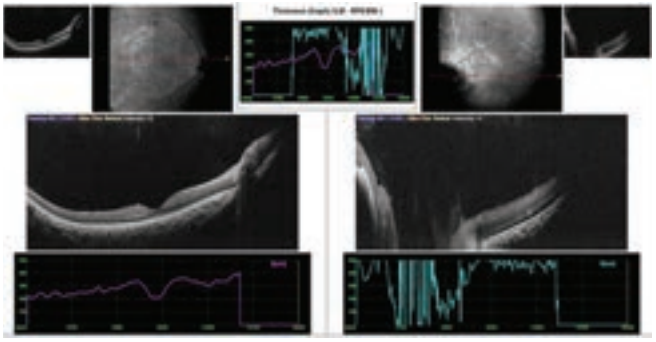

Figure 3. OCT of the left eye shows altered foveal contour with subretinal fluid suggestive of a retinal detachment associated with morning glory syndrome.

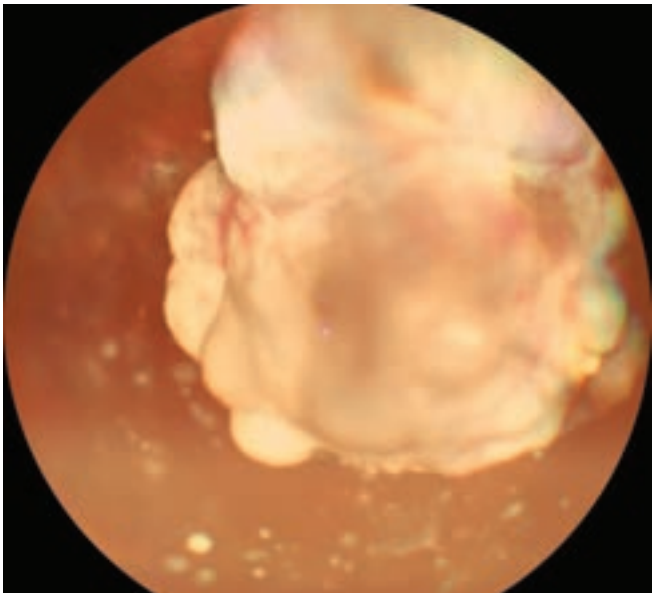

Figure 4. Widefield color imaging of the right eye shows multiple whitish nodular masses with vitreous seeding associated with retinoblastoma.

CASE 5

A 5-year-old boy presented with dimness of vision with squinting in the right eye for 1 year. Dilated fundus examination of the right eye revealed a falciform fold extending temporally from the disc with straightening of the vessels with peripheral avascularity (Figure 5). The left eye had flat traction temporally with straightening of the vessels with peripheral avascularity inferiorly. OCT of each eye showed altered foveal contour. No vitreoretinal intervention was recommended, and the patient was scheduled for follow up every 3 months.

CASE 6

A 6-year-old boy presented with outward deviation of the left eye and dimness of vision (more at night) in each eye since he was 2.5 years of age. BCVA was 6/60 OU. Dilated fundus examination of each eye revealed a granular fundus suggestive of heredomacular degeneration. OCT of each eye showed altered foveal contour with thinning. Fundus

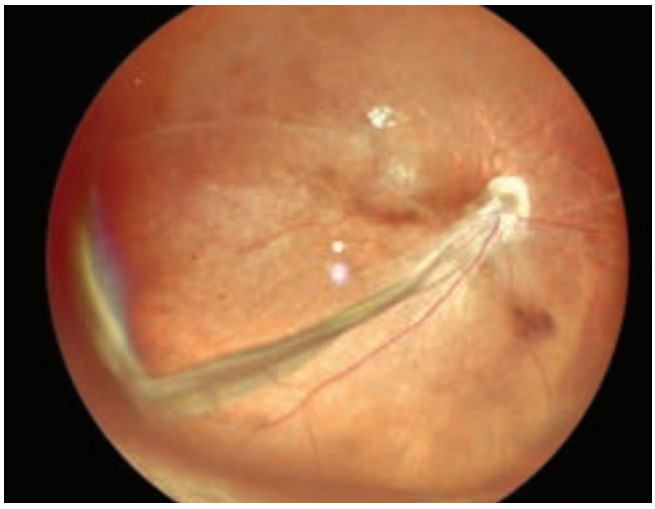

Figure 6. Widefield color imaging of the right eye reveals falciform extending temporally from the disc with straightening of the vessels with peripheral avascularity.

autofluorescence showed hypoautofluorescence with a ring of hyperautofluorescence in each eye, suggestive of heredomacular degeneration (Figure 6). The patient was advised to undergo pattern electroretinography and visual evoked potential testing but was lost to follow-up.

CASE 7

A 1.5-year-old boy, born prematurely at 7.5 month's gestation, presented with dimness of vision in each eye since birth. The patient had received anti-VEGF injections for stage 4 retinopathy of prematurity elsewhere. Dilated fundus examination of each eye showed fibrovascular proliferation at the disc with large areas of avascularization

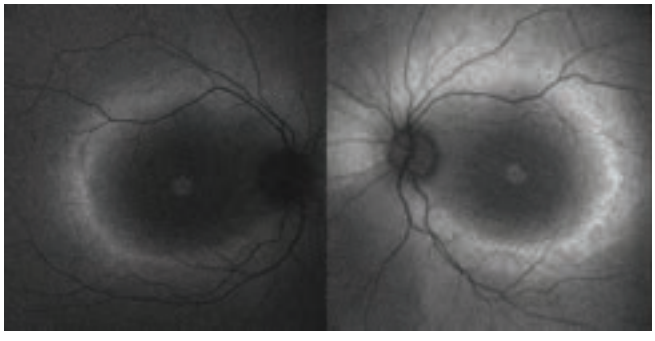

Figure 6. Fundus autofluorescence of each eye shows hypoautofluorescence with a ring of hyperautofluorescence, suggestive of heredomacular degeneration.

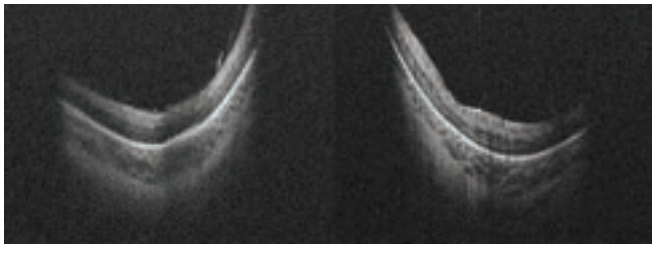

Figure 7. OCT of each eye shows an altered foveal contour.

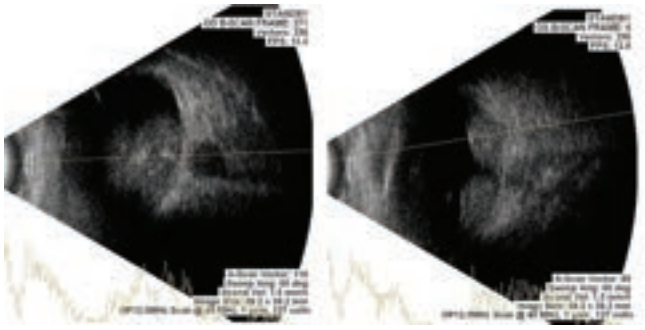

Figure 8. Ultrasound of each eye shows heterogenous mass-like lesions with moderate to high spikes, suggestive of calcification associated with retinoblastoma.

in the left eye. OCT of each eye showed an altered foveal contour (Figure 7). The patient underwent barrage laser treatment to the avascular zones.

CASE 8

A 9-month-old boy presented with leukocoria in each eye since he was 2 months of age. Dilated fundus examination of each eye revealed multiple white lesions at the posterior pole with venous tortuosity and prominence involving the disc and macula, likely suggesting retinoblastoma. Ultrasound of each eye showed heterogenous mass-like lesions with moderate to high spikes suggestive of calcification associated with retinoblastoma (Figure 8). The patient was referred to an ocular oncologist. ■

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THE ROLE OF ULTRASONOGRAPHY IN CHOROIDAL MELANOMA


Tumor shape, readily identified on ultrasound, may have significant prognostic value.

BY EUGENIA M. RAMOS-DÁVILA, MD, AND LAUREN A. DALVIN, MD

The diagnosis of uveal melanoma is primarily based on biomicroscopic examination and multimodal imaging, including ultrasonography.[1] A typical finding during fundoscopy is a pigmented, dome-shaped nodular mass beneath the retinal pigment epithelium. However, some patients present with atypical clinical features or smaller lesions, for which ultrasonography can help confirm the diagnosis.[2] B-scan ultrasonography can further reveal various tumor shapes, including the characteristic mushroom or collar-stud morphology, dome-shaped lesions, and, less frequently, multilobulated or minimally elevated tumors (Figure 1).[3]

In this article, we explain how ultrasonographic features of choroidal tumors, such as their shape, may provide valuable prognostic insights.

ULTRASOUND TECHNIQUES

When diagnosing choroidal tumors, two types of ultrasonography are available: A-mode using an 8-MHz probe and B-mode using a 10-MHz probe.[3] B-scan ultrasonography identifies choroidal melanoma as a homogeneous mass with a low acoustic profile (acoustic hollowness). Due to the higher reflectivity of the extraocular space compared with the tumor, extrascleral extension can be detected by areas of hyporeflectivity beyond the scleral boundary marked by echoes from the orbital tissues.[3] The B-scan can also visualize tumors as small as 1.5 mm in thickness.[2] As such, this imaging modality is particularly valuable for evaluating the classification criteria outlined by the American Joint Committee on Cancer (AJCC)—which is based on tumor size, ciliary body involvement, and extraocular extension—and for determining key prognostic indicators, such as tumor diameter.[4,5] Of note, a largest basal diameter exceeding 12 mm has been strongly associated with a worse prognosis.[6]

A-scan ultrasonography can reveal lesions with low-to-medium reflectivity and a gradual decrease in amplitude, which is attributed to the tumor's acoustically hollow nature, a feature referred to as a *positive angle kappa* (Figure 2).[2,7] However, this characteristic is observed in approximately half of all cases and may appear in other types of choroidal lesions, such as metastasis, hemangioma, or benign nevus.[7,8]

Techniques using higher frequencies of up to 50 MHz, such as ultrasound biomicroscopy, enhance the visualization of anterior uveal melanomas and allow the identification of ciliary body involvement, which, according to the AJCC, represents an important prognostic finding.[4] A statistically

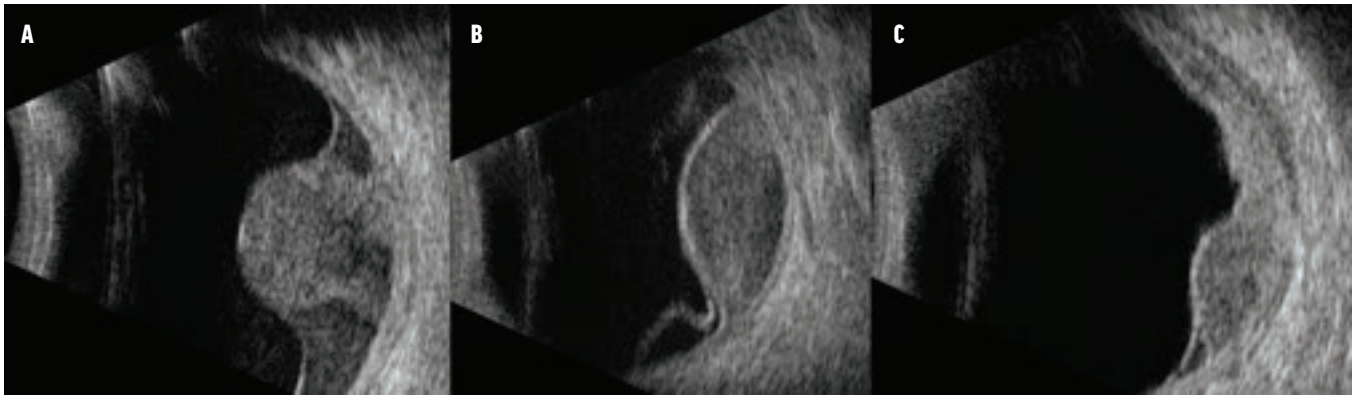

Figure 1. A mushroom-shaped tumor generally exhibits heterogeneous reflectivity characterized by acoustic hollowness at the tumor base and higher reflectivity toward the head (A). Note the distinguished homogeneous consistency of the dome-shaped choroidal lesion (B) and multilobulated melanoma (C).

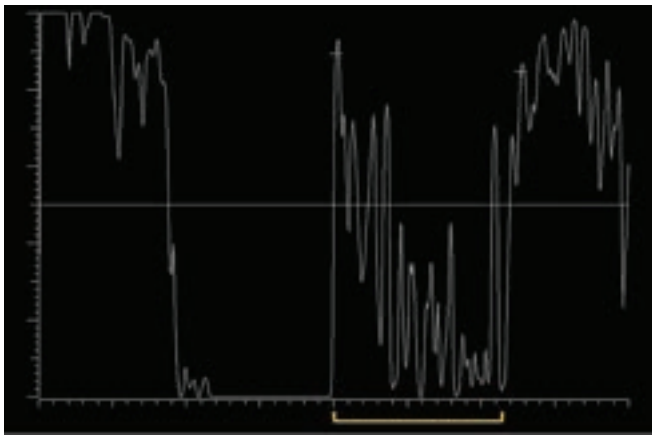

Figure 2. This A-scan ultrasound of a mushroom-shaped tumor illustrates a positive angle kappa, characterized by a gradual decrease in reflectivity from the tumor's head to its base (yellow bracket).

significant shorter metastasis-free survival has been observed in melanomas involving the ciliary body.[9]

IDENTIFYING TUMOR SHAPE

Studies have explored the relationship between tumor size, volume, and even regression patterns with molecular findings and treatment outcomes, but recent findings suggest tumor shape may represent a novel prognostic biomarker.[10-13] The Prospective Ocular Tumor Study evaluated clinical features and outcomes associated with different choroidal melanoma shapes and found that dome-shaped lesions were the most prevalent (72.4%), followed by mushroom-shaped (11.7%), multilobulated (8.3%), minimally elevated (7.5%), and diffuse (0.1%) forms.[13]

Choroidal melanomas have traditionally been characterized as lesions with low-to-medium reflectivity.[13] However, up to 23% of minimally elevated tumors exhibited high reflectivity patterns, a feature observed in only 1.2% of the other groups.[13] Additionally, mushroom-shaped melanomas demonstrated variations in internal reflectivity across their anatomy, with low reflectivity frequently seen at the base and high reflectivity at the apex.[13]

Mushroom-shaped and multilobulated tumors were commonly diagnosed at advanced stages, classified as stage IIB according to AJCC criteria (in 37% and 22% of cases, respectively). In contrast, dome-shaped and minimally elevated tumors were more frequently diagnosed at stage IA (in 44% and 51% of cases, respectively).[13] Multilobulated and minimally elevated melanomas often present diagnostic challenges, especially if they are partially or mainly amelanotic, as they can be mistaken for metastatic lesions.[14,15] Minimally elevated tumors tended to be located near the macula, which could explain the earlier detection.[13]

The majority of mushroom-shaped and multilobulated tumors presented with a basal diameter of at least 12 mm (73.9% and 84.7%, respectively), a significantly higher proportion compared with findings observed in dome-shaped (47%) and minimally elevated (35%) lesions. Moreover, mushroom-shaped lesions more frequently presented a thickness of at least 8 mm (49.6%) compared with the other groups (0% to 14%); consequently, a higher overall enucleation rate was reported in mushroom-shaped (40.3%) and multilobulated (23.5%) melanomas compared with other groups (7% to 11%).[13] Survival analyses estimated that at 36 months, approximately 40% of patients with mushroom-shaped tumors would have undergone enucleation compared with 14% of those with dome-shaped lesions.[13]

Notably, mortality and metastasis rates were significantly higher in the multilobulated group (34% and 35%, respectively) even compared with mushroom-shaped tumors (10.9% and 19.3%, respectively), which had similar mean tumor thickness and diameter. Survival calculations estimated that 32% of patients in the multilobulated group would have developed metastasis and 27% would have passed away at 36 months. These predictions were significantly higher than those calculated for other groups, in which metastasis estimations ranged from 2.6% to 20.9% and death rates from 5.3% to 8.6% at 36 months. Hazard ratios revealed a 2.08-fold increased risk of metastasis and a 2.38-fold higher risk of death for multilobulated melanomas compared with the other groups.[13] Importantly, these findings were confirmed in a multivariate analysis adjusted for tumor size; multilobulated melanomas remained an independent prognostic feature even after accounting for tumor dimensions.[13]

Molecular data available in 160 cases showed that a class 2 gene expression profile was more frequently associated with mushroom-shaped (31.9%) and multilobulated (14.1%) melanomas than with dome-shaped tumors (5%).[13]

GENES AND SHAPES

Tumors with faster growth rates typically harbor a more aggressive underlying genetic profile.[1,10,11,16] The reasons why tumors adopt specific shapes remain unknown but could share a similar molecular explanation.

The worse prognosis associated with multilobulated melanomas could be due to a delay in diagnosis or referral. Nonetheless, high genetic heterogeneity within multilobulated masses should also be carefully considered.[17,18] Heterogeneity seems to be more pronounced at the base of the tumor, suggesting biopsies be considered for each lobule.[17,18] This approach could offer a better understanding of the genetic landscape of multilobulated tumors and help avoid underestimating the risk of metastasis. Further studies are needed to outline the genetic profile across tumor shapes and gain a deeper understanding of the pathophysiology underlying the different morphologies.

(Continued on page 46)

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

FUNDAMENTALS OF ICD-10 CODING IN RETINA

Keep these in mind to avoid claim denials.

BY JOY WOODKE, COE, OCS, OCSR

Published in the ICD-10-CM are specific fundamental coding principles that ensure accurate claim submission and help clinicians and their office staff reduce claim denials. Here are a few rules that pertain to retina coding.

CODE TO THE HIGHEST LEVEL OF SPECIFICITY

Medicare and other payers require ICD-10 codes to be billed to the highest level of specificity. For example, Medicare Administrative Contractor Novitas states in its local coverage article A57804 that it is the physician's "responsibility to select codes carried out to the highest level of specificity and selected from the ICD-10-CM book appropriate to the year" of the encounter.[1]

Using the AAO's *ICD-10-CM For Ophthalmology: The Complete Reference* or other resources, always search a diagnosis code by the main term in the alphabetical index, and then verify by cross-referencing the code in the tabular list to ensure you select the most specific code. A dash following ICD-10 codes listed in the alphabetical index indicates there are additional digits to add for a higher level of specificity. ICD-10 codes without the remaining digits are not reportable and will be denied.

For example, dry AMD is listed in the alphabetical index as H35.31-. Under the tabular list, the sixth character is associated with laterality: 1 for right eye, 2 for left eye, and 3 for bilateral involvement. The seventh character is associated with the stage of the disease: 1 for early, 2 for intermediate, 3 for advanced without subfoveal involvement, and 4 for advanced with subfoveal involvement. Thus, intermediate dry AMD in the left eye in order of increasing specification would be reported as:

- H35.31-, dry AMD
- H35.312-, dry AMD, left eye
- H35.3122, dry AMD, left eye, intermediate

PAY ATTENTION TO EXCLUDES1 NOTES

Chapter 7 of the ICD-10-CM includes the diseases of the eye and adnexa and provides subchapters by condition in conjunction with Excludes1 notes for each section. When included, these notes mean the codes provided can't be billed with the ICD-10 codes in that subchapter.

For example, subchapter H35.4-, peripheral retinal degeneration, includes an Excludes1 note for H33.3-, retinal breaks without detachment. H33.3- codes cannot be billed with those listed in subchapter H35.4-. If these codes were reported together, the payer may deny the claim. Report only the condition that was the primary reason for the visit in these cases.

DON'T REPORT CONDITIONS UNTIL THEY ARE CONFIRMED

Do not report any ICD-10 code associated with the differential diagnoses; wait to report until the correct condition is diagnosed.

APPROPRIATELY LINK CPT CODES TO ICD-10-CM CODES

The ICD-10 code that supports medical necessity for a particular service should be linked correctly to the CPT

Access AAO Coding Resources Here:

ICD-10-CM for Ophthalmology

Practice Management for Retina

code on the claim. The ICD-10 codes are listed in item 21 of the claim form (A-L), and the link to the CPT code is designated in item 24e. For example, a patient is seen for a posterior vitreous detachment (PVD), right eye, and retinal tear with multiple breaks, left eye. An examination and laser are billed. The appropriately linked CPT code and ICD-10 code would be:

- Examination code, 9XXXX – H33.332, H43.811
- Laser code, 67145 – H33.332

If both the PVD and retinal tear ICD-10 codes are linked to CPT code 67145, the claim may be denied because PVD does not support medical necessity.

Another common claim denial is incorrectly linking laterality to treatment. For an intravitreal injection in the right eye, CPT code 67028, linking a bilateral wet AMD ICD-10 code can prompt a denial. Instead, link CPT code 67028-RT to H35.3211, wet AMD with active choroidal neovascularization, right eye.

ACCESS RESOURCES

AAO members can access valuable ICD-10 resources at aao.org/icd10. The *ICD-10-CM For Ophthalmology: The Complete Reference* provides all the necessary fundamentals, rules, and ophthalmic ICD-10 codes to code correctly the first time. ■

1. Billing and coding: scanning computerized ophthalmic diagnostic imaging (SCODI). CMS. Accessed February 27, 2025. www.cms.gov/medicare-coverage-database/view/article.aspx?articleid=57804

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(Continued from page 44)

Multilobulated melanomas are seldom mentioned in the literature; therefore, heightened awareness and suspicion are crucial when encountering lesions with atypical shapes. Moreover, when genetic profiling is not readily available, certain prognostic features such as tumor size and shape, which are easily identifiable on ultrasound, may assist clinicians in tailoring treatment and surveillance strategies. ■

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1. Jager MJ, Shields CL, Cebulla CM, et al. Uveal melanoma. *Nat Rev Dis Prim*. 2020;6(1):24.
2. Branisteanu DC, Bogdanici CM, Branisteanu DE, et al. Uveal melanoma diagnosis and current treatment options (Review). *Exp Ther Med*. 2021;22(6):1428.
3. Solnik M, Paduszyńska N, Czarnecka AM, et al. Imaging of uveal melanoma–current standard and methods in development. *Cancers (Basel)*. 2022;14(13):3147.
4. Shields CL, Kaliki S, Furuta M, Fulco E, Alarcon C, Shields JA. American Joint Committee on Cancer classification of posterior uveal melanoma (tumor size category) predicts prognosis in 7731 patients. *Ophthalmology*. 2013;120(10):2066-2071.
5. Harbour JW, Correa ZM, Schefler AC, et al. 15-Gene Expression Profile and PRAME as integrated prognostic test for uveal melanoma: first report of Collaborative Ocular Oncology Group Study No. 2 (COOG2.1). *J Clin Oncol*. 2024;42(28):3319-3329.
6. Walter SD, Chao DL, Feuer W, Schiffman J, Char DH, Harbour JW. Prognostic implications of tumor diameter in association with gene expression profile for uveal melanoma. *JAMA Ophthalmol*. 2016;134(7):734.
7. Kaiserman I, Amer R, Kaiserman N, Pe'er J. Ultrasonographic tissue characteristics of mushroom-shaped uveal melanoma. *Curr Eye Res*. 2005;30(3):171-177.
8. Singh N, Fonkeu Y, Lorek BH, Singh AD. Diagnostic A-scan of choroidal tumors: comparison of quantified parameters. *Ocul Oncol Pathol*. 2019;5(5):358-368.
9. Gill VT, Sabazade S, Herrspiegel C, et al. A prognostic classification system for uveal melanoma based on a combination of patient age and sex, the American Joint Committee on Cancer and the Cancer Genome Atlas models. *Acta Ophthalmol*. 2023;101(1):34-48.
10. Plasseraud KM, Wilkinson JK, Oelschlager KM, et al. Gene expression profiling in uveal melanoma: technical reliability and correlation of molecular class with pathologic characteristics. *Diagn Pathol*. 2017;12(1):59.
11. Shields CL, Say EAT, Hasanreisoglu M, et al. Cytogenetic abnormalities in uveal melanoma based on tumor features and size in 1059 patients: the 2016 W. Richard Green lecture. *Ophthalmology*. 2017;124(5):609-618.
12. Fang R, Wang H, Li Y, Liu YM, Wei WB. Regression patterns of uveal melanoma after iodine-125 plaque brachytherapy. *BMC Ophthalmol*. 2021;21(1):137.
13. Ramos-Dávila EM, Dalvin LA. Clinical implications of ultrasound-based morphology in choroidal melanoma. *Ophthalmol Retina*. 2025;9(3):263-271.
14. Mathis T, Jardel P, Loria O, et al. New concepts in the diagnosis and management of choroidal metastases. *Prog Retin Eye Res*. 2019;68:144-176.
15. Vishnevskia-Dai V, Zur D, Yaacobi S, Moroz I, Newman H, Neudorfer M. Optical coherence tomography: an adjunctive tool for differentiating between choroidal melanoma and metastasis [published online ahead of print February 22, 2016]. *J Ophthalmol*.
16. Kennedy S, Owens S, Ivers L, et al. Prognostic value of BAP1 protein expression in uveal melanoma. *Am J Surg Pathol*. 2024;48(3):329-336.
17. Mensink HW, Vaarwater J, Kilic, E, et al. Chromosome 3 intratumor heterogeneity in uveal melanoma. *Invest Opthalmology Vis Sci*. 2009;50(2):500-504.
18. Bagger MM. Intraocular biopsy of uveal melanoma risk assessment and identification of genetic prognostic markers. *Acta Ophthalmol*. 2018;96(A112):1-28.

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LOOK BEYOND THE FLOATERS


This rare cause of vitreous opacities requires a high degree of clinical suspicion.

BY SIDRA ZAFAR, MD, AND ROSELIND NI, BS

An 82-year-old man with a medical history of hypertension and hyperlipidemia but no significant ocular history was referred to our clinic for persistent vitreous floaters in the right eye. Here's what we found.

EXAMINATION

The patient's VA was 20/40 OD and 20/25 OS. His IOP was within normal limits, and no relative afferent pupillary defect was noted. Anterior segment examination showed 2+ nuclear sclerosis cataracts in each eye. Dilated fundus examination of the right eye showed prominent vitreous opacities; the left eye was normal (Figure 1).

Given the lack of hypopyon and significant anterior chamber reaction, suspicion for an underlying infectious process was low. The vitreous opacities were presumed to be secondary to either an old vitreous hemorrhage or a lymphoproliferative process. Observation was recommended to see if the opacities resolved with time.

At the 3-month follow-up, the vitreous opacities had worsened. The patient underwent an uncomplicated diagnostic pars plana vitrectomy (PPV). Histopathology results of the vitreous sample did not show neoplastic cells, and no organisms were identified. The sample was also negative for *MYD88* mutation. It did, however, demonstrate amorphous eosinophilic material that stained with Congo red, revealing the characteristic red-green birefringence of amyloidosis (Figure 2).

The patient subsequently underwent genetic testing, which showed a missense mutation in the *transthyretin* gene consistent with familial systemic amyloidosis. Late-phase ICG showed characteristic hyperfluorescent spots along the choroidal vessels, and OCT showed needle-shaped deposits on the retina (Figure 3).

One year post-PPV, there was some recurrence of the amyloid opacities. The patient's course was complicated by neovascular glaucoma requiring a series of three intravitreal anti-VEGF injections.

DISCUSSION

Amyloidosis encompasses a diverse group of disorders characterized by the deposition of amyloid in various parts of the body.[1] Involvement of the eye and/or ocular adnexal structures is not a feature of all amyloidosis cases, but when it does occur, the resulting clinical phenotypes are highly variable. Extraocular manifestations can vary from waxy

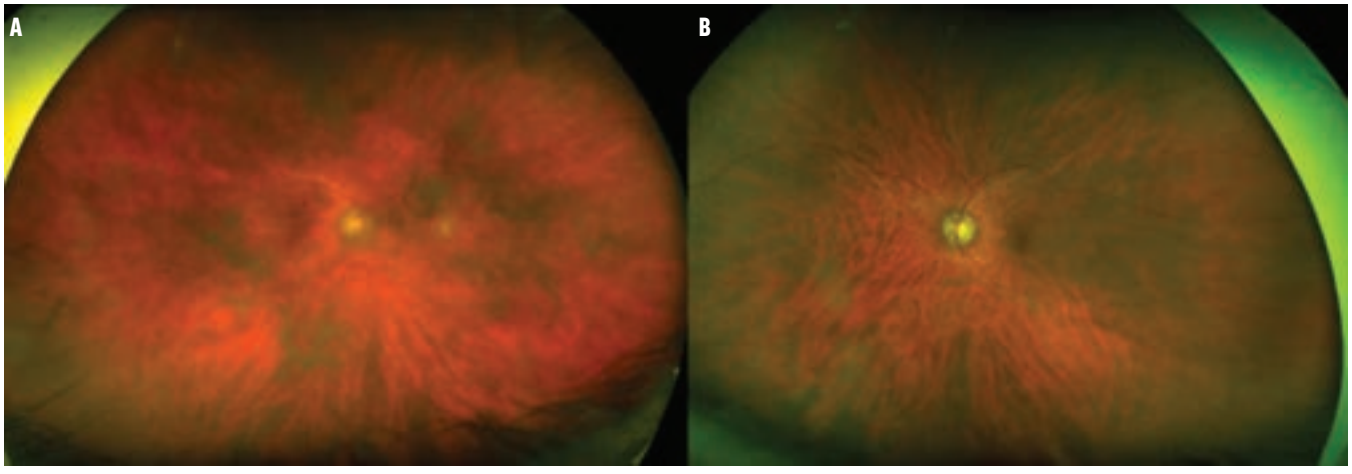

Figure 1. Ultra-widefield fundus photography of the right eye (A) shows prominent vitreous opacities compared with the normal left eye (B).

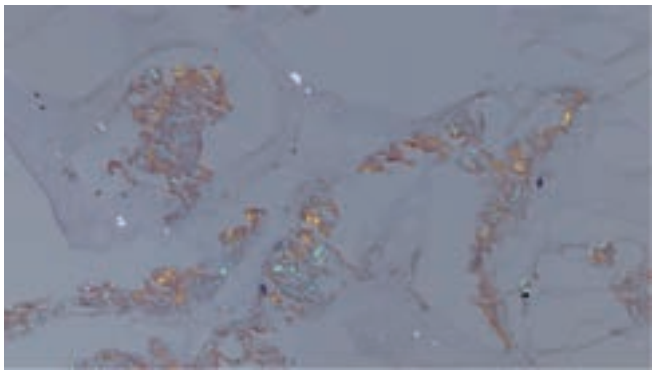

Figure 2. Congo red staining of the vitreous sample shows the characteristic red-green birefringence of amyloidosis.

eyelid papules to infiltration of the extraocular muscles and orbital adnexa, which can lead to progressive proptosis, ptosis, and restrictive ophthalmoplegia. Recurrent atraumatic subconjunctival hemorrhages, conjunctival nodules, glaucoma, and a scalloped pupil are among the anterior segment findings that have been described.[1,2]

Among the posterior segment findings, vitreous opacities are the most common. Vitreous amyloidosis is typically bilateral and asymmetrical. The opacities can be debilitating and, in some cases, can cause severe vision loss.[3] They recur in up to 20% of cases following PPV, which is thought to be secondary to intraocular amyloid production by the retinal pigment epithelium. Luckily, PPV allows for almost complete visual acuity recovery in these patients. One study reported an improvement in VA from 20/100 preoperatively to 20/20 postoperatively among 31 eyes with vitreous amyloidosis following PPV.[4] Another study found that BCVA improved to 20/25 or better for all 14 study patients following PPV.[5]

Diagnosing ocular amyloidosis requires a high degree of suspicion. Although PPV remains the standard to confirm vitreous involvement, several imaging features have been described that can aid clinicians in these cases. Choroidal amyloid angiopathy, which appears as hyperfluorescent streaks on late-phase ICG, has been described in several studies.[6,7] At least 10 minutes of staining are required to demonstrate these findings, with maximal staining seen around 12.5 minutes.[6] On OCT, needle-shaped deposits, presumably depicting amyloid deposition on the retina, have been described, which can persist even after PPV.[8]

Glaucoma is a major cause of vision loss in patients with amyloidosis. In many cases, the glaucoma is very difficult to control, often requiring multiple medications and/or multiple surgeries. The risk of glaucoma increases after PPV, with up to 74% of patients developing elevated IOP postoperatively.[4] Vitrectomy is thought to cause both diffusion of amyloid fibrils into the trabecular meshwork and IOP elevation. One study compared the incidence of glaucoma among eyes that underwent complete PPV

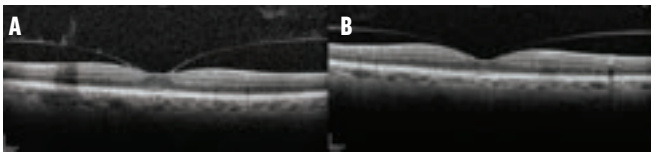

Figure 3. OCT of the right eye (A) shows the characteristic needle-shaped deposits on the retina compared with the normal left eye (B).

versus incomplete vitrectomy and found that 75% of patients in the complete vitrectomy group developed glaucoma over a mean follow-up of 8 years compared with 25% of patients in the incomplete vitrectomy group over a mean follow-up of 28.5 years.[9] The authors hypothesized that the residual vitreous in incomplete PPV may act as a filter that retains mutant amyloid protein and promotes its deposits in the vitreous itself, decreasing and delaying amyloid deposition in the trabecular meshwork. Incomplete vitrectomy is also associated with reduced damage of the trabecular meshwork, explaining the less frequent and delayed progression to glaucoma.

RARE BUT CONSEQUENTIAL

Amyloidosis is a rare cause of vitreous opacities and requires a high degree of clinical suspicion. Imaging modalities such as ICG and OCT can aid in making the diagnosis. These patients can have serious organ involvement and require lifelong monitoring of their IOP, especially after PPV. ■

1. Mathew R, Zeppieri M. Ocular Amyloidosis. In: StatPearls. StatPearls Publishing; 2025.
2. Beirão JM, Malheiro J, Lemos C, Beirão I, Costa P, Torres P. Ophthalmological manifestations in hereditary transthyretin (ATTR V30M) carriers: a review of 513 cases. *Amyloid*. 2015;22(2):117-122.
3. Reynolds MM, Veverka KK, Gertz MA, et al. Ocular manifestations of familial transthyretin amyloidosis. *Am J Ophthalmol*. 2017;183:156-162.
4. Kakihara S, Hirano T, Imai A, Miyahara T, Murata T. Small gauge vitrectomy for vitreous amyloidosis and subsequent management of secondary glaucoma in patients with hereditary transthyretin amyloidosis. *Sci Rep*. 2020;10(1):5574.
5. Koga T, Ando E, Hirata A, et al. Vitreous opacities and outcome of vitreous surgery in patients with familial amyloidotic polyneuropathy. *Am J Ophthalmol*. 2003;135(2):188-193.
6. Mano F, Yonekawa Y, Kakihara S, et al. Choroidal amyloid deposition: a multicenter study of amyloid lesions identified in late indocyanine green angiography. *Retina*. 2022;42(10):1989-1994.
7. Attia S, Kahloun R, Mbarek S, et al. Indocyanine green angiography findings in patients with nonfamilial amyloidosis. *J Ophthalmic Inflamm Infect*. 2012;2(4):199-203.
8. Tasiopoulou A, Ong D, Lightman S. Characteristic needle-shaped pattern seen on OCT in a patient with ocular amyloidosis. *Ophthalmol Retina*. 2021;5(1):99-101.
9. Beirão NM, Matos ME, Meneres MJ, Beirão IM, Costa PP, Torres PA. Vitreous surgery impact in glaucoma development in liver transplanted familial amyloidosis ATTR V30M Portuguese patients. *Amyloid*. 2012;19(3):146-151.

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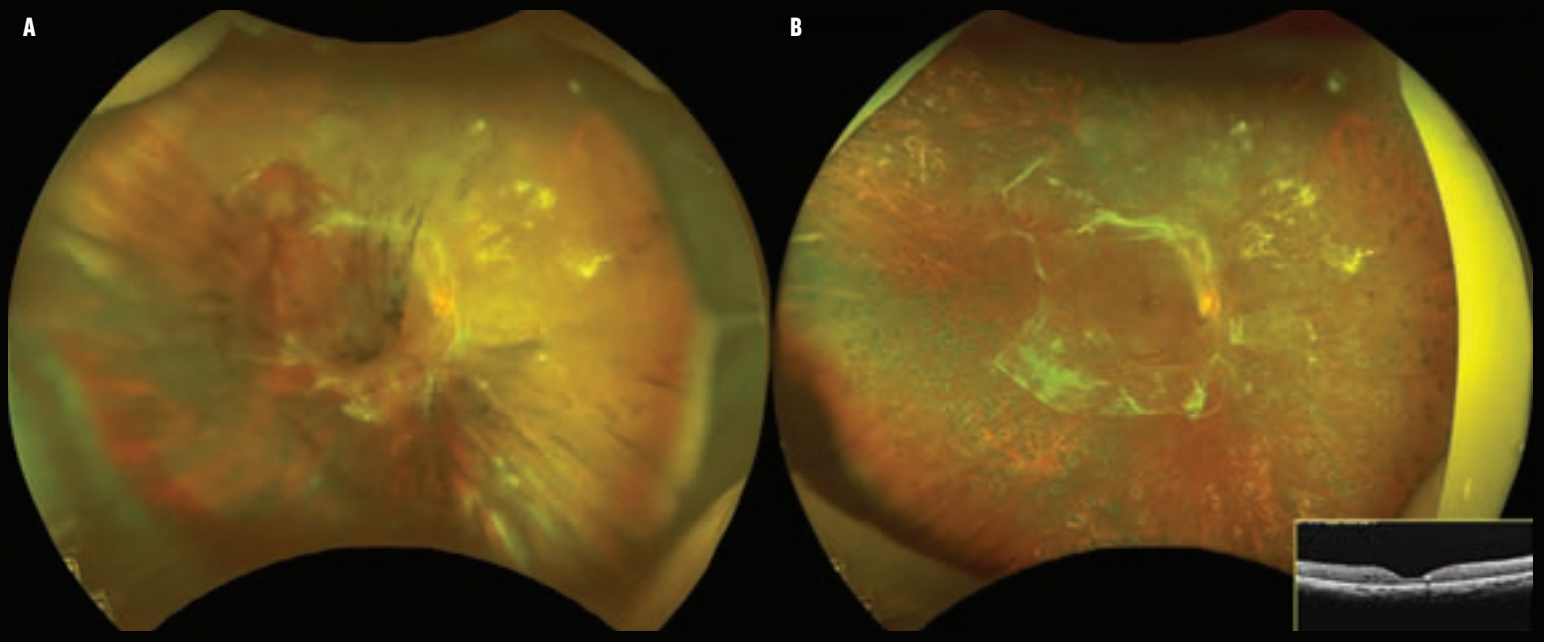

FIGURE 1

LIMITED MEMBRANECTOMY FOR DIABETIC TRD


This technique may be an effective option for select patients with diabetic tractional retinal detachment.

BY TAKU WAKABAYASHI, MD, PHD, AND YUSUKE OSHIMA, MD, PHD

A 59-year-old woman presented with vision loss in each eye. She had a 20-year history of type 2 diabetes, and her BCVA was 20/500 OD and light perception OS. She complained of recent vision loss in her right eye. On initial examination, her right eye showed a tractional retinal detachment (TRD) with a ring-shaped fibrovascular membrane and vitreous hemorrhage due to proliferative diabetic retinopathy (Figure 1A). Widefield fluorescein angiography (FA) showed peripheral retinal nonperfusion and extensive leakage from retinal neovascularization (Figure 2, top row).

SURGICAL MANAGEMENT

Given the risk of progression, we performed a 25-gauge vitrectomy in the right eye. The core vitrectomy was followed by peripheral vitreous shaving and segmentation and delamination of the fibrovascular membrane along the vascular arcade.

During the surgery, we carefully released the traction by performing a limited membranectomy with a vitreous cutter while minimizing membrane dissection and avoiding iatrogenic breaks. We intentionally left some membranes intact without removal.

We also conducted brilliant blue G-assisted internal limiting membrane peeling and then released the anteroposterior traction from the equator to the periphery in the superior, inferior, and temporal areas, leaving the nasal fibrovascular membranes intact.

At the end of the surgery, we applied panretinal photocoagulation up to the far periphery.

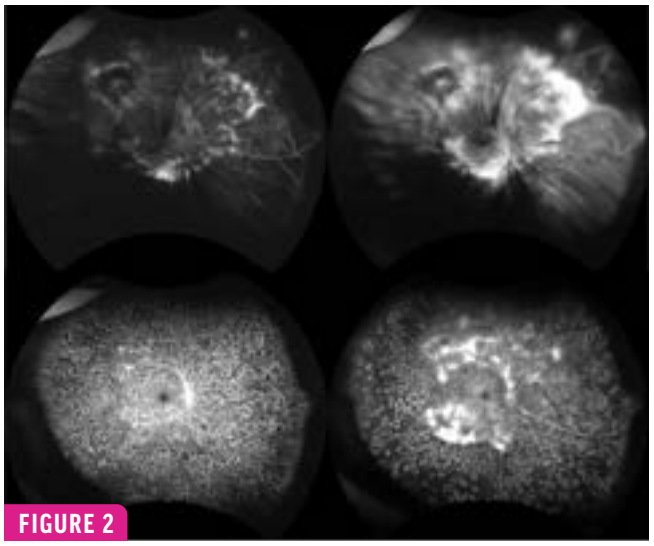

FIGURE 2

OUTCOMES

Six months after surgery, the patient's retina was attached, and her vision had recovered to 20/40 OD (Figure 1B). Some leakage remained in the postoperative FA (Figure 2, bottom row); however, no postoperative vitreous hemorrhage or membrane reproliferation occurred. The optic disc was well perfused without appearing pale.

A GOOD OPTION FOR HIGH-RISK PATIENTS

Indications for limited membranectomy include eyes with mature fibrovascular membranes and TRD without a rhegmatogenous component, eyes without posterior vitreous detachment or with partial posterior vitreous detachment, and high-risk monocular eyes for which avoiding intraoperative complications is paramount, as was the case for this patient. Long-term anatomic and visual outcomes should be explored in future studies. ■

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

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

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

1 INDICATIONS AND USAGE

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

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1.2 Diabetic Macular Edema (DME)

1.3 Macular Edema Following Retinal Vein Occlusion (RVO)

4 CONTRAINDICATIONS

4.1 Ocular or Periocular Infections

VABYSMO is contraindicated in patients with ocular or periocular infections.

4.2 Active Intraocular Inflammation

VABYSMO is contraindicated in patients with active intraocular inflammation.

4.3 Hypersensitivity

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

5 WARNINGS AND PRECAUTIONS

5.1 Endophthalmitis and Retinal Detachments

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

5.2 Increase in Intraocular Pressure

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

5.3 Thromboembolic Events

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

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

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

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

5.4 Retinal Vasculitis and/or Retinal Vascular Occlusion

Retinal vasculitis and/or retinal vascular occlusion, typically in the presence of intraocular inflammation, have been reported with the use of VABYSMO *[see Adverse Reactions (6.2)]*. Discontinue treatment with VABYSMO in patients who develop these events. Patients should be instructed to report any change in vision without delay.

6 ADVERSE REACTIONS

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

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

6.1 Clinical Trial Experience

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

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

Table 1: Common Adverse Reactions (≥ 1%)

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

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

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

6.2 Postmarketing Experience

The following adverse reactions have been identified during postapproval use of VABYSMO. Because these reactions are reported voluntarily from a population of uncertain size, it is not always possible to reliably estimate their frequency or establish a causal relationship to drug exposure.

Eye disorders: retinal vasculitis with or without retinal vascular occlusion.

8 USE IN SPECIFIC POPULATIONS

8.1 Pregnancy

Risk Summary

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

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

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

Data

Animal Data

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

8.2 Lactation

Risk Summary

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

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

8.3 Females and Males of Reproductive Potential

Contraception

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

Infertility

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

8.4 Pediatric Use

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

8.5 Geriatric Use

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

17 PATIENT COUNSELING INFORMATION

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

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

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

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VABYSMO®
faricimab-svoa injection 6 mg

VABYSMO IS THE #1 PRESCRIBED IVT IN nAMD[1]*

*Verana Health® data: nAMD patient share in October 2024, with biologic intravitreal injections approved under separate BLAs considered individually.

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

IMPORTANT SAFETY INFORMATION

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

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

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

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

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

BLA=biologics license application.

References: 1. Data on file. South San Francisco, CA: Genentech, Inc.

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