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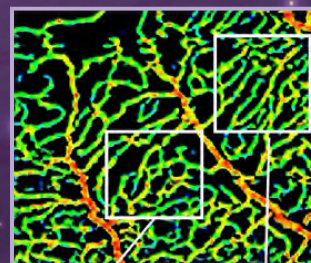
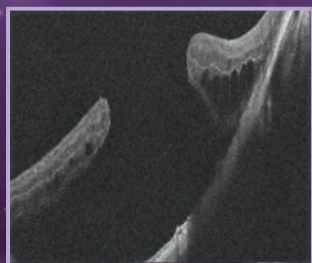
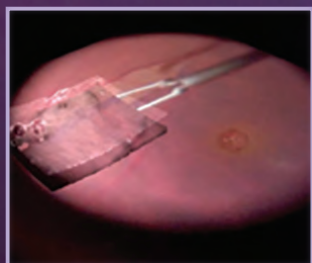
Retina Today

APRIL 2026 VOL. 21, NO. 3  
RETINATODAY.COM



# IMAGING AND VISUALIZATION IN RETINA

A spotlight on the technology improving diagnosis and management.



THE VALUE OF OCTA IN VASCULAR DISEASE

OR UPDATE: HEADS-UP DISPLAYS, AI, AND ROBOTICS

IMAGING EPIRETINAL PROLIFERATION

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# THE OCT ISSUE

BY GEMMY CHEUNG, MBBS, FRCOPHTH, FAMS, MCI, AND SRINIVAS R. SADDA, MD, FARVO



Since it was first introduced in 1991,<sup>1</sup> OCT has become integral to nearly every aspect of retina care—from screening and

diagnosis to prognostication, treatment monitoring, and clinical trial design. At this year's Angiogenesis, Exudation, and Degeneration virtual meeting, more than 20 sessions were dedicated to OCT-based findings, underscoring just how central this technology has become to both research and day-to-day clinical decision making. An OCT biomarker, ellipsoid zone attenuation, is even an approved clinical trial endpoint.

Twenty years ago, OCT was limited to specialty clinics, and we weren't relying on it for most of our clinical decisions (for more on the journey of OCT in our field, check out this issue's *Retina: Then and Now* series with Jay S. Duker, MD). Now, OCT angiography (OCTA), widefield imaging, microscope-integrated OCT, 3D overlays, and even home-based OCT systems are expanding how (and where) we visualize retinal layers and blood flow.

This issue looks at the current state of retinal imaging with OCT, highlighting both the technological advances and the clinical and surgical considerations that accompany them. Amir H. Kashani, MD, PhD, and colleagues explore the role of OCTA in evaluating retinal vascular diseases such as diabetic retinopathy, macular degeneration, and central serous retinopathy.

Widefield structural imaging has become increasingly important as we learn more about retinal pathologies, and the team at Doheny Eye Institute provides an overview of widefield OCT devices and how they are extending our view into the periphery.

For a closer look at the day-to-day clinical utility of OCT imaging, Kotaro Tsuboi, MD, PhD, explains how to identify epiretinal proliferation with en face OCT and proposes its inclusion in the preoperative imaging for macular holes.

OCT is also beginning to reshape our ORs. Lejla Vajzovic, MD, and her team at Duke Eye Center review the surgical applications of microscope-integrated OCT, including the use of an investigational swept-source device, and discuss the future of single-channel visualization platforms. Complementing this, Jayanth Sridhar, MD, and colleagues examine recent advances in 3D visualization in the OR, along with the growing integration of AI and robotics into surgical workflows.

This issue offers a comprehensive view of how far OCT imaging has come. As these technologies become more sophisticated and integrated across clinical settings (and yet simpler to use in the clinic and beyond), they are influencing how we think about diagnosis, management, and outcomes. We hope this issue provides both practical insight and a broader perspective on the expanding role of OCT in retina care. ■

1. Huang D, Swanson EA, Lin CP, et al. Optical coherence tomography. *Science*. 1991;254(5035):1178-1181.

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We are thrilled to welcome several new members to *Retina Today's* Editorial Advisor Board.

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# UNDERSTANDING THE OPHTHALMIC RISKS OF SYSTEMIC TYROSINE KINASE INHIBITORS

A study published in *Ophthalmology Retina* sought to characterize the risks of retinal artery occlusion (RAO) and retinal vein occlusion (RVO) associated with use of systemic tyrosine kinase inhibitors (TKIs),<sup>1</sup> which are used in treating patients with cancer.

The retrospective cohort study used data from electronic health records of multiple institutions across the United States and included adults who had been diagnosed with cancer and had no prior history of RVOs or maculopathy. Patients treated with systemic TKIs both with and without anti-VEGF therapy were compared with matched control patients treated with non-TKI antineoplastic drugs. Lifetime risks of RAO, central RAO (CRAO), branch RAO (BRAO), RVO, central RVO (CRVO), and branch RVO (BRVO) were compared via risk ratios (RRs), and rates of outcomes within 3 years of antineoplastic initiation were also evaluated via hazard ratios (HRs).<sup>1</sup>

The results showed that the anytime risks of RAO and RVO were comparable between the anti-VEGF/TKI cohort and control group; however, the anti-VEGF/TKI cohort had a significantly greater risk of CRVO within 3 years of TKI initiation (HR = 2.86).<sup>1</sup> While the non-anti-VEGF/TKI cohort had a lower risk of RAO (RR = 0.61) and BRVO (RR = 0.51) compared with the non-TKI control group, no significant difference in outcomes via HR was identified. The authors

concluded that patients starting anti-VEGF/TKI therapy may require closer monitoring for CRVO during the first few years of treatment, while non-anti-VEGF/TKI therapy may have a more favorable safety profile regarding BRVO and RAO.<sup>1</sup>

In addition, other researchers explored the implications of systemic TKI therapy with the development of AMD.<sup>2</sup> The results of their study suggest TKIs were not consistently associated with AMD diagnosis compared with matched controls at 1, 3, and 5 years.<sup>2</sup> A subgroup analysis of TKIs with anti-VEGF therapy did show a significant reduction of AMD, but only at the 5-year mark; the findings were not considered to support a population-level protective effect of systemic TKIs against AMD risk, according to the study authors.<sup>2</sup>

1. Jeong H, Yue SC, Kaelber DC, Singh RP, Talcott KE. Risks of retinal vascular occlusions with the systemic use of tyrosine kinase inhibitors. [published online ahead of print March 4, 2026.] *Ophthalmol Retina*.

2. Wu S, Jeong H, Reed HA, et al. Associations between systemic tyrosine kinase inhibitors and development of age-related macular degeneration in patients with cancer. [published online ahead of print March 4, 2026.] *Ophthalmol Retina*.



## FURTHER READING

### Ocular Toxicity From New Oncology Agents

By Sarah Touhami, MD, PhD



READ NOW

## STUDY SHOWS POTENTIAL OF VENDOR-AGNOSTIC DEEP LEARNING MODEL FOR IMAGING ANALYSIS

A multicenter retrospective study conducted in Hong Kong and Vietnam sought to train and evaluate a vendor-agnostic deep learning (DL) model for analyzing 3D OCT scans. The model was trained on 3D scans from the Spectralis OCT (Heidelberg Engineering; vendor 1). Nine external datasets, including 2D and 3D scans from Spectralis and 3D scans from a Cirrus OCT (Carl Zeiss Meditec; vendor 2), were used for testing, and an “uncertain” category was introduced to

handle previously unseen macular conditions.<sup>1</sup>

A total of 6,756 OCT scans from 1,669 patients were used for model development, and 12,236 scans from 4,336 patients were used for external testing. The model was evaluated in terms of area under the receiver operating characteristic curve (AUROC), micro-average positive predictive value (PPV), micro-average negative predictive value (NPV), and clinically important miss rate. The results showed that AUROC ranged from 0.779 to 0.999 for vendor 1, 0.754 to 0.991 for vendor 2, and 0.801 to 0.950 for the 2D scans. Micro-average PPVs ranged from 56.7% to 72.0% for vendor 1 and 46.0% to 60.4% for vendor 2. All micro-average NPVs exceeded 97.5%. The uncertain

category demonstrated high specificity (> 95%) and accuracy (> 92.7%), but varied sensitivity (from 14.3%). The clinically important miss rates were 6.16% and 6.70% for urgent cases and 4.41% and 8.67% for semi-urgent cases for vendors 1 and 2, respectively.<sup>1</sup>

These results suggest the possibility of vendor-agnostic DL models for imaging analysis, which could streamline detection of retinal conditions, according to the study authors.<sup>1</sup>

1. Tang ZQ, Zhang YH, Ran AR, et al. Domain-shift AI technology for vendor-agnostic multiple macular disease detection from 3D OCT scans [published online ahead of print February 26, 2026]. *JAMA Ophthalmol*.

## INVESTIGATIONAL VISUAL PROSTHESIS RECEIVES FDA BREAKTHROUGH DEVICE DESIGNATION

The FDA has granted Breakthrough Device designation to Belgium-based ReVision Implant's device, Occular, a visual cortical prosthesis that uses a brain implant to bypass the eyes and interface directly with the brain. The implant is designed to provide patients with untreatable vision loss the means to

identify objects, perceive obstacles, and navigate their environment, thus offering a greater degree of independence.<sup>1</sup>

The Occular device uses a miniature camera mounted on a wireless headset to capture visual data from the patient's surroundings. These captured data are then transmitted to an implant in the patient's brain, which stimulates neurons in the visual cortex in specific patterns. These patterns are, in turn, interpreted by the brain as points of light, combining to form basic visual representations, according to the company.<sup>1</sup>

The company plans to conduct a short-term clinical evaluation later this year, with a scheduled brain surgery in October. If regulatory approvals are obtained, early-stage human clinical trials could begin in summer 2027.<sup>1</sup>

1. Belgian neurotech startup ReVision Implant secures FDA breakthrough status for brain-implant vision technology. Eyewire+. March 9, 2026. Accessed March 16, 2026. [eyewire.news/news/belgian-neurotech-startup-revision-implant-secures-fda-breakthrough-status-for-brain-implant-vision-technology](https://eyewire.news/news/belgian-neurotech-startup-revision-implant-secures-fda-breakthrough-status-for-brain-implant-vision-technology)

## CHANGES IN PERIPHERAL RETINA COULD HELP DETECT EARLY ALZHEIMER DISEASE

A recent study published in the *Journal of Alzheimer's Disease* suggests changes in the outer peripheral zone of the retina—not only in the central retina—may serve as a useful biomarker for detecting early-stage Alzheimer disease.<sup>1</sup>

In the study, fluorescent immunostaining of mouse retinas was performed to evaluate Müller glia cell function. The findings showed increased levels of Aquaporin-4, a protein crucial for clearing metabolic waste in the peripheral retina, in the earliest stages of disease, which signaled stress in the retinal glymphatic system. This stress corresponds to waste-clearance failures observed in the brains of individuals with Alzheimer disease.<sup>1</sup>

Given the current techniques for diagnosing Alzheimer disease, such as positron emission tomography scans or cerebrospinal fluid assays, these findings indicate that wide-field retinal imaging may offer a less invasive, clinically useful option for detecting disease in its very early states.<sup>1</sup> ■

1. International research shows peripheral retina could unlock early detection of Alzheimer's disease. Eyewire+. February 27, 2026. Accessed March 16, 2026. [eyewire.news/news/international-research-shows-peripheral-retina-could-unlock-early-detection-of-alzheimers-disease](https://eyewire.news/news/international-research-shows-peripheral-retina-could-unlock-early-detection-of-alzheimers-disease)

### Eyewire+ Pharma Update

- **NovaBridge Biosciences** reported positive topline results for its phase 2a trial of VIS-101, a dual VEGF-A and Ang-2 inhibitor being developed for retinal vascular diseases such as wet AMD. The therapy demonstrated significant visual acuity improvements, reductions in retinal thickness, and durability.
- **Ocugen** completed enrollment of its phase 3 liMeliGHt trial evaluating OCU400, a gene-agnostic modifier gene therapy for patients with retinitis pigmentosa. The company has plans to submit a rolling biologics licensing application in 2026 with potential approval in 2027.
- New 3-year data show that **Nanoscope's MCO-010** optogenetic gene therapy produced sustained, clinically meaningful vision improvements of approximately 3 ETDRS lines in patients with advanced retinitis pigmentosa.
- **Cirrus Therapeutics** has expanded into Singapore with a multimillion-dollar collaboration with A\*STAR's Institute of Molecular and Cell Biology. The company also announced a next-generation retinal pigment epithelium cell therapy for geographic atrophy.
- **EyePoint Pharmaceuticals** dosed the first patients in its two phase 3 global trials, COMO and CAPRI, evaluating its vorolanib intravitreal insert (Duravyu), a selective tyrosine kinase inhibitor, for the treatment of diabetic macular edema.

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# RETINA: THEN AND NOW



As part of our 20th anniversary, *Retina Today* is digging into the archives to reflect on how much the profession has changed.

## APRIL SPOTLIGHT: OCT

In 2006, Jay S. Duker, MD, contributed an article titled *Advances in OCT Improve Understanding of Disease States*. After a brief introduction to the technology itself, he highlighted two innovations—ultrahigh-resolution OCT and spectral OCT systems—that allowed for a better understanding of many retinal pathologies and, at least with the latter, faster acquisition speeds.

Here, Dr. Duker reflects on the advances in OCT imaging since *Retina Today* launched in 2006, and the tools poised to change the paradigm again.

### RETINA TODAY (RT): HOW WERE YOU INCORPORATING OCT INTO CLINICAL PRACTICE BACK IN 2006?

**Jay S. Duker, MD:** Twenty years ago, OCT was really limited to specialty ophthalmologists, mostly retina and glaucoma specialists. Very few comprehensive ophthalmologists appreciated the value at the time. Outside ophthalmology, there was virtually no use of OCT. Since then, OCT has become an indispensable tool for all eye care professionals, both ophthalmologists and optometrists, to diagnose and manage ocular diseases such as diabetic macular edema, AMD, and retinal vein occlusion. You can't practice modern eye care without an OCT.

Beyond eye care, it's now become routine in neurology and gastroenterology, and you're going to see OCT technology continue to branch out into other areas of medicine.

### RT: HOW HAS OCT TECHNOLOGY EVOLVED OVER THE LAST 2 DECADES?

**Dr. Duker:** Spectral-domain OCT is now routine, which means faster imaging speeds and better

signal-to-noise ratio. You can do oversampling of the images to get better quality images, and you have widefield scans of 12 mm x 12 mm or even larger. This assists not just with disease diagnosis, but screening.

The interface between the machines and the operator is much easier—it's a single button capture now. Our examinations are more accurate from visit to visit with OCT comparisons.

In addition, multimodal imaging has improved our practice, with fluorescein angiography, ICG angiography, fundus autofluorescence, and widefield OCT all in one imaging device.

As for software, the biggest improvement has been normative databases, allowing us to tell from a scan whether a patient is within the normal limits for any given parameter. The software now allows us to monitor changes in full thickness retina, nerve fiber layer, and the ganglion cell complex.

### RT: WHAT NEW IMAGING TOOLS/UPDATES ARE YOU HOPING TO SEE IN THE FUTURE?

**Dr. Duker:** I think it's going in two directions. First, OCT will continue to

become simpler, cheaper, and more widespread; think of home OCT, which was a theory 20 years ago but now exists. Machines built to monitor disease in the patient's home don't need the same robustness that a subspecialist's OCT might need, but they're certainly effective at taking images to compare with normals or a patient's historical data. Even as the devices are simplified, they will continue to innovate to be faster with higher quality images.

Second, more dense scanning is going to give us better accuracy and provide complete widefield scanning with the real hope of someday scanning from ora serrata to ora serrata; we may one day have software that can detect where disease is present and automatically focus on that area.

It's incredible, having been there at the start of the OCT era and to see how far we have come; at one point at the New England Eye Center at Tufts Medical Center, we had the only OCT device outside the laboratory. Now, it exists in virtually every eye care clinic.

This is a technology that it will continue to evolve and help us take better care of patients. ■

### FURTHER READING

*Advances in OCT Improve Understanding of Disease States*  
March 20026  
By Jay S. Duker, MD



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# ONE TO WATCH

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Samir N. Patel, MD

## WHERE IT ALL BEGAN

I was born and raised in the suburbs of Philadelphia. As a child, I fell in love with the intricacies of computers and technological gadgets; I would pore over instructional books, learning to build and fix computers, and eventually got my first job as a computer technician. I completed my undergraduate studies at Pennsylvania State University, majoring in Biology and Economics, before moving to New York City to attend medical school at Weill Cornell Medical College.

## MY PATH TO RETINA

Ophthalmology was not on my radar at the start of medical school. In college, I spent a significant amount of time developing telemedicine-based global health initiatives. During Weill Cornell's introductory coursework in global health, I connected with R.V. Paul Chan, MD, MSc, MBA,



and Michael F. Chiang, MD, who approached global ophthalmology from an educational and technological perspective. From there, I was hooked on ophthalmology and retina.

## SUPPORT ALONG THE WAY

I have many amazing mentors who have played a crucial role at every step of my training. Drs. Chan and Chiang were instrumental in guiding me to ophthalmology when I was a young medical student at Cornell.

During residency and fellowship at Wills Eye Hospital, I was fortunate to work with many amazing mentors, of which there are too many to list individually. These mentors were instrumental in fostering my development as a clinician, surgeon, and researcher. Beyond imparting their clinical and surgical wisdom, they taught me the importance of Wills Eye's motto of "Skill with Compassion":

**Dr. Patel's advice: In a field as demanding as ours, it is easy to dwell on failures and overlook successes. Always remember that being entrusted with a patient's vision is a rare honor that should sustain you through the toughest moments of your career.**

provide the highest quality of care with respect for the individual needs of each patient. I'm lucky to be working with them, and they continue to serve as a constant source of advice for everything retina and beyond.

## AN EXPERIENCE TO REMEMBER

While clinical milestones are rewarding, the most memorable aspect of my career thus far has been the opportunity to train our vitreoretinal surgery fellows. There is a unique fulfillment in watching a fellow master complex surgical maneuvers for the first time and knowing that you played a small part in their journey toward becoming an independent surgeon. ■

To read about our other Ones to Watch, scan the QR code or visit [retinatoday.com](http://retinatoday.com).



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# RETINA FELLOWS FORUM 2026: PEARLS FOR TRANSITIONING TO PRACTICE



World-class retina experts shared their tips and tricks to help fellows prepare for the real world ahead.

**BY PRASHANT D. TAILOR, MD, AND ALEJANDRO ITZAM MARIN, MD**

The 26th Annual Retina Fellows Forum, held January 30-31, 2026, in Chicago, convened second-year vitreoretinal fellows for 2 days of surgical cases and videos, networking, and lively debate. Carl C. Awh, MD, FASRS; David R. Chow, MD, FASRS; and Tarek S. Hassan, MD, FASRS, hosted a program built to sharpen clinical decision making and strengthen professional connections (Figure 1).

## INNOVATIONS IN RETINA

For the first panel, Adrienne W. Scott, MD, FASRS, framed wet AMD therapy around durability and the widening gap between trial cadence and real-world adherence. She reviewed contemporary options such as faricimab (Vabysmo, Genentech/Roche), aflibercept 8 mg (Eylea HD, Regeneron), and the port delivery system with ranibizumab (Susvimo, Genentech/Roche), and highlighted gene therapy and tyrosine kinase inhibitor platforms as potential next-wave approaches.

The discussion then narrowed to one of the daily decisions fellows will face as attendings: when to switch a patient's therapeutic option. The recurring pearl was to define your heuristics before the clinic day defines them for you. Margaret A. Chang, MD, MS, FASRS, emphasized the value in applying consistent criteria so these changes feel deliberate. The panel added that step therapy and payer rules may drive parts of the sequence, making clear documentation and patient-facing explanations essential.

Emmanuel Y. Chang, MD, PhD, then reviewed the

management of submacular hemorrhage. He discussed everything from anti-VEGF monotherapy and intravitreal tissue plasminogen activator (tPA) with pneumatic displacement to subretinal tPA displacement with vitrectomy. Dr. Chang cautioned against relying on a single OCT cutoff to guide intervention. Instead, the panel endorsed an individualized, patient-centered approach, encouraging fellows to carefully document the clinical factors informing their decision making, including hemorrhage size and thickness, chronicity, location, baseline visual acuity, and whether the patient can position and follow-up promptly.

Surgical pearls included controlled subretinal access, gentle injection into the thickest area of the clot, and strict attention to postoperative positioning as a critical determinant of success.

## EXPERT SURGICAL ADVICE

The surgical video panels, moderated by Dr. Chow and Sunir J. Garg, MD, highlighted that the success of high-expectation cases, such as symptomatic floaters and epiretinal membrane, is dictated as much by patient-reported symptoms and thoughtful counseling as it is the surgical technique itself. The faculty emphasized that careful selection, alignment of symptoms with clinical findings, and clear communication about realistic outcomes are central to surgical success and patient satisfaction.

When discussing epiretinal membrane and macular hole repair, the faculty focused on reproducible fundamentals: optimize visualization, stay tangential, and protect the

## FELLOWS FORUM

Images courtesy of Kevin Caldwell Photography



Figure 1. The 2026 meeting boasted a stellar faculty, including (left to right) Drs. Garg, Scott, Chow, Rachitskaya, Awh, Emmanuel Chang, Elliott, Hassan, Chee, and Margaret Chang.

inner retina. Most endorsed the use of dye and thoughtful light management, and several discussed contact lens viewing and digital visualization as safety multipliers. Tools such as the micro-vacuum pick (Katalyst) and the Finesse Flex Loop (Alcon) were mentioned as ways to reduce instrument exchanges, but the message was consistent across preferences: If the peel becomes forceful or the view degrades, re-stain, change your approach, or stop rather than risk nerve fiber layer injury.

### COMPLICATIONS AS CURRICULUM

Aleksandra V. Rachitskaya, MD, FASRS, reframed complications as a shared learning tool and a leadership test. She touched on themes such as maintaining control of the surgical environment, proactively anticipating high-risk steps, and implementing small technical adjustments that reduce complication risk. When faced with a complication, the faculty emphasized the need for calm surgical judgment under pressure, including a willingness to stage a case when visualization or safety deteriorates.

Postoperative communication was treated as a critical part of complication management. Faculty advocated for direct language, ownership, and presence. The take-home for fellows was that technical competence is necessary, but composure and clarity are what preserve trust.

### SURGICAL CASE INSIGHTS

The fellows' case presentations, moderated by Dr. Margaret Chang, and Yewlin E. Chee, MD, delivered practical pearls across trauma, oncology, and complex retinal detachment. Trauma cases included

**SAVE THE DATE: 27th Annual Retina Fellows Forum**

January 29-30, 2027, in Chicago



Figure 2. Drs. Hassan, Awh, and Chow, present Dr. Elliott with a gift to commemorate his talk as this year's distinguished guest speaker.

glass intraocular foreign body retrieval (by Joseph C. Giacalone, MD, PhD) and post-injury retinal detachment repair (by Jonathan Lin, MD, PhD), emphasizing the value of preoperative planning, secure wound strategy, and staged surgery when appropriate. Additional presentations—including a bungee-cord injury (by Prithvi R. Bomdica MD, MBA) and a modified sutured IOL technique (by Rui Wang, MD)—reinforced that the “small” choices, such as incision planning, hemostasis, and fixation redundancy, often determine whether a challenging case stays under control.

On day 2, fellow presentations included a case of submacular hemorrhage (by Caroline C. Awh, MD), vitreoretinal biopsy planning for suspected intraocular lymphoma (by Patrick Hughes, MD), and combined tractional and exudative detachment management in hemangioblastoma-related disease (by Yuxi Zheng, MD). Abdulrahman Alotaibi, MD, discussed a pneumatic-first maneuver before vitrectomy to calm a bullous detachment in select cases. Across sessions, the faculty kept the discussion pointed: Identify the inflection point that changes management, define plan B before making an incision, and know that “doing less” can be the right first move.

Dr. Hassan's diabetic vitrectomy pearls aligned with that mindset. Timing should follow macular threat and traction, not just visual acuity, and posterior hyaloid management remains central. Modern cutters support efficient unimanual work in many cases, but fellows were encouraged to stay bimanual-ready for dense fibrovascular disease.

### BUSINESS 101

The business of retina panel led by Dr. Margaret Chang discussed how financial systems are essential aspects of vitreoretinal clinical practice. Prior authorization

*(Continued on page 41)*

# VIGABATRIN-RELATED RETINAL TOXICITY



Patients taking this medication for epilepsy should be monitored carefully for visual disturbances.

BY NATALIA LONDOÑO, MD; RAFAEL MÉNDEZ, MD; DANIELA ROJAS, MD; CLEMENCIA DE VIVERO, MD; AND ÁLVARO MEJÍA, MD

**V**igabatrin, an adjuvant therapy for refractory focal onset epilepsy and the treatment of infantile spasms, is a structural analog of gamma-aminobutyric acid (GABA) that irreversibly inhibits GABA transaminase.<sup>1,2</sup> It has a high response rate and overall good tolerability.<sup>2</sup>

In 1997, researchers reported a series of cases of bilateral concentric visual field constriction related to vigabatrin,<sup>3</sup> with a frequency of 52% in adults and 34% in children.<sup>1</sup> Although approximately 90% of cases are asymptomatic, severity can range from mild to severe, including potential compromise of central vision and reduced quality of life.<sup>2</sup>

Herein, we report a case of severe, fast-onset vigabatrin retinal toxicity in a pediatric patient.<sup>4</sup>

## CASE REPORT

A 13-year-old Hispanic girl with a long-standing history of refractory epilepsy since her second year of life presented with difficulties going down a staircase due to bilateral inferior scotomas. The patient had been prescribed vigabatrin 3 months earlier, and symptoms began within 3 weeks of use.

She had no prior visual complaints and a past medical history of prior ictal frequency of two seizures per week and approximately one status epilepticus per month. She was being treated with levetiracetam, lamotrigine, and lacosamide, but her seizures persisted, so she was started on vigabatrin initially at a dose of 500 mg twice daily and later 1,000 mg twice daily. The patient also reported obstructive sleep apnea with use of a continuous positive airway pressure machine at night.

The ophthalmic examination showed a VA of 20/20 OU, normal Ishihara plates in each eye, and 0.6 log units of an

afferent pupillary defect in her left eye. Motility and anterior segment examinations were normal in each eye. On dilated fundus examination, each optic nerve appeared normal, and a mottled pattern was noted in the midperipheral retina in each eye (Figure 1). Visual field testing demonstrated a concentric loss of sensitivity in the gray-scale with a concentric scotoma present in the mean and pattern deviation of each eye (Figure 2).

Optic nerve OCT demonstrated normal peripapillary retinal nerve fiber layer (pRNFL) and a mild thinning of the ganglion cell layer-inner plexiform layer (GCL-IPL)

## KEY TAKEAWAYS

- ▶ Vigabatrin, a drug used as an adjuvant therapy for refractory focal onset epilepsy and for the treatment of infantile spasms, can lead to retinal toxicity in some cases.
- ▶ Onset of retinal toxicity has been reported between 6 months to 5 years after initiating treatment, with a 5.3% risk of developing toxicity at 6 months in pediatric patients.
- ▶ Multifocal electroretinogram can be helpful in confirming a diagnosis of vigabatrin-related retinal toxicity.



Figure 1. Funduscopy of the right eye showed a mottled pattern in the midperipheral retina.

complex in each eye (Figure 3). Multifocal electroretinogram (mfERG) was decreased in P1 and N2 waves in the third, fourth, and fifth rings in each eye without electrical changes of the fovea. These results were deemed compatible with cone toxicity.

Vigabatrin was immediately discontinued, and clobazam was prescribed. The patient also underwent a left frontal lobotomy. At the 3-month follow-up visit, her visual acuity remained stable, and no further visual field changes were noted.

### VAVFL EXPLAINED

Vigabatrin-associated visual field loss (VAVFL) was first recognized approximately 9 years after the drug's approval.<sup>2</sup> Its toxic mechanism is not completely understood, but data suggest a multifactorial mechanism in which the selective deposition of vigabatrin in the retinal tissue reaches concentrations between five and 18 times of those in the brain.<sup>5</sup> This leads to an increase in GABA concentrations up to five times its normal value in the retina, which triggers an intense activation of GABA receptors, inducing excitotoxicity through an osmotic imbalance due to the entry of chlorine, sodium, and water inside the cell.<sup>5</sup> Decreased ocular blood flow and an increased production of reactive oxygen species also appears to be associated with VAVFL.<sup>5</sup> Other potential factors include the accumulation of ornithine due to a nonselective inhibition of ornithine transferase by vigabatrin and the depletion of taurine, which acts as an antioxidant in retinal tissue.<sup>5</sup>

The prevalence of vigabatrin retinal toxicity has been reported between 14% and 92%.<sup>6,7</sup> A systematic review by Maguire et al found a mean proportion of VAVFL of

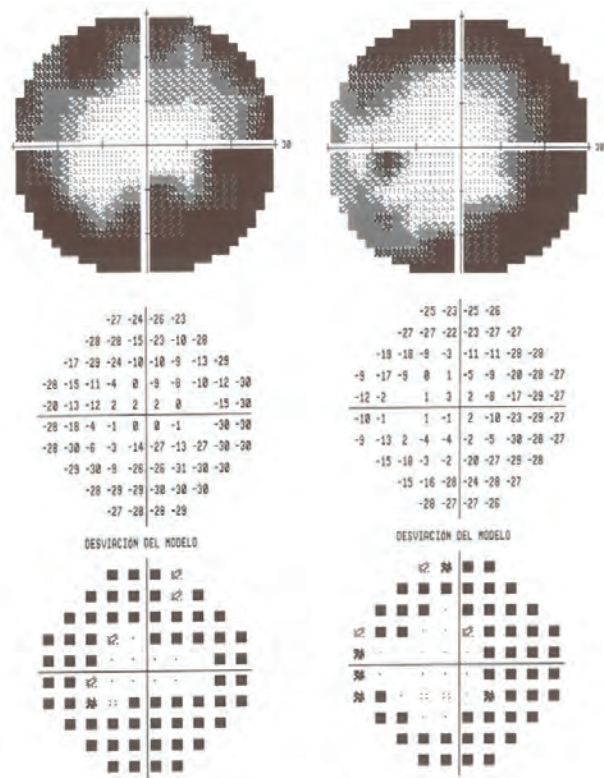


Figure 2. A 30-2 stimulus III SITA standard Humphrey visual field demonstrated a concentric loss of sensitivity in the grayscale with a concentric scotoma present in the mean and pattern deviation of each eye.

52% in adults and 34% in children compared with 7% in non-vigabatrin exposed patients.<sup>1</sup> Risk factors for the development of retinal toxicity include mean age, cumulative dose, and duration of treatment.<sup>1</sup>

Average onset of retinal toxicity has been reported between 6 months to 5 years after initiating treatment, with a 5.3% risk of developing toxicity at 6 months in pediatric patients.<sup>1-3,8</sup> To our knowledge, our report describes the earliest case of retinal toxicity only 3 weeks after starting vigabatrin.

Clinically, VAVFL manifests in perimetry as a bilateral concentric constriction of the visual field.<sup>1,2</sup> The deficit is variable in severity and has a facultative nasal preponderance that is deemed specific but not always present.<sup>2</sup> Many patients fail to perceive the scotomas, compensating with head movements until central vision is compromised; this “asymptomatic” presentation corresponds to 73% to 88% of those affected.<sup>1,2,6</sup> About 2% of patients experience severe compromise involving the central 30° of vision.<sup>2,6</sup>

The diagnosis of retinal toxicity depends on the identification of a bilateral, concentric constriction of the peripheral visual field.<sup>2</sup> Fundoscopic findings tend to be nonspecific, but some authors have described optic nerve head pallor, arterial narrowing, surface wrinkling

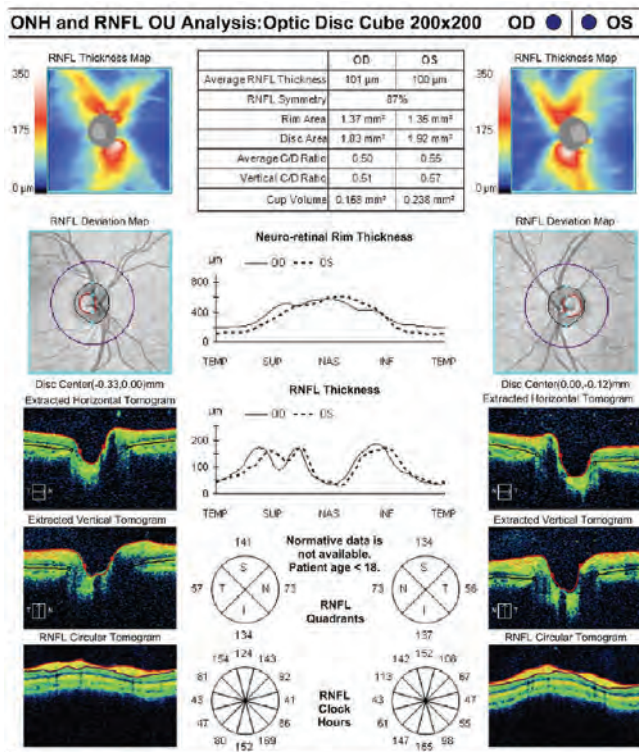


Figure 3. OCT of each eye showed normal pRNFL and mild GCL-IPL thinning.

retinopathy, irregular sheen at the macula, and abnormal pigmentation at the macula or peripheral retina.<sup>2</sup> Our patient had a midperipheral mottled pattern compatible with previously described findings.

OCT of the optic nerves may show a generalized attenuation of the pRNFL thickness with variable involvement of the upper, nasal, and lower quadrants; the temporal quadrant is usually respected.<sup>7,9</sup> OCT may be an alternative clinical tool for patients who cannot undergo perimetry; some authors have calculated a sensitivity between 66% and 100% for OCT findings.<sup>7,9</sup> Another pending challenge is establishing a set of standardized pRNFL values for pediatric populations.

Retinal toxicity can be further confirmed by mfERG.<sup>10</sup> The focal peripheral points demonstrate a decrease in amplitude, which is directly related to scotomas in the perimetry.<sup>10</sup> Moreover, in one study, up to 24% of pediatric control patients may have visual field disturbances even if they were not exposed to vigabatrin, while only those patients exposed to vigabatrin (n = 204) showed mfERG changes.<sup>10</sup>

### MONITOR THESE PATIENTS CLOSELY

Currently, there is no effective treatment for VAVFL, and the nature of its damage appears to be irreversible and nonprogressive once vigabatrin is suspended.<sup>2</sup> Some associations yet to be confirmed include the role of interactions with partial GABA agonists, such as

valproic acid, in the development of severe presentations. Vigabatrin retinal toxicity should be monitored in all patients using this drug, considering the idiosyncratic nature of the presentation and the potentially serious visual outcomes. ■

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# The Value of OCTA in Retinal Vascular Disease

Measuring retinal blood flow is easier than ever before, with new tools under investigation to further improve our ability to assess changes in the retinal vasculature.

By Sarah Aman, MD; Viet-Hoan Le, PhD; Ruikang K. Wang, PhD; and Amir H. Kashani, MD, PhD



OCT angiography (OCTA) has dramatically changed the landscape of retinal disease diagnosis because it allows clinicians to noninvasively evaluate early vascular changes at the capillary level in asymptomatic patients. This has significant clinical potential, as ischemic microangiopathies remain a leading cause of vision loss in developed countries.<sup>1</sup>

Here, we review the clinical utility of qualitative blood flow assessment in three major retinal diseases—diabetic retinopathy (DR), AMD, and central serous retinopathy (CSR)—and highlight evidence demonstrating the utility of additional blood flow quantification (Table).

## AN OVERVIEW OF OCTA

OCTA visualizes blood flow by detecting motion contrast of individual red blood cells. This technology has high axial resolution (ie, 5-10  $\mu\text{m}$  or better) and provides depth-resolved images of the retinal and choroidal vasculature at the capillary level, allowing clinicians to pinpoint the exact layer in which perfusion is present or absent.<sup>2</sup>

Currently, OCTA devices provide pseudocolor maps of retinal capillaries based on the presence or absence of red blood cell flow within a certain range of velocities (typically 0.3-3 mm/sec); they do not provide information about exact blood velocity in one region versus another. However, experimental OCT-based algorithms now allow quantification

of red blood cell velocity at the capillary level.<sup>3-5</sup> Known as *velocimetry*, these techniques take advantage of faster laser scanning speeds and more sophisticated scan patterns to understand disease onset and progression at a much more granular scale than standard OCTA (Figure). OCTA-based velocimetry has demonstrated that blood velocity varies across different retinal capillary beds, laying the foundation upon which abnormal blood flow—leading to diseases such as DR and others—can be categorized.<sup>3</sup>

## DIABETIC RETINOPATHY

DR is rooted in capillary nonperfusion, endothelial dysfunction, and autoregulatory failure.<sup>6,7</sup> Quantitative flow measurements have demonstrated a range of retinal blood flow alterations in patients with diabetes, even in the absence of overt retinopathy.<sup>8</sup> Doppler-based studies have demonstrated various changes in blood flow in the large retinal vessels among patients with diabetes but without retinopathy.<sup>9-12</sup> Other doppler-based studies have shown a reduction in retinal blood flow in eyes with severe nonproliferative DR (NPDR) and proliferative DR (PDR).<sup>13,14</sup> At the capillary level, OCTA studies show a decrease in vessel perfusion across the superficial and deep capillary plexuses correlating with disease severity and progression.<sup>15</sup> Even patients with minimal or no retinopathy demonstrate impaired capillary perfusion on OCTA.<sup>16,17</sup>

A recent study using OCTA-based second-generation variable interscan time analysis revealed an increase in the red blood cell velocity in the deep capillary plexus of

**TABLE. RETINAL BLOOD FLOW CHANGES IN RETINAL DISEASE**

Disease	Flow Changes	Potential Clinical Role
Diabetic Retinopathy	<ul style="list-style-type: none"> <li>• Early impaired capillary perfusion</li> <li>• Reduced capillary density, altered blood flow speed, and autoregulatory dysfunction in the deep capillary plexus</li> </ul>	<ul style="list-style-type: none"> <li>• Monitoring treatment response (anti-VEGF injection, panretinal photocoagulation)</li> <li>• Identifying preclinical high-risk eyes</li> </ul>
AMD	<ul style="list-style-type: none"> <li>• Choriocapillaris hypoperfusion in early/intermediate AMD, with reduced perfusion predicting progression to geographic atrophy</li> <li>• Altered macular neovascularization (MNV) hemodynamics in active vs quiescent lesions</li> </ul>	<ul style="list-style-type: none"> <li>• Early detection before visible atrophy</li> <li>• Potential prognostic marker for geographic atrophy progression</li> <li>• Evaluating treatment response and recurrence risk in MNV</li> </ul>
Central Serous Retinopathy (CSR)	<ul style="list-style-type: none"> <li>• Choroidal hyperperfusion and hyperpermeability in acute and chronic CSR, especially in the vortex venous system</li> <li>• Choroidal flow normalization after therapy</li> <li>• Detection of MNV</li> </ul>	<ul style="list-style-type: none"> <li>• Distinguishing acute vs chronic CSR</li> <li>• Persistent hyperperfusion as a biomarker for chronic CSR and risk of recurrence</li> <li>• Guiding choice of therapy with evidence of flow normalization with photodynamic or mineralocorticoid therapy</li> <li>• Tracking recovery</li> </ul>

patients with DR, which correlated with a decreased vessel density in patients with NPDR.<sup>18</sup> Longitudinal work also indicates that eyes with early flow deficits, especially in the deep retinal layer, are more likely to progress to vision-threatening stages of DR, including PDR.<sup>19-21</sup>

### Clinical Applications In DR

For clinicians, the most compelling potential of blood flow measurement in DR lies in its ability to guide both early diagnosis and personalized care. By identifying subtle flow deficits before retinopathy becomes apparent, clinicians can stratify which patients are at highest risk for progression, allowing more targeted surveillance and earlier intervention.

Beyond screening, new quantitative flow metrics from velocimetry-based algorithms will provide a useful biomarker of treatment response for novel early interventions. For example, flow changes measured after anti-VEGF therapy or panretinal photocoagulation have been shown to correlate with anatomic and functional improvement.<sup>22,23</sup>

Finally, offering patients a concrete demonstration of early microvascular dysfunction could motivate tighter systemic control of diabetes.

### MACULAR DEGENERATION

A central feature of early AMD is loss of choriocapillaris perfusion, which impairs metabolic support to the retinal pigment epithelium (RPE) and photoreceptors.<sup>24</sup> In wet AMD, aberrant macular neovascularization (MNV) reflects a maladaptive response to hypoxia and vascular insufficiency.<sup>25</sup>

Studies using OCTA have shown that choriocapillaris, choroidal, and retinal blood flow alterations are detectable in early and intermediate AMD, often preceding active MNV or atrophy.<sup>26-29</sup> In addition, reduced choriocapillaris perfusion is associated with faster progression to geographic atrophy (GA), suggesting it may serve as a

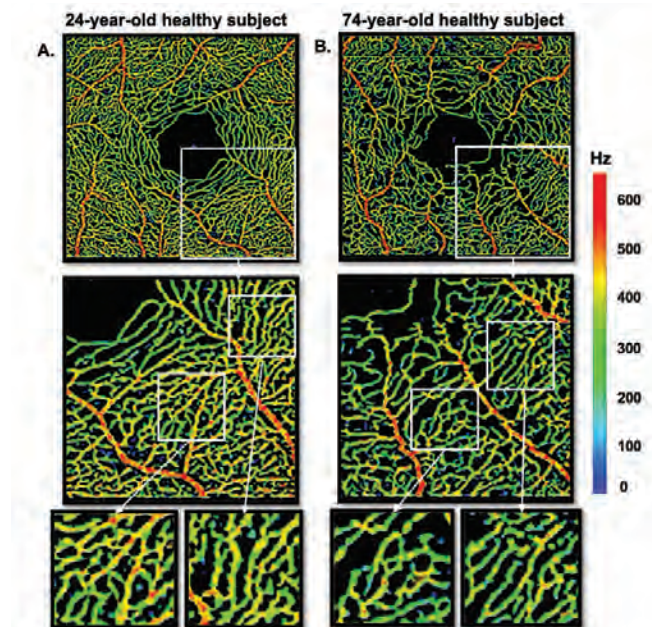


Figure. These pseudocolor flow velocity maps illustrate the age-related differences in retinal capillary flow within the superficial retinal layer. A 24-year-old healthy subject demonstrates higher capillary flow velocities, represented by higher color saturation (A), whereas a 74-year-old healthy subject shows lower overall flow (B), with differences most evident at the capillary level. Magnified views highlight the flow patterns within individual capillary networks. The color bar indicates mean frequency in Hertz (Hz), used as a surrogate measure of capillary flow velocity. Adapted with permission from Aman et al.<sup>3</sup>

valuable prognostic biomarker.<sup>30-32</sup> OCTA has been used to detect MNV before the presence of exudation in subjects with clinically apparent and intermediate AMD.<sup>33,34</sup> In wet AMD, OCTA provides unique insight into MNV hemodynamics, where flow patterns can distinguish potentially active lesions from quiescent subretinal fibrosis,<sup>35</sup> and where lower choroidal perfusion can serve as a risk factor for MNV development in the fellow eye of patients with

## KEY TAKEAWAYS

- ▶ Subclinical changes in retinal and choroidal blood flow are qualitatively detectable using commercially available OCT angiography (OCTA).
- ▶ Quantitative blood flow measurements obtained from non-FDA cleared research devices have demonstrated correlations with disease severity, progression, and treatment response in studies of diabetic retinopathy, geographic atrophy risk in AMD, and central serous retinopathy.
- ▶ OCTA-based velocimetry and variable interscan time analysis represent emerging strategies for quantitative assessment of capillary perfusion.

unilateral MNV.<sup>36</sup> Anti-VEGF therapy also alters MNV perfusion, and flow changes measured on OCTA correlate with treatment efficacy and recurrence risk.<sup>37-39</sup>

### Clinical Applications in AMD

Retinal blood flow measurement enables early detection of AMD by revealing subtle choriocapillaris flow deficits, which has the potential to flag high-risk eyes for closer monitoring of MNV or RPE loss.

In addition, flow mapping provides a functional biomarker of treatment response. By capturing MNV perfusion changes alongside structural OCT metrics, clinicians can make more refined decisions about retreatment and long-term management. Clinicians can also monitor patients with nonexudative MNV more closely for progression to active exudation.

Information about blood flow abnormalities holds value in prognostic counseling, as they correlate with rates of atrophy progression and visual decline. For example, reduced choriocapillaris flow deficits on OCTA predict faster GA enlargement,<sup>40</sup> and baseline OCTA parameters such as fractal dimension and blood flow surface area are associated with treatment burden in wet AMD.<sup>41</sup>

### CENTRAL SEROUS RETINOPATHY

CSR is thought to occur due to dysregulation of the choroidal circulation. The hallmark is a state of choroidal hyperperfusion and hyperpermeability, which leads to leakage through the RPE and subsequent accumulation of subretinal fluid.<sup>42-44</sup>

Laser speckle flowgraphy studies have consistently shown elevated choroidal blood flow in acute CSR compared with unaffected eyes, with levels that normalize following spontaneous resolution or treatment.<sup>45-47</sup> OCT and OCTA have further demonstrated evidence of choroidal vascular

dysregulation, with dilated choroidal vessels and focal zones of hyperperfusion in both acute and chronic cases.<sup>43,48-51</sup>

Adaptive optics (AO) imaging has helped clarify regional alterations in choroidal perfusion, with evidence of significant RPE changes.<sup>52</sup> OCT has also demonstrated evidence of an asymmetric vortex venous system in CSR eyes, with relative hyperperfusion in all vortex veins.<sup>53</sup> Importantly, persistent hyperperfusion is associated with disease chronicity and a higher risk of recurrence.<sup>45</sup>

Lastly, OCTA is probably the most useful tool to assess the presence of MNV in chronic CSR lesions, while fluorescein angiography and ICG angiography often show diffuse areas of non-specific staining.

### Clinical Applications in CSR

Blood flow assessment in CSR may aid in distinguishing acute from chronic disease, and quantitative flow measures could guide treatment selection. For example, normalization of choroidal hyperperfusion following photodynamic therapy has been observed, reinforcing its role in restoring hemodynamic balance.<sup>54-56</sup> This dynamic biomarker could allow physicians to monitor therapeutic response more directly than structural OCT alone. Flow abnormalities could serve as prognostic indicators, identifying patients more likely to experience recurrent or persistent subretinal fluid, and thereby guiding closer follow-up. In the future, integrating choroidal flow assessment into CSR care may provide a more tailored, patient-specific approach to what has historically been a challenging condition to manage.

### BARRIERS TO CLINICAL INTEGRATION

Despite significant progress in imaging technologies, the clinical adoption of quantitative retinal blood flow measurement remains limited. A major barrier is inter-device variability, with various devices differing in acquisition principles, algorithms, output parameters, and measurement sensitivity. This makes it difficult to compare results across platforms or establish standardized clinical cutoffs.

Other challenging caveats include the lack of robust normative databases and the need for standardized metrics. For example, studies use a variety of parameters, such as vessel density, perfusion density, capillary flux, red blood cell velocity, and mean blur rate, all of which are often defined differently between research groups. Such heterogeneity has led to conflicting results in the literature.

To see a listing of current devices, their field of view, availability, and advantages and limitations, read this article online at [retinatoday.com](http://retinatoday.com).



## THE BENEFITS OF OCTA IN THE CLINIC

OCTA (and its velocity-based extensions) is reaching a level of maturity that allows reliable, reproducible data collection in clinical settings. Still, challenges remain. Inter-device variability, a lack of normative databases, and workflow integration are significant barriers to adoption.

Despite these limitations, clinical trials incorporating flow endpoints, AI-driven image analysis, and growing interest in multimodal integration are all accelerating the pathway to clinical translation. ■

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# Clinical Applications of Microscope-Integrated OCT

Recent advances have improved the utility of intraoperative visualization, with more innovation on the way.

By Bani Aguirre, MD, MPH; Anjali Saini, BS; Vahid Ownagh, MD; and Lejla Vajzovic, MD



The high resolution and noninvasive nature of OCT have established it as a cornerstone of retinal disease imaging. Recognizing the diagnostic value of this tool, surgeons have sought to incorporate it into surgical settings to enable real-time intraoperative feedback. Continuous investigation has led to the development of intraoperative

microscope-integrated OCT (MIOCT), designed to integrate the optical path of the spectral-domain OCT (SD-OCT) scanner into the surgical microscope, enabling real-time imaging of active vitreoretinal surgical maneuvers.<sup>1-3</sup> The feasibility and advantages of MIOCT in macular surgery were reported in a 3-year study, in which information from the device influenced surgical decisions in 29% of cases.<sup>4</sup>

Today, several commercially available systems offer MIOCT for vitreoretinal surgery, differing in the degree of OCT integration and 3D visualization capabilities. Three SD-MIOCT systems provide real-time cross-sectional B-scan imaging: the Zeiss Rescan 700, the Haag-Streit iOCT, and the Leica Proveo 8 with EnFocus, which offers SD-OCT with en face imaging. The Artevo 800 digital microscope (Carl Zeiss Meditec) and Ngenuity (Alcon) 3D visualization system advance this further by integrating SD-OCT with a stereoscopic 4K heads-up display on a single platform, enabling simultaneous real-time OCT imaging and 3D visualization of the surgical field. Notably, none of these systems currently support real-time volumetric quantification of intraocular structures.

However, in the research domain, next-generation

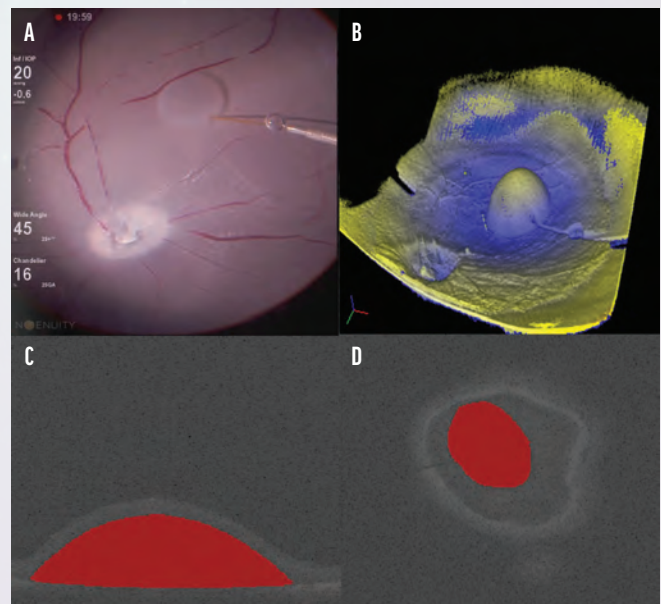


Figure 1. This is the microscope view with the Ngenuity (Alcon) 3D visualization system (A) with a 3D MIOCT volume reconstruction during bleb formation (B). The system provides segmentation of the MIOCT bleb B-scans (C) and a coronal view of the bleb (D).

models have introduced swept-source technology and 4D volumetric imaging.<sup>5</sup> These enhancements allow dynamic visualization of residual membranes, foveal deformations, and subretinal fluid quantification, resulting in more precise real-time surgical adjustments.<sup>6-9</sup>

Furthermore, MIOCT has facilitated the integration of novel surgical approaches, including subretinal gene therapy delivery, where precise cannula placement and bleb formation are critical for therapeutic efficiency.<sup>10</sup> Intraoperative OCT has also proven valuable in educational settings, providing retina fellows with immediate visual

Images courtesy of Robert Toub

feedback while they practice advanced surgical procedures.

The rapid evolution of MIOCT continues to redefine standards in vitreoretinal surgery, connecting diagnostic imaging with surgical execution to enhance safety and precision. In this article, we review the clinical applications and future directions of MIOCT to highlight its transformative role in retinal surgery, including real-time volume estimation and image fusion of color microscopy.

## VOLUME ESTIMATION

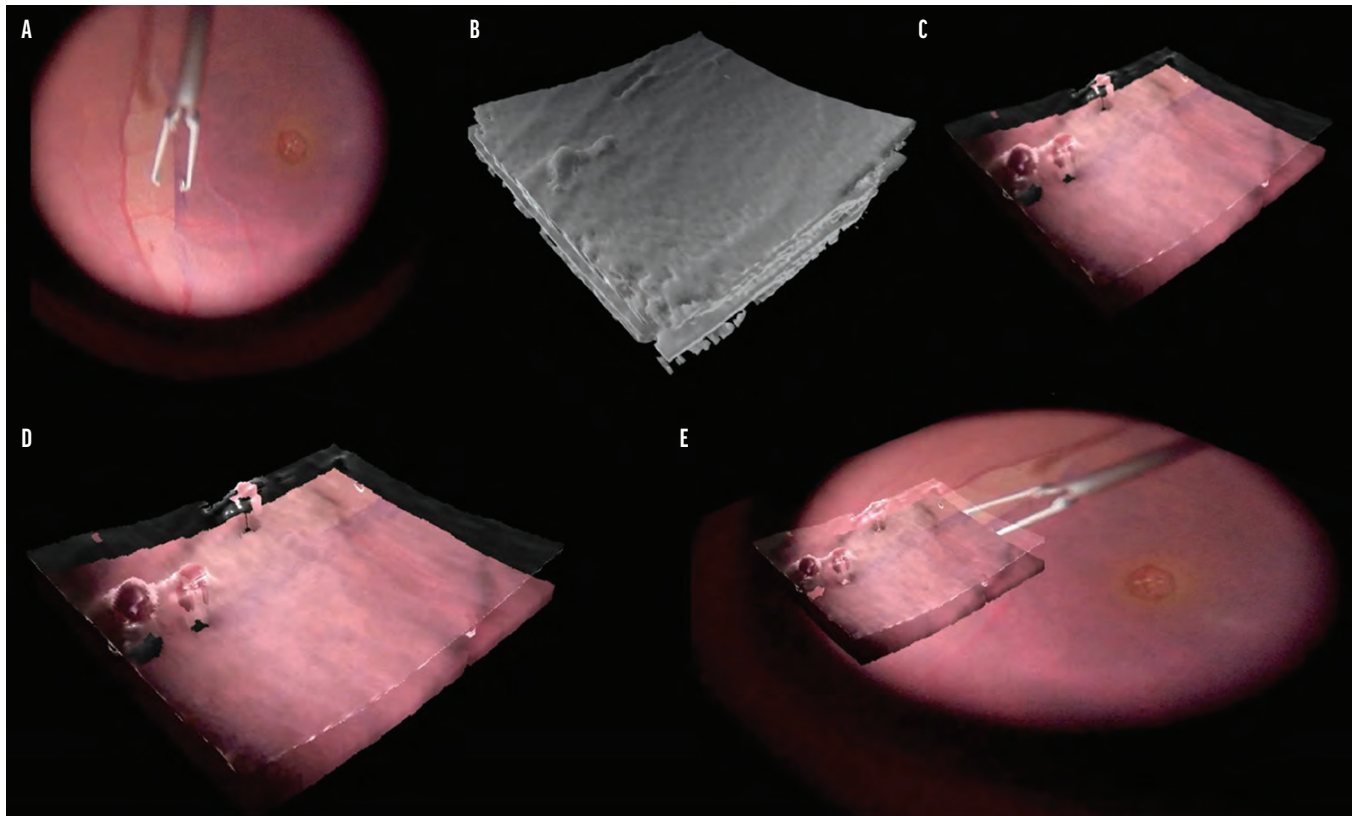
Swept-source MIOCT (SS-MIOCT), such as the investigational Duke MIOCT, has addressed key limitations of SD-MIOCT—most notably depth penetration and scanning speed—enabling the real-time, high-resolution volumetric imaging of subretinal blebs.<sup>11</sup> This system, which has been validated in phantom eyes and in vitro, allows for direct 4D visualization of subretinal blebs and suprachoroidal cannulas, and, through voxel dimension calibration, enables a quantitative assessment of segmented scans (Figure 1).<sup>12,13</sup> Moreover, The Duke MIOCT is currently being used in human clinical trials for subretinal bleb visualization and volumetric quantification, providing real-time volumetric assessment of subretinal structures.

This advance has significantly deepened our

## KEY TAKEAWAYS

- ▶ The evolution of intraoperative microscope-integrated OCT (MIOCT) connects diagnostic imaging with surgical execution to enhance safety and precision.
- ▶ In the research setting, swept-source MIOCT technology and 4D volumetric imaging allow dynamic visualization of residual membranes, subretinal fluid, and foveal deformations.
- ▶ In the future, transitioning from side-by-side displays to unified, single-channel visualization platforms will provide surgeons with enhanced depth perception and spatial orientation.

understanding of surgical precision in subretinal gene therapy. Hsu et al compared bleb volumes in porcine eyes measured with SS-MIOCT against the intended injection volume and the surgeon's estimated leakage. In eyes with minimal leakage, surgeons successfully delivered an average



Images courtesy of Robert Trout

Figure 2. The digital microscope view (A) has a corresponding volume render (B) that is integrated to generate a single fused visualization (C). The rendered image (D) is then fused with the 2D image in the periphery (E). Image adapted from Trout et al.<sup>17</sup>

of  $32 \pm 12.5 \mu\text{L}$  of the intended  $50 \mu\text{L}$ . To confirm the system's precision, a validation study was conducted in model eyes using an object of known volume. This study demonstrated an accuracy of  $1.0 \mu\text{L}$  (6% of the measured volume) with no statistically significant variation across different imaging settings.<sup>13</sup>

Following this work, Sastry et al sought to improve SS-MIOCT quantification by implementing a widefield viewing system capable of capturing larger or more peripheral blebs. Using a suprachoroidal subretinal cannula, the team created subretinal blebs in porcine eyes and demonstrated that 82.48% of the intended injection volume was accurately delivered in ex vivo experiments. Validation studies using ceramic spheres confirmed the accuracy of image-based volume measurements, showing precision to  $\pm 0.029 \mu\text{L}$  for objects imaged over the posterior pole and  $\pm 0.025 \mu\text{L}$  for those imaged over the peripheral retina.<sup>12</sup>

Recently, Valikodath et al conducted the first human study to implement MIOCT for volumetric bleb measurement. Using an investigational intraoperative MIOCT system with a modified widefield noncontact indirect viewing platform, the team quantified subretinal tissue plasminogen activator delivery in three patients with submacular hemorrhage. This proof-of-concept study revealed discrepancies of 9% to 64% between the intended and actual injection volumes, likely driven by variability in bleb morphology and leakage at the injection site.<sup>10</sup>

These studies have shown that MIOCT can enhance the safety, accuracy, and evaluation of subretinal drug delivery.<sup>10</sup> In addition, these insights have motivated the development of next-generation devices that facilitate the more efficient delivery of therapeutic agents and reduce the steep learning curve for surgeons.<sup>14</sup> Additionally, quantification techniques will allow us to understand the dynamics and technique modifications that lead to larger blebs and less leakage.<sup>15</sup>

## IMAGE FUSION OF COLOR MICROSCOPY

The next transformative event for user-centered surgical visualization is the integration and perception of intraoperative visual information. By transitioning from traditional side-by-side displays to unified, single-channel visualization platforms, surgeons will benefit from enhanced depth perception and spatial orientation (Figure 2).

Our team used boundary-based shading to further refine 3D structural details and adapted virtual reality interfaces to better delineate critical retinal layers. In parallel, these adaptations offer a more immersive and flexible visualization for surgical navigation.<sup>16</sup>

As we continue to develop this technology and implement features such as retinal thickness maps, we will be able to study the tissue–tool interactions and surface features that lead to optimized surgical outcomes.<sup>17</sup> ■

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# Imaging Epiretinal Proliferation Using OCT

En face OCT-based identification of proliferative changes may guide surgical strategies in full-thickness macular holes.

By Kotaro Tsuboi, MD, PhD



Epiretinal proliferation (EP), first described by Witkin et al in 2006, is a medium-reflective material that fills the space between the inner border of the epiretinal membrane (ERM) and the retinal nerve fiber layer on spectral-domain OCT (Figure 1A).<sup>1</sup> EP is frequently observed in eyes with lamellar macular hole (LMH) and full-thickness macular hole (FTMH).<sup>2</sup> When EP is identified with preoperative OCT, surgeons often encounter sticky yellowish tissues around the MH during surgery (Figure 1B).

Here, I discuss the value of EP detection with en face OCT and propose its inclusion in preoperative imaging for MHs.

## WHY EPIRETINAL PROLIFERATION MATTERS

The presence of EP is an important biomarker for determining surgical strategy. For eyes with LMH, an EP embedding technique improves vision and reduces the risk of postoperative FTMH compared with conventional internal limiting membrane (ILM) peeling alone.<sup>3</sup> In eyes with FTMH and EP, ILM peeling is recommended because of the improvement in the primary closure rate.<sup>4</sup> Additionally, our recent paper demonstrated that EP sparing in eyes with FTMH is beneficial in terms of visual and anatomic outcomes.<sup>5</sup>

In our daily clinic, clinicians perform cross-sectional OCT to diagnose and classify FTMH. Thus, preoperative cross-sectional OCT is the standard technique for detecting EP. However, in some cases, preoperative cross-sectional OCT images do not reveal EP, but yellowish tissues around the MH can be identified during the surgery (Figure 2). To address this limitation, we need more precise examination techniques to identify EP. Recently, Grondin et al demonstrated that high-resolution en face OCT can

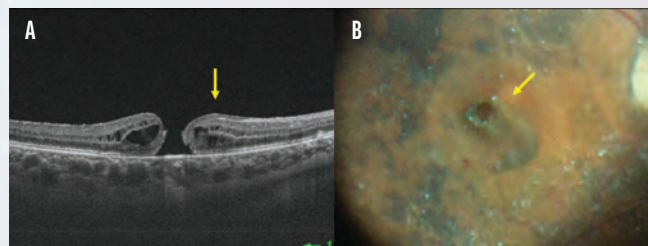


Figure 1. This preoperative cross-sectional OCT image demonstrates EP as a medium-reflective material (arrow) located between the inner border of the ERM and the retinal nerve fiber layer (A). Intraoperatively, EP is seen as a sticky yellowish tissue contiguous to the MH during membrane peeling (B, arrow).

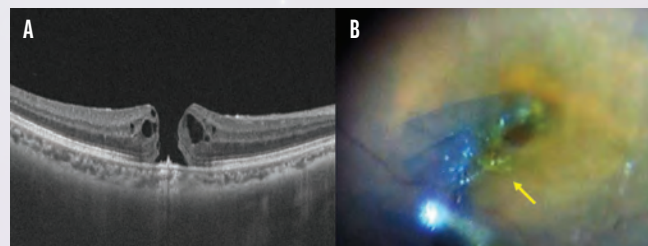


Figure 2. This patient's preoperative cross-sectional OCT image did not indicate the presence of EP (A), although the surgeon encountered the characteristic yellowish tissue consistent with EP during ILM peeling around the MH, as shown in the intraoperative image (B, arrow).

visualize a subclinical proliferative change on the retinal surface that later developed into contractile ERM.<sup>6</sup> We then used this technique in eyes with FTMH to identify EP.

## DETECTING PROLIFERATIVE CHANGE

En face OCT is generated by reconstructing hundreds of cross-sectional OCT images from volumetric OCT data. Clinicians often obtain an OCT angiography (OCTA)

# IMAGING AND VISUALIZATION IN RETINA

scan for generating en face OCT because the OCTA scan protocol provides high-density 3D data, enabling high-resolution en face OCT images. En face OCT is created by projecting OCT signals between predefined segmentation boundaries onto one plane. In Figure 3, the original superficial slab of OCT image is defined as a depth range between ILM to inner plexiform layer (IPL) of  $-9\ \mu\text{m}$  (ie,  $9\ \mu\text{m}$  above the IPL). The superficial slab does not illustrate any abnormalities (Figure 3A). Most OCT devices allow customizable segmentation settings to illustrate layer-specific retinal pathology. When we set a custom slab defined as ILM  $+3\ \mu\text{m}$  to  $+9\ \mu\text{m}$ , en face OCT clearly visualizes a subclinical proliferative change barely seen on en face OCT with the superficial slab or cross-sectional OCT image (Figure 3B, arrow). With this technique, we found that one quarter of eyes with FTMH have subtle proliferative change around the hole, termed *preretinal abnormal tissue* (PAT).<sup>7</sup>

Because brilliant blue G (BBG) selectively stains ILM, the macular area is completely stained if there is no ERM or PAT (Figure 4A). However, surgeons often observe nonstaining areas (Figure 4B), and the nonstaining pattern is similar to the distribution of PAT on en face OCT, as illustrated by the corresponding fundus appearance and en face OCT findings in representative cases. Steel et al demonstrated that there

## KEY TAKEAWAYS

- ▶ The presence of epiretinal proliferation is an important biomarker for determining surgical strategy when treating lamellar macular holes and full-thickness macular holes.
- ▶ Researchers can capture en face OCT imaging with customized segmentation settings to clearly visualize a subclinical proliferative change barely seen on traditional en face OCT with the superficial slab or cross-sectional image, termed *preretinal abnormal tissue*.
- ▶ The author proposes incorporating en face OCT imaging to improve the classification of full-thickness macular holes and identify preretinal abnormal tissue preoperatively.
- ▶ The author also recommends membrane peeling when preretinal abnormal tissue is detected on en face OCT.

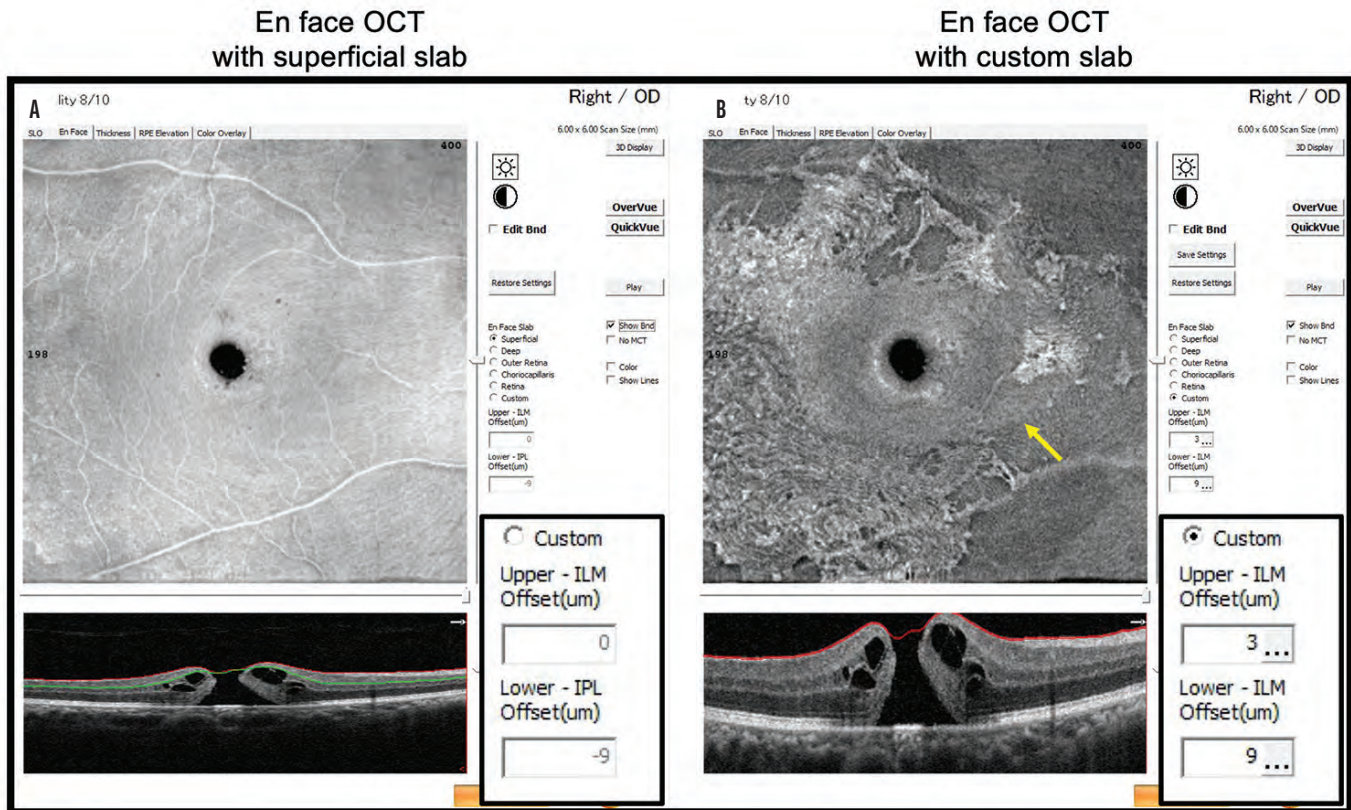
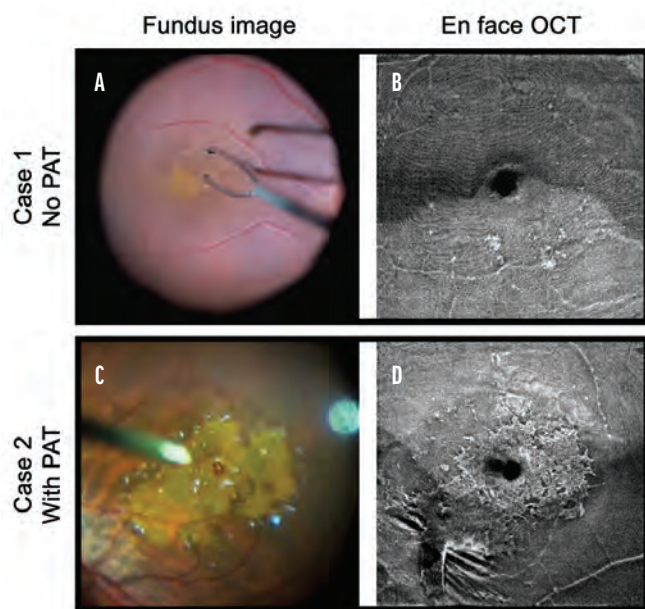


Figure 3. This en face OCT image (XR Avanti, Optovue), generated using the original superficial slab (ILM to IPL,  $-9\ \mu\text{m}$ ), show no apparent abnormality (A). However, the en face OCT image obtained using a custom slab (ILM,  $+3\ \mu\text{m}$  to  $+9\ \mu\text{m}$ ) clearly shows subtle PAT surrounding the MH (B).



**Figure 4.** This intraoperative fundus image shows uniform staining around the MH (A). The corresponding en face OCT image obtained with a custom slab (ILM +3  $\mu$ m to +9  $\mu$ m) demonstrates the absence of PAT surrounding the hole (B). The intraoperative fundus image of another eye demonstrates an area of nonstaining around the MH (PAT; C). The corresponding en face OCT image reveals PAT distributed around the MH (D).

are a variety of nonstaining patterns around the hole using BBG, and eyes with incomplete BBG staining pattern had more multicellular layers and new collagen on the ILM.<sup>8</sup> This suggests that BBG staining pattern may help to detect subclinical proliferative change in eyes with FTMH.

## IDENTIFYING EP WITH EN FACE OCT

My team conducted a retrospective study to assess the detection of EP using BBG staining patterns and en face OCT.<sup>9</sup> We defined the presence of EP as yellowish tissues contiguous to the hole observed during membrane peeling. In a total of 110 eyes, preoperative cross-sectional OCT revealed EP in 26 eyes (24%); however, we identified EP intraoperatively, termed *surgical EP*, in 30 eyes (27%), indicating that preoperative cross-sectional OCT overlooked surgical EP in approximately 10% of eyes.<sup>9</sup>

In four cases with this discrepancy, we observed peri-MH nonstaining patterns (Figure 4C and D). Using surgical EP as the ground truth, the presence of peri-MH nonstaining showed a sensitivity of 100% and a specificity of 89% for detecting EP. This suggests that if no nonstaining areas are observed after BBG application, the presence of EP is unlikely. When we analyzed eyes with peri-MH nonstaining, those with surgical EP showed a significantly larger average nonstaining area than eyes without surgical EP ( $2.8 \pm 1$  disc diameters [DD] vs  $1.4 \pm 0.9$  DD,  $P < .001$ ).

In 55 eyes with available preoperative en face OCT, 37 eyes had no PAT around the hole, whereas 18 eyes

showed PAT. Using surgical EP as the ground truth, the sensitivity of PAT on en face OCT for detecting surgical EP was 100%, with a specificity of 84%. The area of peri-MH PAT was significantly larger in eyes with surgical EP than in eyes without surgical EP ( $18.8 \pm 11.2$  mm<sup>2</sup> vs  $3.4 \pm 2.5$  mm<sup>2</sup>,  $P = .0029$ ). These results suggest that eyes without PAT are less likely to have EP around the hole.

## NEXT STEPS IN RESEARCH AND THE OR

Based on our findings, we propose that incorporating en face OCT may improve the classification of FTMH. Because the presence of PAT likely reflects EP or subclinical membrane formation, membrane and ILM peeling would be recommended when PAT is detected on en face OCT.

An important remaining question is whether ILM peeling is truly necessary in eyes with FTMH without PAT. Although ILM peeling improves the primary MH closure rate by approximately 20%, a recent meta-analysis showed that when closure is successfully achieved, eyes without ILM peeling have better visual outcomes than those with ILM peeling.<sup>10</sup> We hypothesize that in the absence of PAT, MHs may close successfully without ILM peeling.

We reported preliminary data at the 2025 ASRS meeting showing that in eyes without PAT and with non-large MHs (< 500  $\mu$ m), the non-ILM peeling group achieved closure rates comparable with those of the ILM peeling group.<sup>11</sup> These findings support the potential value of a new en face OCT-based classification, which warrants further prospective validation. ■

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# Widefield OCT: Extending Structural Imaging into the Periphery

These new tools are improving our view.

By Alberto Quarta, MD; Ceren Soylu, MD; and Srinivas R. Sadda, MD, FARVO



Widefield OCT (WF-OCT) and wide-coverage OCT extend our structural and vascular assessment

well beyond the central 30° to 50° field of conventional OCT, addressing a critical need when diagnosing and monitoring diseases where peripheral pathology drives clinical decision making.

Enabled by swept-source architectures (~1,050 nm), high A-scan rates, optimized beam optics, eye tracking, motion correction, and montaging algorithms, these systems deliver expanded scan areas with deep penetration and high signal-to-noise ratios. WF-OCT angiography (OCTA) further permits noninvasive visualization of peripheral nonperfusion and microvascular remodeling.

Clinically, WF-OCT supports detection and monitoring of diabetic retinopathy, retinal vein occlusions, uveitis, peripheral vitreoretinal interface disorders, and peripheral degeneration by directly visualizing retinal thickness profiles, tractional changes, breaks, and neovascular complexes across a broader anatomical region.

Current WF-OCT systems include the following (Table):

**Optos Silverstone RGB.** This tool combines approximately 200° ultra-widefield scanning laser ophthalmoscopy with guided swept-source OCT for targeted peripheral B-scans.

**Canon Xephilio OCT-S1.** This device offers wide single-capture swept-source scans up to approximately 23 mm with high speed and AI-assisted OCTA.

**Intalight DREAM OCT.** This device was granted a CE

mark in Europe with FDA approval pending. Along with the emerging TowardPi platforms, it provides very high-speed swept-source and broad scan fields.

Additional wide-coverage approaches include the Optos MonacoPro with integrated spectral-domain OCT and ultra-WF imaging, the Heidelberg Spectralis + WF imaging module and ultra-WF OCTA module, and multimodal platforms such as the Nidek Mirante scanning laser ophthalmoscope/OCT that combines ultra-WF fundus capture with wide area OCT/OCTA.

## IMAGING WHERE YOU NEED IT

These platforms enhance our ability to image the retina, allowing better diagnosis and monitoring of conditions with peripheral changes. As innovation in this area continues, we look forward to even faster devices with higher resolution, increased automation, and more detailed analytics. ■

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**TABLE. CURRENTLY AVAILABLE WIDEFIELD AND ULTRA-WIDEFIELD OCT PLATFORMS**

System	Widefield Approach	OCT Details	Speed (A-Scan Rate)	Max Single-Capture Width/Angle (Claimed <sup>1-9</sup> )	Montage/Expanded Coverage	OCTA	Practical Strengths
Optos Silverstone RGB <sup>1</sup>	True color cSLO UWF (optomap) + guided OCT to periphery	Guided SS-OCT, 1,050 nm wavelength, < 7 µm and < 20 µm integrated with 200° optomap imaging	Up to 100k A-scans/sec	200° single-shot optomap; OCT guided to peripheral lesions	Peripheral targeting via UWF guidance	Not yet available	Best "see-periphery-then-scan-it" workflow via UWF guidance
Optos MonacoPro <sup>2</sup>	UWF cSLO pseudocolor fundus image + integrated OCT	SD-OCT (integrated), 840 nm, < 7 µm and < 20 µm	Up to 70k A-scans/sec	200° optomap imaging; OCT described as ~40° views	Not primarily montage-based	Not highlighted as core feature	Integrated UWF + OCT for macula/ONH/peripheral targeting
Canon Xephilio OCT-S1 <sup>3</sup>	True wide single-capture OCT (large scan geometry)	SS-OCT, 1,060 nm, 8 µm and 30 µm	100k A-scans/sec	Up to 23 mm single scan (~80°)	Wide coverage without montage for posterior/midperipheral view	Yes	Excellent "big single scan" structural + OCTA workflow
Intalight DREAM OCT <sup>4,5</sup>	Ultra-wide single-scan OCT/OCTA + auto montage	SS-OCT, 1,050 nm, 3.8 µm and 10 µm	Up to 400k A-scans/sec	26 mm × 21 mm single scan (~130°)	Auto montage to ~200°	Yes	Very large structural/OCTA capture; montage toward more panretinal coverage
TowardPi BMizar (BM-400K) <sup>6</sup>	UWF full-range SS-OCT/OCTA	SS-OCT, 1,060 nm, ≤ 6 µm and 10 µm "full-range" UWF SS-OCTA positioning	400k A-scans/sec	120° UWF full-range SS-OCTA in ~7 to 15 sec	Large areas via montage	Yes	Designed for very wide OCTA + fast acquisition
Heidelberg Spectralis + Widefield Imaging Module <sup>7</sup>	cSLO widefield fundus + OCT (module-based)	Module expands OCT + fundus modalities	Not specified	55° FOV for fundus imaging and OCT	Panning/steering and multimodal capture; can extend region with technique-dependent mosaics	Depends on system configuration	High-quality multimodal imaging with a defined 55° OCT-enabled widefield module
Heidelberg Spectralis + UWF Angiography Module <sup>8</sup>	cSLO UWF angiography optics (module-based)	UWF angiography module	Not specified	102°	Can be combined with technique-dependent mosaics for peripheral documentation	Yes; OCT depends on configuration/workflow	Strong for wide OCTA; WF-OCT is best represented by the 55° module
Nidek Mirante SLO/OCT <sup>9</sup>	UWF cSLO + integrated OCT workflow	Multimodal SLO/SD-OCT platform, 880 nm, 7 µm and 20 µm (widefield adapter)	Up to 85k A-scans/sec	Up to 163° UWF SLO with widefield adapter	Widefield is primarily via SLO FOV; OCT coverage described as part of SLO/OCT combo	Depends on configuration	Strong multimodal UWF SLO context with integrated OCT capability

Abbreviations: cSLO, confocal scanning laser ophthalmoscopy; FOV, field of view; OCTA, OCT angiography; ONH, optic nerve head; SD-OCT, spectral-domain OCT; SS-OCT, swept-source OCT; UWF, ultra-widefield.

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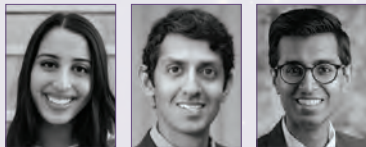
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# OR Tech Update: 3D Displays, AI, and Robotics

New visualization tools are expanding what's possible in the OR.

By Kareena Chawla, BS; Jayanth Sridhar, MD; and Prashant D. Tailor, MD



The clinical integration of 3D digital visualization, AI, and robotics is reshaping the surgical experience for both

patients and surgeons, from preoperative forecasting models that guide patient counseling to technologies that enhance precision and efficiency in the OR. Together, these innovations are redefining the modern ophthalmic workflow, linking data-driven prediction with real-time intraoperative performance. Here, we review the current evidence supporting the use of heads-up display systems (HUDS) in the OR, intraoperative AI, and robotic-assisted surgical techniques.

## VISUALIZATION IN THE RETINA OR

HUDS—such as the Artevo 800 (Carl Zeiss Meditec) and Ngenuity (Alcon)—have emerged as an important alternative to standard operating microscopes (SOMs), offering surgeons a customizable 3D digital view of the operative field with superior ergonomics and enhanced depth perception (Figure). Moreover, their shared-screen capability enables real-time telementoring, supporting the growing evidence for remote proctoring and 3D telesurgery as effective tools for ophthalmic education.<sup>1</sup>

## Performance and Learning Curve

Comparative studies suggest that HUDS can deliver surgical outcomes comparable to those of SOMs, but with distinct differences in ergonomics, visualization, and learning curves.<sup>2-4</sup> In a prospective comparative cohort, Kelkar et al evaluated 342 phacoemulsification cases performed with the Artevo 800 (n = 100) and the OPMI Lumera 700 SOM (n = 242). Surgical times were significantly longer with the



Figure. 3D HUDS enable shared viewing for the surgical team while enhancing depth perception, precision, and ergonomics.

HUDS than the SOM ( $8.4 \pm 2.1$  min vs  $6.5 \pm 1.8$  min), but complication rates remained low and similar (2% vs 2.5%).<sup>4</sup> Importantly, all complications in the HUDS group occurred during the first 50% of cases,<sup>4</sup> illustrating the learning curve with these systems.

In a vitreoretinal surgery study of 241 consecutive cases, surgical duration was similar between HUDS and conventional microscopy ( $45.5 \pm 20.1$  vs  $46.0 \pm 19.8$  minutes), with comparable complication and anatomic outcomes, including 3-month retinal detachment recurrence (10% vs 18%) and macular hole closure rates (82% vs 88%).<sup>5</sup>

Thus, the learning curve associated with HUDS may differ between anterior and posterior segment surgery, as

demonstrated by differences in operative times. Inefficiencies may be mitigated by initially performing simpler cases, optimizing system presets, and incorporating ergonomic training during the adoption phase.

## Ergonomics And Wellbeing

A consistent advantage of HUDS is improved surgeon comfort and ergonomics. In a comparative analysis of 80 cataract surgeons, those using the Artevo 800 maintained a more neutral neck posture, with less flexion during capsulorhexis, phacoemulsification, and IOL placement. Postoperative musculoskeletal discomfort was also lower.<sup>6</sup>

Similarly, ophthalmologists using HUDS for simulated minimally invasive glaucoma surgery rated HUDS superior to conventional microscopy for ergonomics, depth of field, and educational training value.<sup>7</sup> Early clinical experience in vitreoretinal surgery further support these findings, with 91.7% of surgeons from a cohort of 20 volunteers preferring the ergonomics of heads-up visualization during standardized microsurgical tasks, alongside retrospective validation in more than 400 routine vitrectomies over 8 months.<sup>8</sup> In a prospective study of retina fellows using the Ngenuity 3D system, early ergonomic and comfort advantages compared with analog microscopes were observed, although these differences leveled over time as training progressed.<sup>9</sup>

Beyond immediate comfort, improved posture with HUDS may have long-term implications for surgeon health and career longevity, as sustained neck flexion and musculoskeletal strain are well-documented contributors to early retirement from the OR.<sup>10</sup>

## Visualization, Safety, and Procedural Tradeoffs

In vitreoretinal surgery, HUDS may enhance visualization in ways that translate to clinically meaningful outcomes. For example, in a trainee series of macular hole repairs, closure rates were significantly higher with the use of HUDS compared with SOMs (86.3% vs 60.3%).<sup>11</sup>

In a randomized controlled trial at Wills Eye Hospital comparing the Artevo 800 with SOM for macular surgery, procedures were performed at substantially lower endoillumination levels (22.7% vs 39.1%) while maintaining comparable safety and postoperative visual outcomes.<sup>12</sup> Because lower light intensity lessens cumulative phototoxic risk,<sup>13</sup> the ability of HUDS to achieve optimal endoillumination at lower light intensities may play a protective role in mitigating retinal phototoxic damage.

Despite the advantages of HUDS, certain tradeoffs remain. Notably, macular peel times were longer with HUDS (14.8 vs 11.9 minutes), underscoring that, despite improved visualization, efficiency still depends on surgeon familiarity and workflow optimization. Thus, structured training is necessary to fully realize HUDS' ergonomic and visualization advantages without prolonging operative time.

## KEY TAKEAWAYS

- ▶ 3D heads-up display systems provide anatomic and visual outcomes comparable to conventional microscopes, while requiring lower levels of endoillumination and offering better ergonomics.
- ▶ Digital image processing and local-dimming 3D monitors improve field clarity and contrast across common steps in vitreoretinal procedures.
- ▶ Intraoperative AI can now perform real-time instrument and landmark detection on the surgical video feed, and robotic platforms are achieving autonomous, motion-compensated subretinal injections guided by intraoperative OCT.

## Software and Hardware Advances for HUDS

Digital image processing has become a key contributor to optimizing HUDS. The real-time application of local contrast and edge-definition sharpening and color adjustment algorithms can enhance intraoperative contrast while reducing objective measures of image clarity (skewness and kurtosis).

In clinical studies, mean visibility scores increased markedly on a 10-point scale, rising from 5.0 at baseline to 7.5 at 50% sharpening levels, and color adjustments significantly improved visualization during delicate steps such as internal limiting membrane (ILM) peeling.<sup>14,15</sup>

In practice, surgeons may begin with moderate contrast sharpening intensities (25% to 50%), as supported by Nakajima et al, who found that visibility improved proportionally with sharpening within this range. Real-time color balance adjustments, though not yet standardized, were shown to further enhance ILM contrast without loss of image clarity.<sup>14-16</sup>

Complementary advances in display technology are producing comparable gains, with next-generation monitors optimizing brightness to improve visualization of the operative field. Nakajima et al evaluated the performance of the Sony LMD-XH550MT 3D monitor with local dimming technology against the conventional Sony monitor. The study demonstrated that the monitor with local dimming technology achieved higher visibility scores and reduced skewness during cataract and vitreous surgery compared with the conventional monitor.<sup>17</sup>

While HUDS offer ergonomic and educational advantages, their high capital cost, OR layout requirements (to maintain clear sightlines to the 55" monitor), and the need for staff to wear polarized 3D glasses can pose barriers to adoption.<sup>1</sup>

## STRUCTURED TRAINING IS NECESSARY TO FULLY REALIZE HUDS' ERGONOMIC AND VISUALIZATION ADVANTAGES WITHOUT PROLONGING OPERATIVE TIME.

### AI AND ROBOTICS

AI has emerged as a key tool for surgical workflow analysis and intraoperative decision support in ophthalmic surgery. By leveraging deep learning (DL) models trained on surgical video and imaging data, AI can identify procedural phases, recognize instrument use, and provide structured feedback for training and quality control.

#### Surgical Workflow and Intraoperative Guidance

Mueller et al evaluated the use of a DL model for surgical phase recognition in cataract surgery. Using the SICS-105 dataset (105 prospectively collected videos of small-incision cataract surgery), the model achieved 85.6% accuracy for SICS and 89.9% for phacoemulsification, confirming that AI can reliably segment complex surgeries into distinct steps.<sup>18</sup>

In a study focused on vitreoretinal surgery, Nespolo et al evaluated a DL model designed to analyze the intraoperative field and detect surgical instruments, classify their tips, and segment key retinal landmarks in real time. Their model was trained on 606 annotated surgical frames and demonstrated strong performance.<sup>19</sup>

By achieving both high precision and real-time speed, DL models show the potential to support intraoperative tasks such as collision avoidance, automated instrument tracking, and surgical data analysis.

#### Robotic Systems and Motion Compensation

AI-integrated robotic platforms are being developed to achieve the motion and positional stability needed for safe and reproducible subretinal therapies. Wu et al introduced a fully autonomous robotic system for subretinal injection delivery designed to compensate for human hand tremor, retinal movement from respiration, and cardiac pulsation. The system achieved insertion error of approximately 9- $\mu$ m root mean squared error and 22- $\mu$ m MaxAE in simulation. In ex vivo porcine eyes, biological variability introduced

greater uncertainty, although five of eight trials still achieved successful retinal bleb formation.<sup>20</sup>

Similarly, Arikan et al tested the Steady-Hand Eye Robot with OCT-based motion feedback to stabilize injections during simulated retinal motion. At low simulated retinal-motion amplitudes (25  $\mu$ m), tracking was stable, while larger amplitudes (100  $\mu$ m) introduced drift and phase lag, and four of seven porcine injections achieved successful subretinal bleb formation.<sup>21</sup>

Recently, Horizon Surgical Systems completed the world's first robotic-assisted cataract surgery using its Polaris platform, marking a major milestone in advancing ophthalmic innovation through robotics and AI.<sup>22</sup>

#### Predictive Models and Outcome Forecasting

AI models have been deployed to predict surgical outcomes and can potentially serve as a valuable tool in preoperative patient counseling and prognostication. Guo et al trained a multimodal DL model to evaluate whether it could accurately predict postoperative visual outcomes following rhegmatogenous retinal detachment (RRD) repair and compared it to OCT-only and fundus-only AI models. Analyzing OCT, ultra-widefield fundus images, and clinical parameters from 184 RRD repairs, the multimodal model provided the strongest predictive performance. In contrast, OCT-only and fundus-only models performed less well.<sup>23</sup>

Godani et al showed that a regression model could predict postoperative visual acuity after macular hole surgery within 0.1 to 0.3 logMAR in 61% to 87% of cases.<sup>24</sup> In a similar study on idiopathic epiretinal membrane surgery, Lin et al found that a DL model trained on OCT scans from 696 eyes with epiretinal membrane slightly outperformed retina specialists when predicting postoperative visual outcomes.<sup>25</sup>

### WHAT'S TO COME IN THE RETINA OR

The convergence of digital HUDs, intraoperative AI, and robotics heralds a transformative era in ophthalmic surgery. Together, these technologies can enhance visualization, ergonomics, and microsurgical precision, while emerging AI and motion-compensated robotic platforms are redefining the boundaries of intraoperative safety and outcome predictability. As adoption accelerates, structured training, workflow optimization, and evidence-based validation will be essential to ensure these innovations fulfill their potential in advancing surgical precision, protecting surgeon well-being, and improving patient outcomes. ■

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(Continued on page 31)

# COMPLEX MYOPIC MHRD: MEMBRANES AND TRANSPLANTS



In the last installment of this three-part series, we describe the latest techniques for managing challenging retinal detachments.

BY CARLOS MATEO, MD, AND ANNIKEN BURÉS-JELSTRUP, MD

**M**acular hole retinal detachments (MHRD) are a significant challenge in vitreoretinal surgery, with high myopia and the presence of a posterior staphyloma the predominant causes. In RDs originating from the posterior pole, retinal breaks other than the MH may be responsible, such as full-thickness tears along the vascular arcades or within areas of chorioretinal atrophy—particularly around the optic disc—which can be difficult to identify.

In addition to the macular buckling technique, several alternative surgical strategies have proven highly effective for achieving both MH closure and retinal reattachment.

## ILM DISSECTION AND INVERTED FLAP TECHNIQUE

First described in 2016 by Michalewska et al for large MHs, the inverted internal limiting membrane (ILM) flap technique has demonstrated a clear superiority over complete ILM removal in terms of MH closure rates and retinal reattachment in various series published in 2016 and 2017.<sup>1-5</sup> Creating an inverted flap when the retina is detached can be cumbersome due to two main challenges:

- During staining, the dye tends to enter the subretinal space, impairing ILM visualization and increasing the risk of retinal pigment epithelium (RPE) toxicity.
- Performing the initial “pinch” maneuver to start the ILM peel on a detached, mobile retina can be technically difficult and traumatic.

To address these issues, a modified technique was described in 2023: Following pars plana vitrectomy (PPV), perfluorocarbon liquid (PFCL) is injected to displace the subretinal fluid peripherally. Using high magnification and a 41-gauge cannula, a partial drainage of subretinal fluid can be performed through the MH. Staining is then achieved by injecting dye with a soft-tip cannula between the retina and the PFCL, which allows almost instantaneous staining without subretinal dye migration. The inverted flap can then be prepared and positioned over the MH. This approach avoids the need for additional posterior retinotomies.<sup>6</sup>

The inverted ILM flap technique has become the first-line surgical approach for MHRD associated with high myopia.

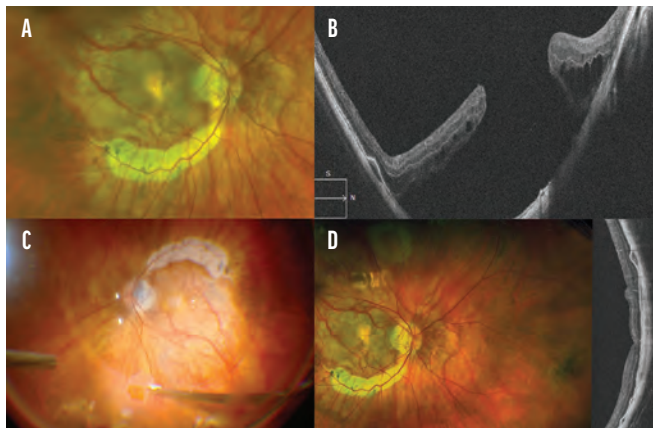
## AUTOLOGOUS RETINAL TRANSPLANTATION

In 2016, Grewal and Mahmoud introduced the concept of autologous retinal transplantation (ART) for the treatment of large refractory MHs (Figure 1).<sup>7</sup> Subsequently, 15% of the patients included in the ART Global Consortium Study had a MHRD that had failed to close after surgery. After ART, 95% of these patients achieved MH closure (complete closure in 68.4% and a small eccentric defect in 26.3%).<sup>7</sup> Reported complications included graft dislocation, redetachment in four eyes, and the presence of subretinal PFCL in two eyes.<sup>8</sup>

A controversial aspect of ART has been whether the graft becomes reperfused. Tabandeh reported two cases that demonstrated vascular reperfusion of large ART grafts,<sup>9</sup> and Kitahata et al documented vascularization in 34.6% of 26 eyes.<sup>10</sup> Conversely, Takeuchi et al observed no changes in fixation points using microperimetry or in absolute scotoma size in cases of very large MHs.<sup>11</sup>

During the initial surgical steps, it is important to estimate the MH size to harvest a graft approximately 25% larger, compensating for postoperative graft contraction. This can be facilitated by placing a Finesse Flex Loop (Alcon) over the MH to estimate its diameter and then transferring the measurement to the peripheral retina (ART is typically harvested from the superior peripheral retina).

Some surgeons prefer to apply diathermy around the donor site to minimize bleeding, although excessive coagulation may devitalize the edges. Maintaining the graft's orientation is crucial. While some surgeons deliver the graft under PFCL to facilitate a correct placement, others prefer to lift the graft and place it directly over the MH, use forceps to position the graft, and stabilize it over the MH using PFCL. (The latter option could avoid potential photoreceptor trauma because the graft is not being dragged into position.) The final exchange with the chosen tamponade agent—either gas or silicone oil—is critical to prevent graft displacement.



**Figure 1.** This eye with high myopia has a large MHRD confined to the macular area (A). Structural OCT shows the central size of the MH (B). Intraoperative imaging with PFCL after creating a peripheral localized RD and cutting the ART that will then be moved to the MH under PFCL (C). Postoperatively, the retina is reattached, and the MH is closed on OCT (D).

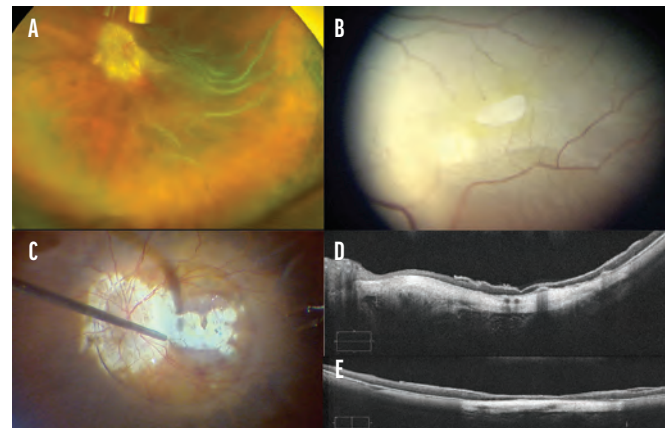
### HUMAN AMNIOTIC MEMBRANE

In 2011, Kiilgaard et al used subretinal human amniotic membrane (HAM) in animal studies as a substitute for damaged RPE and Bruch membrane.<sup>12</sup> Later, Rizzo et al applied small, cryopreserved HAM implants subretinally without specific orientation to promote MH closure.<sup>13</sup> In 2019, Caporossi et al reported a 94% closure rate in highly myopic eyes (mean axial length 30.89 mm) using subretinal HAM placed with chorion-RPE orientation. Importantly, 69% of eyes demonstrated visual improvement, with BCVA better than 20/63 in 56% of eyes.<sup>14</sup>

The technique involves preparing a HAM disc (1 to 2 mm in diameter, depending on MH size) and positioning it beneath the MH edges (Figure 2). Mechanical elevation of the edges is often necessary to insert the implant and prevent its loss during fluid-air exchange. In cases of MHRD, once the HAM is placed subretinally (preferably with the chorion facing the RPE), it should be stabilized with PFCL to prevent subretinal displacement. Subretinal fluid should then be drained either through a peripheral retinal break or a small, intentionally created peripheral retinotomy.<sup>15</sup>

In 2020, Moharram et al reported the use of a large epiretinal HAM patch in 14 eyes with MHRD, achieving MH closure and retinal reattachment in 93% of cases.<sup>16</sup> In 2021, Garcin et al applied the same technique in two groups—those with large MHs and those with MHRD—achieving 80% hole closure and 100% retinal reattachment, respectively.<sup>17</sup>

Whether the optimal form of HAM is cryopreserved or lyophilized remains unclear. Cryopreserved HAM is stored at very low temperatures (-80°C to -196°C), preserving histological integrity but showing some basal lamina and stromal protein degradation after 3 months. Conversely, lyophilized HAM is thinner, can be stored at room temperature, and is immediately available. Regarding growth factors, Allen et al demonstrated that dried HAM retained higher



**Figure 2.** A total RD is caused by a large MH (A). Intraoperatively, the hole has atrophic areas seen through the translucent detached retina (B). The HAM is stabilized under PFCL, and the surgeon centers and unrolls the HAM (C). Horizontal (D) and vertical (E) OCT scans crossing the foveal center show the centered HAM.

concentrations of growth factors compared with cryopreserved HAM when a modified preservation process was used.<sup>18</sup> Orientation also remains controversial—whether the chorionic side should face upward or toward the RPE. Cryopreserved HAM shows greater adherence on its chorionic surface, so many surgeons prefer placing this surface toward the RPE to enhance adherence and reduce the risk of implant displacement during the final fluid-air exchange.

### THE BENEFITS OF MH COVERAGE

MHRD remains one of the most complex scenarios in vitreoretinal surgery, particularly in highly myopic eyes with posterior staphyloma. Recent advances such as the inverted ILM flap technique, ART, and HAM implantation provide effective alternatives for achieving both MH closure and retinal reattachment in challenging cases. However, we still have barriers to overcome, including the need to achieve not only closure and retinal reattachment, but also complete restoration of the retinal layers.

Careful patient selection, meticulous surgical technique, and awareness of potential complications are essential to optimize outcomes. As instrumentation and adjuncts evolve, these strategies may further improve both anatomic success and functional recovery in eyes with MHRD. ■

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## FURTHER READING

### MYOPIC TRACTION MACULOPATHY: SURGICAL TIMING AND TECHNIQUES

Part one explores various management considerations when faced with complications of pathologic myopia.

By Taku Wakabayashi, MD, PhD



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### MACULAR BUCKLING FOR MYOPIC TRACTION MACULOPATHY

Part two shares the value of treating the staphyloma without fear that buckling will damage the choroid.

By Barbara Parolini, MD, and Aurelio Apuzzo, MD



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(Continued from page 28)

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# CODING ADVISOR

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## USING CATEGORY III CODES



Five tips to help improve accuracy, payment, and compliance.

BY MATTHEW BAUGH, MHA, COT, OCS, OCSR

Accurate coding for emerging retinal technologies requires more than familiarity with the standard American Medical Association (AMA) Current Procedural Terminology (CPT) Category I and Healthcare Common Procedure Coding System (HCPCS) codes; it also requires understanding CPT Category III codes. These temporary tracking codes, or “T” codes, are increasingly common in retina as innovation accelerates, yet they remain a frequent source of confusion, denials, and compliance risk.

CPT Category III codes consist of four numeric characters followed by the letter “T.” Although they are valid CPT codes, they do not have assigned relative value units (RVUs) or national Medicare payment rates. As a result, coverage and carrier pricing for reimbursement are determined by the Medicare Administrative Contractor (MAC) or the individual payer.

The following five practical tips outline how retina practices can use CPT Category III codes correctly to improve payer outcomes and position emerging services for future CPT Category I promotion.

### TIP NO. 1: DON'T DEFAULT TO PATIENT PAY

A common misconception is that Category III codes are inherently noncovered and should automatically be billed to the patient. However, Category III status does not always mean investigational or noncovered. Rather, when a procedure is best described with a Category III code, it should be billed as such on the claim. Coverage decisions are based on medical necessity and payer policy—not the code category alone. Bypassing payer adjudication increases compliance risk and may leave reimbursement uncollected.

Verify payer coverage and submit the claim to the payer first. When Medicare Part B coverage is uncertain or considered noncovered, the physician is required to obtain

a valid Advance Beneficiary Notice (ABN), rather than defaulting to self-pay.<sup>1</sup>

### Practical Considerations

- Verify written payer policies for each Category III code used.
- Use ABNs with Medicare Part B patients when coverage is uncertain.
- Educate front desk and billing staff that Category III does not equate to automatic patient responsibility.

### TIP NO. 2: REPORT CATEGORY III CODES INSTEAD OF UNLISTED CODES

When a Category III code exists that accurately describes the service performed, it must be reported instead of an unlisted Category I code. Substituting an unlisted code (eg, CPT code 67299, unlisted code, posterior segment) when a Category III option is available is incorrect coding and may trigger denials or post-payment review.

A retina-specific example is 0810T for subretinal injection of a pharmacologic agent (including vitrectomy and retinotomy), such as voretigene neparvovec-rzyl (Luxturna, Spark Therapeutics). Note: It would not be appropriate to bill CPT code 67036, pars plana vitrectomy and/or 67299 in place of or together with 0810T due to the descriptor.

Using the correct Category III code allows payers to price the service appropriately and supports the AMA CPT Editorial Panel in collecting usage data for a new and emerging service required for potential promotion to Category I status.<sup>2</sup>

### Practical Considerations

- Use audit charge masters and electronic health record order sets to ensure Category III codes are available and mapped correctly.

# A COMMON MISCONCEPTION IS THAT CATEGORY III CODES ARE INHERENTLY NONCOVERED AND SHOULD AUTOMATICALLY BE BILLED TO THE PATIENT. HOWEVER, CATEGORY III STATUS DOES NOT ALWAYS MEAN INVESTIGATIONAL OR NONCOVERED.

- Build payer-specific rules to prevent staff from defaulting to unlisted codes.

### TIP NO. 3: EXPECT HEIGHTENED DOCUMENTATION SCRUTINY

Because Category III codes lack RVUs and national payment rates, documentation often determines whether a claim is paid and is considered medically necessary per the payers. Some MACs require submission of operative notes or supporting records upon claim acceptance for all Category III services.<sup>3</sup> Failure to submit properly or respond in a timely manner will prompt an additional documentation request, which can delay or deny payment.

Documentation should clearly reflect the full service performed, matching the Category III code descriptor, the clinical rationale and diagnosis, the operative or procedure notes (as appropriate), and the formal interpretation and report, when required.

### Practical Considerations

- Create templated operative notes with language and supporting documentation for each Category III code used.
- Train staff on MAC paperwork workflows for submission.
- Document measurable findings and their effect on clinical decision making.

### TIP NO. 4: ALIGN PROFESSIONAL AND FACILITY BILLING

Many Category III services involve both professional and facility components. Misalignment between physician and facility billing can result in duplicate charges, missing modifiers, or denials. For example, when 0810T is performed in a facility, the physician reports 0810T, and the facility should also report 0810T and the drug. Clarifying the appropriate code(s) and who bills each component before claim submission is essential.

### Practical Considerations

- Develop a shared billing checklist with the ambulatory surgery center or hospital partners.
- Confirm modifier usage (-RT/-LT, -50) and drug billing responsibilities.

### TIP NO. 5: TRACK SEMIANNUAL UPDATES AND CODE TRANSITIONS

Category III codes are temporary by design and are released twice yearly (January and July). They are assigned a defined sunset date, which represents the point at which the AMA reevaluates the code based on usage and clinical evidence. At that time, a code may be promoted to a Category I permanent code, revised, or deleted, if adoption had been limited. Their sunset date can also be extended if more data are needed.

Retina has seen this lifecycle repeatedly:

- 0465T (suprachoroidal injection) was replaced by Category I 67516 in 2024.
- Subretinal delivery was assigned to Category III (0810T) in 2023.
- New technologies, such as photobiomodulation therapy (0936T), are also currently tracked under Category III.

Failure to monitor updates can result in the use of deleted codes or missed billing opportunities.

### Practical Considerations

- Schedule internal CPT reviews every January and July.
- Update superbills, electronic health record pick lists, and charge masters promptly.
- Educate clinicians and staff on coding changes before patient care is delivered.

### RETINA-SPECIFIC CATEGORY III EXAMPLES

- **0472T:** Device evaluation, interrogation, and initial programming of intraocular retinal electrode array (eg, retinal prosthesis), in person, with iterative adjustment of the implantable device to test functionality, select optimal permanent programmed values with analysis, including visual training, with review and report by a qualified health care professional.
  - New code effective July 1, 2017
  - Sunset January 2028
- **0506T:** Macular pigment optical density measurement by heterochromatic flicker photometry, unilateral or bilateral, with interpretation and report.
  - New code effective July 2018
  - Sunset January 2029

*(Continued on page 40)*



# RISING STARS IN RETINA

**RT**  
Retina Today

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## Get to know outstanding retina fellows from the class of 2026.



**Prashant D. Tailor, MD**

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

My decision to pursue retina was personal. When I was 7 years old, my mother—a high myope with -20 D refractive error—suffered a retinal detachment. Witnessing the toll multiple detachments took on her quality of life demonstrated the profound value of preserving vision. I chose medicine, and specifically the field of retina, to provide others with the same security and independence that successful surgical intervention restored to my family.

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

I have been fortunate to train under exceptional mentors. Timothy Olsen, MD, laid the foundation for my career at Emory, teaching me scientific rigor.

During residency training at the Mayo Clinic, Matthew Starr, MD; John Chen, MD; Lauren Dalvin, MD; Raymond Iezzi Jr, MD; Brittni Scruggs, MD, PhD; Arthur Sit, MD; Andrew Barkmeier, MD; and Sophie Bakri, MD, instilled in me the core value that the needs of the

patient always come first.

As a fellow at the University of California Los Angeles, Jayanth Sridhar, MD; Kirk Hou, MD; Pradeep Prasad, MD; Hamid Hosseini, MD, Colin McCannel, MD; Tara McCannel, MD, PhD; David Sarraf, MD; Edmund Tsui, MD; and Irena Tsui, MD, have challenged me to refine my surgical and medical technique and strive for perfection in every case.

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

Transitioning from learner to teacher has been the highlight of my fellowship training. Staffing residents on complex cataracts and vitrectomies is incredibly rewarding—specifically, watching surgical principles “click” for them in real-time. Seeing their confidence grow throughout the year reinforces my own understanding of the field and desire to mentor future trainees.

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

Push yourself to be the best comprehensive ophthalmologist you can be before narrowing your focus to retina, because the best retina specialists understand the eye as a whole system.

Above all, if you always put the needs of the patient first, you will never make the wrong decision. ■

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# RISING STARS IN RETINA

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# INCONTINENTIA PIGMENTI-ASSOCIATED RETINOPATHY



Early screening of these patients is imperative for accurate risk assessment and timely intervention.

BY ŞENGÜL ÖZDEK, MD, FEBO, FASRS, AND ECE ÖZDEMİR ZEYDANLI, MD, FEBO, FICO, FRCS

Incontinentia pigmenti (IP), or Bloch-Sulzberger syndrome, is a rare X-linked dominant neuroectodermal dysplasia that presents a unique clinical challenge for vitreoretinal surgeons.<sup>1,2</sup> Caused primarily by mutations in the *IKBKG* (formerly *NEMO*) gene, IP is typically lethal in males, leading to a more than 96% female cohort.<sup>1</sup> While a cutaneous “marble cake” hyperpigmentation is the clinical hallmark, ocular manifestations—specifically, IP-related retinopathy—carry the highest risk for permanent morbidity.

As our understanding of the vascular pathogenesis of IP evolves, management is shifting from reactive observation toward a more proactive, risk-adapted strategy. Using insights from a recent multicenter study involving more than 400 eyes, together with emerging literature, we describe how to identify high-risk patients and determine when intervention is most critical.

## REMARKABLE HETEROGENEITY

IP-related retinal disease is marked by striking heterogeneity in both presentation and disease course. Some infants demonstrate peripheral avascular retinal findings that remains stable for years, while others develop rapid neovascularization and tractional retinal detachment (TRD) within months (Figure).<sup>3-5</sup> At the extreme end of the spectrum, neonates may present with advanced fibrovascular proliferation or total TRD at birth, suggesting aggressive disease can begin in utero.<sup>3,4</sup> The biological basis for this variability remains unclear; although all patients share disruption of the NF- $\kappa$ B signaling pathway, genotype-phenotype correlations have not yet been established. It is possible that additional modifying genetic factors contribute to disease severity, but this hypothesis remains speculative and, as yet, lacks definitive evidence.

What is clear, however, is that IP-associated retinopathy

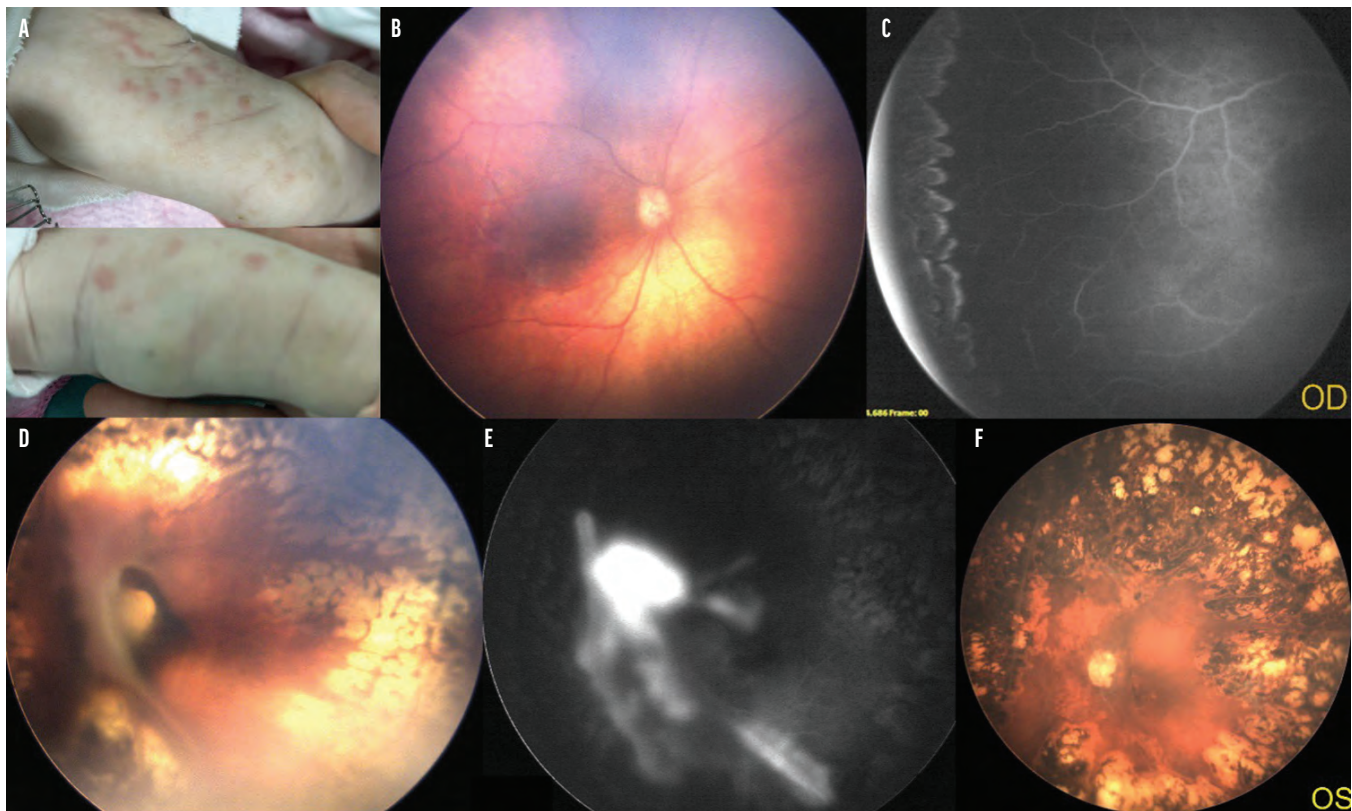
does not behave like retinopathy of prematurity (ROP), despite their similarities as ischemic pediatric retinopathies.<sup>6</sup> While vascular development follows a relatively predictable timeline in RP, IP may demonstrate prolonged, quiescent avascular retina with late-onset neovascularization, sometimes emerging years after initial stability. Moreover, IP can exhibit a dynamic vaso-occlusive course: New areas of peripheral—or even posterior—nonperfusion may arise in previously vascularized areas, a phenomenon not characteristic of ROP.<sup>6</sup> In addition, some infants with IP display an aggressive phenotype, progressing rapidly to vitreous hemorrhage or TRD within the first months of life, sometimes despite timely laser intervention.<sup>5</sup>

## DIAGNOSTIC INSIGHTS

### Assessing Risk

Recent literature suggests as many as 70% of infants with IP exhibit angiographic signs of retinal disease.<sup>7</sup> Similarly, in our recent multicenter cohort of 434 eyes, fluorescein angiography (FA) identified retinal pathology in 65% of eyes at a median of 3 months of age.<sup>8</sup> Notably, we also found that 25% of eyes that appeared normal on indirect ophthalmoscopy demonstrated angiographic abnormalities. This mismatch is clinically significant, as subtle peripheral nonperfusion or late-phase leakage may be invisible on routine examination yet carry prognostic implications. For this reason, baseline widefield FA early in life is central to stratifying risk.

Prior reports have emphasized that IP-associated retinopathy is dynamic, with both progression and, less commonly, possible spontaneous involution.<sup>3-5</sup> Nevertheless, our multicenter data suggest baseline clinical features, particularly angiographic phenotype, provide meaningful risk stratification. In our cohort, FA findings were able to independently predict disease course: Compared with eyes



**Figure.** A full-term infant with IP was referred for progressive RD in her left eye 6 weeks after bilateral laser photocoagulation performed at 3 weeks of age. Cutaneous lesions typical of IP were present (A). Her right eye showed an attached and stable retina with 360° peripheral laser scars (B) and no new vascular activity on FA (C). Her left eye showed partial TRD involving the nasal and peripapillary retina with 360° laser scars extending toward the macula (D). FA demonstrated severe leakage from neovascular tissue associated with TRD (E), and fundus photography obtained 9 months postoperatively showed resolution of the TRD (F).

with a normal FA, eyes with isolated nonperfusion carried a five-fold increased risk of progression, while the presence of angiographic leakage or neovascularization increased risk 10- to 15-fold. In practical terms, the presence of vascular activity signals biologically active disease and a substantially higher likelihood of continued progression, warranting closer monitoring and earlier intervention.

### Predicting RD

For clinicians and families, the greatest concern with IP-associated retinopathy tends to be the development of an RD. Encouragingly, only 2.6% of eyes in our cohort developed RD over a median follow-up of 4 years. When RD occurred, it tended to be within the first years of life. This early vulnerability mirrored a report by Chen et al,<sup>5</sup> who observed RD in 22% of eyes over extended follow-up and described a bimodal distribution: TRD occurred predominantly in infancy and early childhood, while rhegmatogenous RD (RRD) developed later in adolescence and adulthood.

In our study, no eyes with a normal baseline FA developed an RD; risk increased stepwise with angiographic severity and was highest in eyes with leakage or neovascularization. Similarly, Chen et al identified retinal

neovascularization as a strong risk factor for RD, whereas peripheral nonperfusion alone was less clearly predictive.<sup>5</sup> Taken together, these findings support an aggressive surveillance strategy in infancy and early childhood, particularly for eyes with vascular activity. In later childhood and adolescence, follow-up intervals may be individualized, but patients and families should be educated about symptoms of RRD and encouraged to monitor vision in each eye separately.

### MANAGEMENT STRATEGIES Laser Photocoagulation

Peripheral laser photocoagulation remains a mainstay of treatment in IP-related retinopathy in which the primary goal is to reduce angiogenic drive by ablating ischemic retina and decreasing the risk of neovascular complications and RD.

That said, laser treatment does not guarantee protection from RD. Chen et al reported that three of four infants treated prophylactically still developed TRD,<sup>5</sup> and in our cohort, most eyes that progressed to RD had received early laser. These observations underscore that early ablation may not reliably prevent RD in biologically aggressive disease. On the other hand, another series demonstrated favorable outcomes when treatment was initiated very early,

# THE PERIOD OF GREATEST VULNERABILITY IS EARLY INFANCY, WHEN DISEASE ACTIVITY AND RETREATMENT BURDEN PEAK; AFTER THIS WINDOW, MANY EYES STABILIZE, ALTHOUGH LONG-TERM VIGILANCE REMAINS ESSENTIAL.

suggesting both timing and disease phenotype are relevant.<sup>9</sup>

In our multicenter study, a subgroup analysis of infants showed that retreatment rates peaked within the first 3 to 6 months after presentation and declined substantially thereafter. After 3 years, additional treatment was relatively uncommon. Accordingly, follow-up intervals can often be gradually extended after early childhood in stable eyes, while maintaining lifelong awareness.

## Anti-VEGF Therapy

Intravitreal anti-VEGF therapy has been reported in select cases of IP-related retinopathy, typically in eyes with severe neovascularization or vitreous hemorrhage.<sup>10</sup> In our cohort, anti-VEGF injections were rare and limited to adjunctive treatment, preventing reliable assessment of efficacy.

There are also theoretical safety concerns, as IP is a multisystem vascular disorder involving the central nervous system, and the systemic effects of VEGF suppression in infants are not fully understood.<sup>11</sup> For now, anti-VEGF therapy is best considered a selective adjunct in cases of severe posterior neovascularization or media opacity limiting laser, rather than as a primary treatment strategy.

## Surgical Management

Data on surgical outcomes in IP are limited, and previously reported results have been guarded.<sup>3,5</sup> In our multicenter study, eyes with TRD undergoing primary vitreoretinal surgery demonstrated greater anatomic stability compared with those managed conservatively or with laser alone. Although visual outcomes remained guarded, surgical intervention appeared to reduce the likelihood of further structural deterioration in some cases.

Importantly, a subset of eyes with peripheral or fovea-sparing TRD remained stable over prolonged follow-up without surgical intervention. This suggests careful observation with or without laser treatment may be reasonable in nonprogressive, non-macula-threatening RD cases, particularly when traction is extrafoveal, localized, and stable, and the fellow eye has better visual potential.

In contrast, outcomes were poor in eyes presenting with advanced TRD. Many of these infants presented within weeks of birth, suggesting an aggressive in-utero phenotype,

rather than delayed recognition. Even with surgical intervention, progression to phthisis was common; in such cases, realistic counseling regarding prognosis is essential.

## REMAIN VIGILANT

IP-related retinopathy is a dynamic, biologically heterogeneous disease that demands early, risk-adapted management. Widefield FA has become central to identifying high-risk eyes, particularly those with vascular activity, who require closer surveillance and often earlier intervention. The period of greatest vulnerability is early infancy, when disease activity and retreatment burden peak; after this window, many eyes stabilize, although long-term vigilance remains essential. ■

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# EXTENDED ILM PEELING FOR PVR



This technique can help prevent recurrent retinal detachment by completely removing traction and the scaffold for repopulation.

BY TAKU WAKABAYASHI, MD, PHD, AND YOSHIHIRO YONEKAWA, MD

**P**roliferative vitreoretinopathy (PVR) remains the leading cause of redetachment after rhegmatogenous retinal detachment (RD) repair and the most formidable nemesis of retina surgeons.<sup>1,2</sup> In particular, grade C PVR, characterized by preretinal and subretinal fibrotic proliferation, star folds, intraretinal contraction, and retinal foreshortening, often requires complex surgical techniques, including membrane dissection, encircling scleral buckle, relaxing retinectomy, lensectomy, and silicone oil tamponade.<sup>2</sup> However, these techniques have changed little over the past decades, and eyes with PVR still pose a high risk of recurrence and suboptimal visual outcomes. Techniques to improve PVR outcomes continue to represent an enduring challenge in vitreoretinal surgery.

To address these limitations, we propose extended internal limiting membrane (ILM) peeling as an additional strategy to reduce PVR recurrence, thereby improving outcomes.<sup>3</sup>

## ILM PEELING IN PVR

There are three rationales for ILM peeling in PVR surgery:

- By removing the ILM, the surgeon is certain that the overlying PVR membranes have been completely removed. The wider the peel, the more PVR is removed.
- By removing the scaffold on which it grows, PVR does not repopulate in that area. The portions of the retina without ILM are known as the *nonproliferation zone*; therefore, the wider the peel, the better.
- Peeling ILM, and consequently any overlying subclinical PVR, disconnects any peripheral traction from the posterior pole, thereby interrupting the tractional forces exerted by the PVR.

The potential benefits include the prevention of membrane repopulation and consequent recurrent RD. Broader ILM peeling—extending to or beyond the vascular arcades—may further attenuate the transmission of peripheral traction toward the posterior pole.<sup>4</sup> Extending the ILM

peeling up to the margin of a planned retinectomy is ideal. This will reduce repopulation along the retinectomy edge, a common site of recurrent detachment. Peeling all the way to the retinectomy edge is technically challenging, however, and not always possible.

## Case Report

A 52-year-old man presented with a 3-year history of progressive vision loss and a recent mature cataract in his left eye. His VA was hand motion OS, and his IOP was 5 mm Hg OS. B-scan ultrasonography revealed a total RD in the left eye, and the patient underwent phacovitrectomy. After cataract extraction, intraoperative findings confirmed a chronic total RD and grade C PVR (Figure 1A).

During vitrectomy, dense preretinal membranes were removed from the posterior pole to the periphery. Subretinal bands were removed bimanually through an inferior retinectomy. The retina was flattened under PFO, followed by extended ILM peeling from within the vascular arcade and beyond the arcade toward the retinectomy site to relieve residual traction (Figure 1B). Endolaser photocoagulation was applied to the inferior retinectomy margin, followed by silicone oil tamponade.

After surgery, the patient's retina remained reattached; his VA improved to 20/400 OS and IOP was 20 mm Hg OS (Figure 1C).

## Results of Our Multicenter Study

We conducted a multicenter study including six institutions in the United States and Japan (Wills Eye Hospital, Mayo Clinic, Osaka University, Aichi Medical University, Oshima Eye Clinic, and Hyogo Medical University) to evaluate the potential efficacy of ILM peeling on anatomic and visual outcomes in grade C PVR.<sup>3</sup> The primary outcome was single-surgery anatomic success at 3 and 6 months. The study included 370 eyes from 370 patients: 157 eyes (42%)

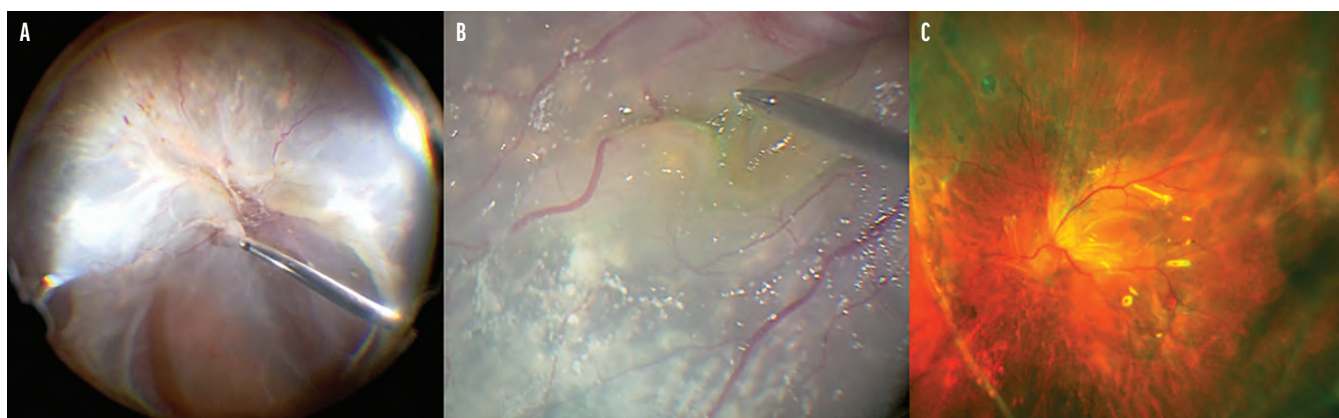


Figure 1. Intraoperative fundus imaging showed a total rhegmatogenous RD with grade C PVR (A). After inferior retinectomy and extended ILM peeling under PFO (B), the retina was successfully reattached postoperatively (C).

with ILM peeling and 213 (58%) eyes without ILM peeling. The mean follow-up was 23 months, and baseline characteristics were similar between groups. Among ILM-peeled eyes, 20% underwent macular peeling, 46% arcade-to-arcade peeling, and 24% extended peeling beyond the arcades.

The single-surgery anatomic success was significantly higher in the ILM peeling group (86.6% vs 73.2% at 3 months and 75.2% vs 64.8% at 6 months). The retinal reattachment rate under fluid without any tamponade was significantly higher in the ILM peeling group at 6 months (68.8% vs 51.6%). Both groups showed significant visual improvement after surgery; however, the ILM peeling group showed significantly better visual acuity and visual improvement ( $1.11 \pm 0.70$  LogMAR vs  $1.29 \pm 0.80$  LogMAR and  $0.48 \pm 0.77$  LogMAR vs  $0.24 \pm 0.90$  LogMAR, respectively). The ILM peeling group had significantly fewer reoperations, including epiretinal membrane surgeries (8.9% vs 17.8%).<sup>3</sup>

In eyes without ILM peeling, 38% developed recurrent RD during follow-up, caused by posterior, mid-peripheral, or peripheral breaks, including macular holes and stretch breaks near the retinectomy margin. In contrast, 28% of eyes with ILM peeling experienced redetachment; however, none showed new breaks within the posterior pole. No ILM peeling was significantly associated with new posterior retinal breaks, suggesting ILM peeling significantly reduced the traction responsible for posterior retinal breaks. Multivariable regression analysis showed that extended ILM peeling was significantly associated with a higher likelihood of retinal reattachment at 6 months and better final visual acuity.<sup>3</sup>

## DISCUSSION

ILM peeling enables complete removal of the overlying preretinal membranes responsible for retinal contraction and prevents repopulation by eliminating the scaffold for membrane proliferation (Figure 2). These effects promote retinal relaxation, resulting in higher single-surgery success

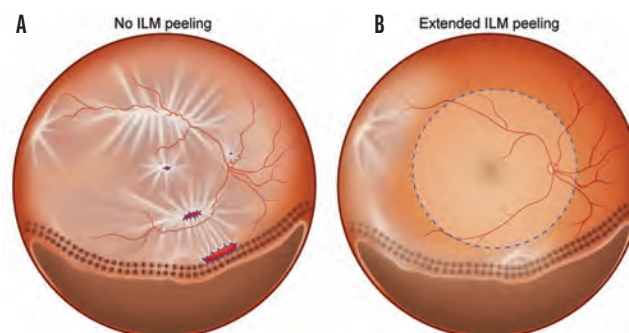


Figure 2. This schematic representation compares no ILM peeling (A) with extended ILM peeling (B). Extended ILM peeling prevents postoperative posterior contraction through broad traction removal.

rates, greater reattachment rates under fluid, and fewer reoperations in eyes with grade C PVR. In addition, extended ILM peeling resulted in even superior outcomes—as such, the more ILM that can be peeled, the more likely we were to achieve long-term stable retinal reattachment. Theoretically, broader ILM peeling extending beyond the arcade up to the midperiphery would provide a greater reduction in the tractional forces at both the posterior pole and the midperiphery. However, both the retina and the ILM become thinner beyond the arcade, making an extension of ILM peeling to the far periphery nearly impossible. Therefore, ILM peeling alone is unlikely to eliminate the traction exerted on the peripheral retina.

In our study, although eyes with ILM peeling did not develop recurrent breaks within the arcade, new breaks did occur, predominantly in the periphery. Thus, additional procedures such as retinectomy or placement of an encircling scleral buckle may be required to address peripheral traction and support the anterior retina. However, stretch breaks may occasionally occur at the posterior edge of the retinectomy site or even on scleral buckles, if the membrane contraction is significant. Thus, ILM peeling extended to the retinectomy site may help prevent stretch breaks originating

at the retinectomy sites and subsequent redetachment. The lower rate of redetachment with ILM peeling may also contribute to better visual outcomes.

One potential disadvantage of ILM peeling is the risk of iatrogenic retinal breaks due to the grasps for the ILM. However, the beneficial effect of ILM peeling in preventing redetachment likely outweighs such disadvantages, particularly in eyes with grade C PVR, which are at high risk of redetachment. Although ILM peeling can be technically challenging on a detached retina, PFO can be inserted and the ILM peeled under PFO, which provides countertraction. Extended ILM peeling can also be challenging in highly myopic eyes due to retinal thinning; in these cases, arcade-to-arcade peeling may be sufficient to reduce the risk of iatrogenic retinal breaks.

Another potential concern regarding ILM peeling is the theoretical retinal toxicity of the vital dyes. However, in our study, eyes that underwent ILM peeling achieved superior visual outcomes, suggesting any potential adverse effects of dyes are minimal compared with the benefits of traction removal and reduced recurrence.

### OPTIMIZE SURGICAL OUTCOMES

We propose ILM peeling as a valuable addition to the surgical strategy for patients with PVR. Increasing the extent of ILM peeling enables a broader removal of traction and suppression of repopulation, resulting in improved anatomic and visual outcomes. The combination of established procedures, such as an encircling buckle and relaxing retinectomy, and extended ILM peeling may further optimize surgical outcomes for this highly challenging condition. ■

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### CODING ADVISOR

(Continued from page 33)

- **0810T:** Subretinal injection of a pharmacologic agent, including vitrectomy and one or more retinotomies.
  - New code January 1, 2023
  - Sunset January 2029
- **0936T:** Photobiomodulation therapy of retina, single session.
  - New code effective January 1, 2025
  - Sunset January 2030

### New in 2026

One new Category III code relevant to retina practice took effect in 2026.

- **0996T:** Insertion and scleral fixation of a capsular bag prosthesis containing an intraocular lens, with vitrectomy, including removal of the crystalline lens or dislocated intraocular lens when performed.
  - New code effective January 1, 2026
  - Sunset January 2030

Do not bill separately for cataract extraction, IOL insertion or exchange, or vitrectomy codes when reporting this code.

If a vitrectomy and removal of the crystalline lens or removal of a dislocated intraocular lens are performed *without* insertion with scleral fixation of a capsular bag prosthesis, this code should not be reported; instead, the appropriate vitrectomy and lens-related procedure codes should be used.

### WHY ACCURATE REPORTING MATTERS

Suprachoroidal injections provide a clear example of why proper Category III reporting is essential. Early services were reported with 0465T, generating the usage data needed for promotion to permanent Category I code 67516 in 2024. CPT Category III codes represent the leading edge of retina innovation. Treating them as automatically noncovered services increases compliance risk and forfeits legitimate reimbursement. Submitting claims to payers, documenting thoroughly, coordinating professional and facility billing, and tracking semiannual CPT updates allows practices to be paid appropriately today—while supporting the pathway to permanent codes tomorrow. ■

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(Continued from page 10)

requirements vary by payer and change quickly, and small documentation errors can derail reimbursement and delay care. Fellows were encouraged to become knowledgeable of their clinical coding practices to prevent avoidable, high-cost errors such as treating an unauthorized eye or administering the wrong drug.

Drug inventory and reimbursement timing were framed as solvency risks for practices carrying high-cost medications. The faculty emphasized tight inventory control, accurate unit billing, and caution with newly approved drugs until coding stabilizes. The panel also noted that cost conversations have become more frequent, reinforcing the need for clear counseling and realistic planning across the year.

#### ADVICE ON STARTING YOUR CAREER

Distinguished guest speaker Dean Elliott, MD, FASRS, delivered outstanding early-career advice with a simple premise: The first year is about stability, not heroics. Limit variables, do what is right for the patient, and know when to stop, he advised. He elaborated on the best preoperative preparations, postoperative follow-up, and managing antagonistic patients. In clinic, be a consultant who thinks deeply and always puts the patient first (Figure 2).

Closing remarks from Dr. Awh and the faculty during the “Starting Your Career: *The Real World*” session reframed

success around sustainability and community. Dr. Awh encouraged fellows to treat location and support systems as strategic career infrastructure and to protect what refuels them, so the early-career acceleration remains durable.

Discussion tables, dinner, and bowling reinforced that the retina community is built in the lecture hall and beyond.

Through candid discussion, surgical transparency, and practical guidance spanning innovation, complications, and business fundamentals, the Retina Fellows Forum equips senior fellows with both technical confidence and professional clarity. The enduring effect of the event reflects the extraordinary dedication of its course directors and organizing faculty, whose commitment continues to strengthen each new generation of vitreoretinal surgeons joining the retina the community. ■

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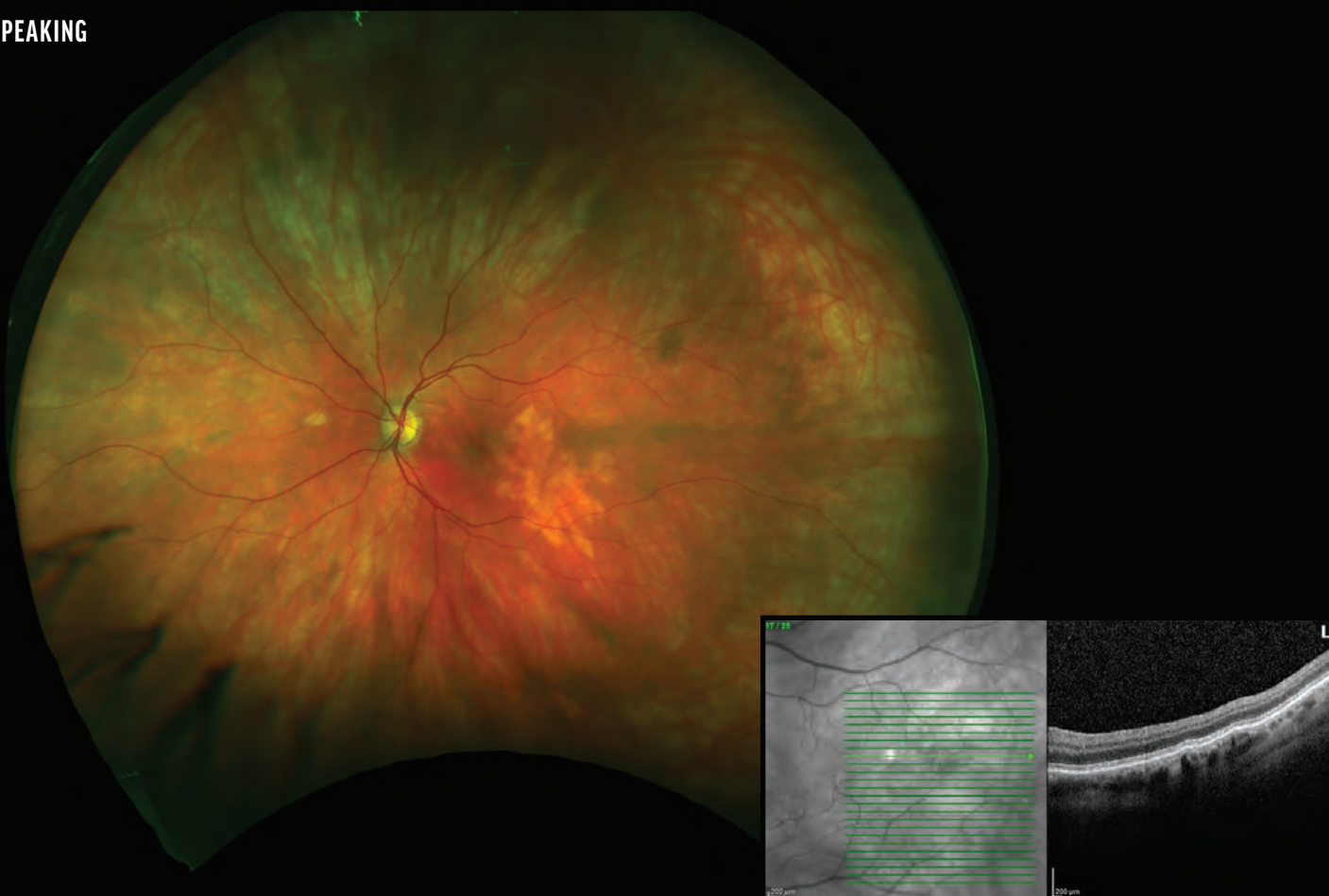


FIGURE 1

# A RARE CASE OF CHOROIDAL VITILIGO



Recognize this uncommon sign of varicella-zoster reactivation.

BY TINA TANG, MD, AND NAUMAN CHAUDHRY, MD

**A** 66-year-old immunocompetent woman with a history of recurrent cutaneous lesions was referred for evaluation of retinal lesions in the left eye noted during a routine examination. Her cutaneous lesions were characterized as discrete erythematous macules and small papules on her lower back. Her BCVA was 20/20 OU with normal IOPs and anterior segment examination.

Dilated fundus examination of her left eye showed irregular yellowish choroidal lesions temporal to the macula and focal areas of hypopigmentation nasal to the disc (Figure 1). OCT of her left eye showed trace epiretinal membrane with no definite mass lesion (Figure 1, Inset). Fundus autofluorescence revealed hyperautofluorescence corresponding to the yellow lesions, along with

hyperfluorescent changes on fluorescein angiography. ICG angiography of the left eye revealed early blocked cyanescence in the area of the lesions temporal to the macula (Figure 2A) with late foci of hyperfluorescence nasal and temporal to the disc (Figure 2B).

Work-up revealed positive varicella-zoster virus (VZV) immunoglobulin G, but immunoglobulin M was negative. The ocular oncology service ruled out ocular lymphoma. Her choroidal lesions slowly enlarged over the next 6 years with regular monitoring and no definite mass on OCT (Figure 3).

## CHOROIDAL VITILIGO

Choroidal vitiligo is an acquired condition characterized by flat depigmentation of the normally pigmented choroid.

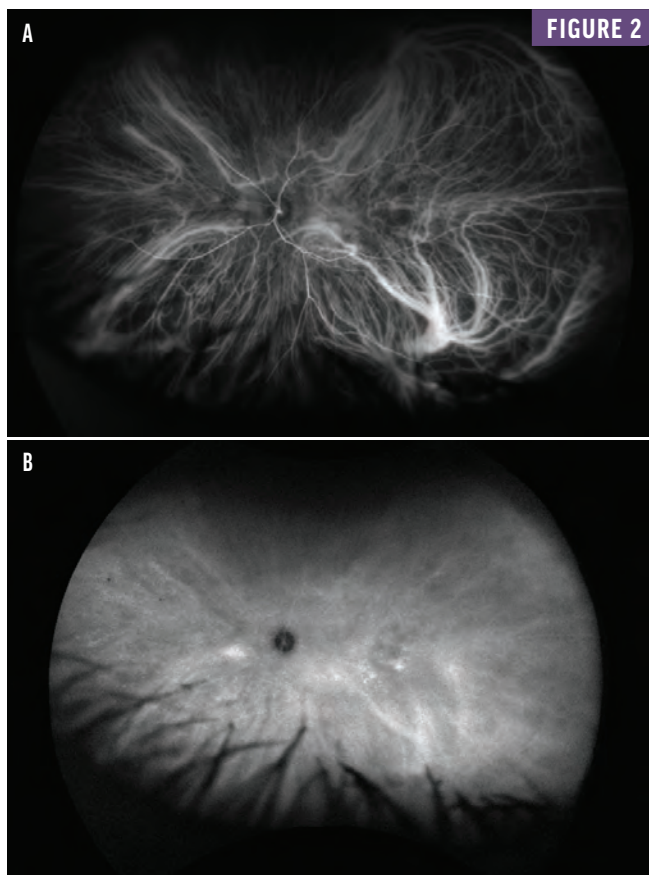


FIGURE 2



FIGURE 3

Primary choroidal vitiligo occurs in patients with cutaneous vitiligo without a history of intraocular inflammation, while secondary choroidal vitiligo typically results from inflammation of the uveal tract, most commonly associated with Vogt-Koyanagi-Harada syndrome.<sup>1</sup> Progressive choroidal vitiligo has also been reported after VZV reactivation with exudative retinal detachment.<sup>2</sup> VZV-associated uveitis can cause focal or multifocal hypopigmented choroidal lesions, often accompanied by choroidal thickening or scarring.<sup>3</sup> To the best of our knowledge, no prior cases have documented choroidal vitiligo associated with a history of zoster rash in the absence of ocular symptoms or inflammation.

#### RARE BUT POSSIBLE

In this case, the absence of systemic or ocular inflammation combined with a history of zoster rash suggested a postinflammatory mechanism related to VZV. Segmental vitiligo, a subtype of vitiligo, is characterized by cutaneous depigmentation in a dermatomal distribution and is hypothesized to have an autoimmune etiology.<sup>4</sup> To extrapolate from dermatological research, VZV may contribute to localized retinal pigment epithelium and choroidal depigmentation. The role of VZV in choroidal pathology remains underexplored, and further studies are needed to elucidate the underlying mechanisms.

This unique case highlights choroidal vitiligo as a rare but possible sequela of VZV reactivation, even in asymptomatic patients. ■

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