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Retina Today

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RETINATODAY.COM

20TH ANNIVERSARY

DIABETIC EYE DISEASE: A GLOBAL PERSPECTIVE

Expert insight on screening efforts and the changing landscape of care delivery.

eyetube

GLOBAL DR SCREENING: WHY AREN'T WE THERE YET?

USING OCTA TO PREDICT DR PROGRESSION

PEARLS FOR MANAGING COMPLEX DIABETIC PPV

SUBSCRIBE FOR FREE

The **first and only** FDA-approved treatment for adults with idiopathic macular telangiectasia type 2 (MacTel)[1]

ENCELTO™
(revakinagene taroretcel-lwey)
implant, for intravitreal use

Proven to **slow disease progression** in two phase 3 studies[1,2]*

*Based on two phase 3, randomized, multicenter, sham-controlled studies (Study A and Study B). Both studies evaluated the rate of ellipsoid zone (EZ) area loss (macular photoreceptor loss) in 228 adults with MacTel type 2 over 24 months. Results for ENCELTO: 54.8% reduction in retinal degeneration in Study A (P<0.0001); 30.6% reduction in Study B (P=0.0186).[1,2]

The permanent J-code for ENCELTO is now available: J3403

Scan the QR code for more information about accessing ENCELTO

INDICATIONS AND USAGE

ENCELTO is an allogeneic encapsulated cell-based gene therapy indicated for the treatment of adults with idiopathic macular telangiectasia type 2 (MacTel).

IMPORTANT SAFETY INFORMATION

CONTRAINDICATIONS

ENCELTO is contraindicated in patients with active or suspected ocular or periocular infections, and in patients with known hypersensitivity to Endothelial Serum Free Media (Endo-SFM).

WARNINGS AND PRECAUTIONS

ENCELTO implantation surgery and/or implantation related procedures have been associated with the following:

Severe Vision Loss

Severe vision loss defined as three or more lines of visual acuity loss [≥15 Early Treatment Diabetic Retinopathy Study (ETDRS) letters] has occurred following ENCELTO implantation. Monitor patients for signs and symptoms of vision loss and manage as clinically indicated.

Infectious Endophthalmitis

Infectious endophthalmitis may occur following ENCELTO implantation. Signs and symptoms of infectious endophthalmitis include progressively worsening eye pain, vision loss, or scleral and conjunctival injection. To mitigate the risk of endophthalmitis, use proper aseptic surgical technique for ENCELTO implantation. Monitor patients for signs or symptoms of infectious endophthalmitis. Remove ENCELTO implant if infectious endophthalmitis occurs and manage symptoms according to clinical practice.

Retinal Tear and Detachment

Retinal tears and retinal detachment may occur following ENCELTO implantation. Signs and symptoms of retinal tears include acute onset of flashing lights, floaters, and/or loss of visual acuity. Signs and symptoms of retinal detachment may include progressive visual field loss and/or loss of visual acuity. Use standard vitreoretinal surgical techniques during ENCELTO implantation to minimize the risk of retinal tears and retinal detachment. Monitor for any signs or symptoms of retinal tear and/or retinal detachment. Treat rhegmatogenous retinal detachment and retinal tears promptly. Remove ENCELTO implant, if vitrectomy with a complete gas fill or silicone oil fill is required.

Vitreous Hemorrhage

Vitreous hemorrhage, which may result in temporary vision loss, has occurred following ENCELTO implantation. Patients receiving antithrombotic medication (e.g., oral anticoagulants, aspirin, nonsteroidal anti-inflammatory drugs) may be at increased risk of vitreous hemorrhage. To reduce the risk of vitreous hemorrhage, interrupt antithrombotic medications prior to the ENCELTO implantation. Vitrectomy surgery may be necessary to clear severe, recurrent, or non-clearing vitreous hemorrhage. If the patient has a late onset vitreous hemorrhage (greater than one year following ENCELTO implantation surgery), examine the ENCELTO implantation site for possible implant extrusion. If implant extrusion has occurred, surgically reposition ENCELTO.

Implant Extrusion

Implant extrusion through the initial scleral wound has occurred following ENCELTO implantation. Signs and symptoms of implant extrusion include recurrent uveitis, vitreous hemorrhage, eye pain more than one year after implantation, or visibility of titanium fixation loop under the conjunctiva. To reduce the risk of implant extrusion, carefully follow the specific surgical steps for ENCELTO implantation.

Evaluate patients after 6 months to confirm proper positioning of ENCELTO and then annually. If ENCELTO begins to extrude, surgically reposition ENCELTO to a proper scleral wound depth either in the same site or in the opposing inferior quadrant of the vitreous cavity.

Cataract Formation

Cataract formation, including cataract cortical, cataract nuclear, cataract subcapsular, cataract traumatic, and lenticular opacities, has occurred following ENCELTO implantation. To reduce the risk of ENCELTO-related cataract formation or progression, carefully follow the specific surgical steps for ENCELTO implantation.

Suture Related Complications

Suture related complications, including conjunctival erosions due to suture tips and suture knots, have occurred following ENCELTO implantation.

To mitigate the risk of suture related complications, carefully follow the specific surgical steps for ENCELTO implantation and manage suture-related complications as clinically indicated.

Delayed Dark Adaptation

Delayed Dark Adaptation, a delay in the ability to adjust vision from a bright lighting condition to a dim lighting, has occurred following ENCELTO administration which remained unchanged for the duration of study follow up. Advise patients to take caution while driving and navigating in the dark.

ADVERSE REACTIONS

The most common adverse reactions (≥2%) reported with ENCELTO were conjunctival hemorrhage, delayed dark adaptation, foreign body sensation, eye pain, suture related complications, miosis, conjunctival hyperemia, eye pruritus, ocular discomfort, vitreous hemorrhage, blurred vision, headache, dry eye, eye irritation, cataract progression or formation, vitreous floaters, severe vision loss, eye discharge, anterior chamber cell, iridocyclitis.

Please see Brief Summary of full Prescribing Information on adjacent pages.

References: 1. ENCELTO [prescribing information]. Cumberland, RI. Neurotech Pharmaceuticals, Inc. **2.** Data on file. Neurotech Pharmaceuticals, Inc. Cumberland, RI.

neurotech

BRIEF SUMMARY OF PRESCRIBING INFORMATION

This Brief Summary does not include all of the information needed to use ENCELTO™ safely and effectively.

See full Prescribing Information for ENCELTO.

ENCELTO (revakinagene taroretcel-lwey) implant, for intravitreal use

Initial U.S. Approval: 2025

INDICATIONS AND USAGE

ENCELTO is indicated for the treatment of adults with idiopathic macular telangiectasia type 2 (MacTel).

DOSAGE AND ADMINISTRATION

Recommended Dose

For intravitreal implantation only

- ENCELTO is administered by a single surgical intravitreal procedure performed by a qualified ophthalmologist.
- The recommended dose is one ENCELTO implant per affected eye. Each ENCELTO implant contains 200,000 to 440,000 allogeneic retinal pigment epithelial cells expressing recombinant human ciliary neurotrophic factor (rhCNTF) (NTC-201-6A cell line), a neurotrophic factor.

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ADVERSE REACTIONS

Clinical Trials Experience

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

ADVERSE REACTIONS (cont'd)

Clinical Trials Experience (cont'd)

The safety data described in this section reflects exposure to ENCELTO in two clinical trials, Study 1 (NTMT-03-A) and Study 2 (NTMT-03-B) and are pooled for analysis. A total of 117 patients received ENCELTO, and 111 patients underwent a sham procedure and were followed for a duration of 24 months.

Serious adverse reactions occurred in six patients (5%) including suture related complications (n=5) and implant extrusion (n=1).

Table 1 lists the most common adverse reactions that occurred in ≥2% patients and with higher frequency in ENCELTO group compared to Sham group in Study 1 and Study 2.

Table 1. Adverse Reactions occurring in ≥2% of Patients and with higher frequency in ENCELTO group compared to Sham group in ENCELTO studies*

Adverse Reactions	ENCELTO (N=117) n (%)	Sham (N=111) n (%)
Conjunctival hemorrhage	36 (31)	29 (26)
Delayed dark adaptation	27 (23.1)	1 (1)
Foreign body sensation in eyes	18 (15)	15 (13.5)
Eye pain	18 (15)	10 (9)
Suture related complication**	18 (15.4)	3 (2.7)
Miosis	18 (15.4)	0 (0.0)
Conjunctival hyperemia	13 (11)	9 (8)
Eye pruritus	10 (9)	4 (3.6)
Ocular discomfort	10 (9)	1 (1)
Vitreous hemorrhage	10 (8.5)	0 (0.0)
Vision blurred	8 (7)	4 (4)
Headache	8 (7)	1 (1)
Dry eye	7 (6)	2 (2)
Eye irritation	6 (5.1)	2 (2)
Cumulative cataract incidence	6 (5)	0 (0)
Vitreous floaters	6 (5)	0 (0.0)
Severe visual loss>15 letters***	4 (3)	0 (0)
Eye discharge	4 (3.4)	1 (0.9)
Anterior chamber cell	4 (3.4)	0 (0.0)
Iridocyclitis	3 (2.6)	0 (0)

*Pooled data from Study 1 and Study 2; Adverse reaction rates were comparable between the two studies

**Suture related complications include exposed suture, foreign body sensation, conjunctival wound dehiscence, painful sutures, suture irritation, suture granuloma, scleral wound opening, and itchy suture

***Includes one case of visual loss due to cataract formation which remained unresolved at the end of the study

USE IN SPECIFIC POPULATIONS

Pregnancy

Risk Summary

There are no data on the use of ENCELTO in pregnant women. Endogenous CNTF is naturally found in maternal plasma, placental cells, and umbilical cord blood. It is not known if the use of ENCELTO increases CNTF above naturally occurring levels in these tissues.

In animal reproduction studies, subcutaneous administration of rhCNTF to pregnant rats and rabbits demonstrated no evidence of teratogenic effects on the fetus. However, when administered to rabbits at a dose level of 10ug/kg/day, a decrease in implantations and live fetuses was observed. When administered to rats at a dose level of 100ug/kg/day a decrease in corpora lutea was observed.

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

Data

Animal Data

See *Risk Summary* for details on data.

Lactation

Risk Summary

There is no data on the presence of ENCELTO in human milk, its effects on the breastfed infant, or its impact on milk production.

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

Pediatric Use

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

Geriatric Use

There were 38 patients (32%) 65 years of age and older and two patients (1%) 75 years of age and older in Study 1 and Study 2 who received ENCELTO. Clinical studies of ENCELTO did not include sufficient numbers of patients aged 65 and over to determine whether they respond differently than younger patients.

Manufactured for:
Neurotech Pharmaceuticals, Inc.
Cumberland, RI 02864

ENCELTO™
(revakinagene taroretcel-lwey)
implant, for intravitreal use

neurotech

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DR CARE: IT TAKES A VILLAGE

Diabetes has been labeled an epidemic and a global crisis for more than 20 years.[1] Despite improved systemic therapies and diabetic eye disease screening efforts, the prevalence of diabetic retinopathy (DR) continues to rise at an alarming rate. In 2021, 22.27% of patients with diabetes had DR, globally.[2] By 2045, researchers estimate the number of adults worldwide with DR will increase to 160.5 million, a more than 55% increase from 2020, with 44.82 million having vision-threatening disease.[2] Needless to say, we desperately need a better way to identify these patients and ensure they get the vision-saving care they need.

Over the years, we have covered many DR screening programs, including a single-day community event that started in Philadelphia, a teleretinal program in Boston, and a national program in Brazil. These efforts are all useful in identifying patients in need of care and connecting them with the larger health care system. Unfortunately, they simply aren't big enough on their own. What we really need is a global initiative—something adaptable to inhospitable locations to serve patients most in need.

To that end, Majda Hadziahmetovic, MD, from Duke Eye Center, spearheaded a global conversation on the unmet needs for our patients with diabetes and the hurdles we must overcome before realizing comprehensive global screening. In our flagship article *Global DR Screening: Why Aren't We There Yet?*, you will learn from a robust lineup of international experts from Brazil, Saudi Arabia, Sierra Leone, Singapore, United Kingdom, and the United States. They explore the unique barriers to adoption in their regions, as well as the benefits of creating organized, technology-assisted, and equitable screening programs.

When it comes to identifying and tracking disease in our clinics right now, fundus photography-based AI models and AI-assisted OCT screening may help, and Scott Song, BA, and T. Y. Alvin Liu, MD, provide information on those. In addition, Amani A. Fawzi, MD, and her team discuss how you can use OCT angiography to track disease progression.

Once patients have established care, novel implants and pharmaceutical mechanisms of action hold promise for more durable and efficacious treatment. Matthew Pfannenstiel, MD, and Leanne Clevenger, MD, explore various implants for DR/DME, while Shawn Kavoussi, MD, provides a granular look at tyrosine kinase inhibitors in the pipeline. Lastly, Dimitra Skondra, MD, PhD, FASRS, and Neil Sheth, MD, MBA, provide important pearls for managing complex diabetic vitrectomy.

This is one of our most comprehensive diabetes issues to date, and we hope it sparks a much-needed larger conversation about how we can all come together, as a retina village, to tackle the diabetes epidemic and reduce the risk of vision-threatening complications. ■

- Allen C. Ho, MD
- Robert L. Avery, MD
- Lejla Vajzovic, MD

1. Bonow RO, Gheorghiade M. The diabetes epidemic: a national and global crisis. *Am J Med.* 2004;116(Suppl 5A):2S-10S. doi.org/10.1016/j.amjmed.2003.10.014
2. Teo ZL, Tham YC, Yu M, et al. Global prevalence of diabetic retinopathy and projection of burden through 2045: systematic review and meta-analysis. *Ophthalmology.* 2021;128(11):1580-1591. doi.org/10.1016/j.ophtha.2021.04.027

FURTHER READING

Teleretinal Screening: Closing the Gap in Diabetic Eye Care
By Alice C. Lorch, MD, MPH

READ NOW

SCREENING EFFORTS CLOSE TO HOME

In 2022, Wills Eye Hospital initiated a single-day community diabetic retinopathy (DR) screening program; since then, participation has risen more than 45%, and nearly half of patients screened are uninsured with English as their secondary language. Approximately one in 36 patients screened had vision-threatening DR. Given the success of the program, it has now expanded to include 18 sites across four states.

After years of feasibility testing and validation for DR screening, Duke Eye Center launched its first organized, institution-wide AI-powered DR screening program in May 2026, marking a major milestone in integrating AI into routine clinical care. In addition to improving early detection, this collaborative aims to increase follow-up adherence, streamline referrals, and optimize the use of ophthalmology clinics.

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RT NEWS

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FDA APPROVES FIRST OPHTHALMIC BEVACIZUMAB

Outlook Therapeutics received FDA approval for Lytenava (bevacizumab-vikg) for the treatment of wet AMD, the first approved ophthalmic formulation of bevacizumab in the United States. The company expects Lytenava to receive 12 years of reference product exclusivity under the Biologics Price Competition and Innovation Act.[1]

"For more than two decades, bevacizumab has served as one of the most widely utilized anti-VEGF therapies in retina care despite the absence of an FDA-approved ophthalmic formulation," said Bob Jahr, MBA, chief executive officer of Outlook Therapeutics, in a press release. "Lytenava fundamentally changes that landscape."[1]

The approval comes 2 months after the FDA granted Outlook's appeal following a Formal Dispute Resolution process tied to its biologics license application for ONS-5010/Lytenava. The FDA's Office of New Drugs concluded that Outlook established "substantial evidence of effectiveness" for Lytenava in treating wet AMD based on the results of the NORSE TWO trial and confirmatory evidence including NORSE EIGHT, natural history, and mechanistic and pharmacodynamic data.[2]

The FDA had issued a Complete Response Letter in December 2025 regarding the company's biologics license application. Altogether, the FDA issued three Complete Response Letters for the drug dating back to 2023.[1]

OUTLOOK ON EYEWIRETV

Outlook Therapeutics CEO Discusses FDA Approval of Lytenava for Wet AMD

WATCH NOW

The company expects the product to become available to eligible US patients before the end of the year. The product is already authorized for use in Europe and the United Kingdom.

1. FDA approves Outlook Therapeutics' Lytenava as first ophthalmic bevacizumab for wet AMD [press release]. Eyewire+. July 24, 2026. Accessed July 29, 2026. tinyurl.com/4ppxa67p

2. Outlook Therapeutics wins appeal following formal dispute resolution process for ONS-5010/Lytenava (bevacizumab-vikg) [press release]. Outlook Therapeutics. May 26, 2026. Accessed July 29, 2026.tinyurl.com/3ch8yjh9

DOES VITRECTOMY INCREASE CME RISK AFTER CATARACT SURGERY?

Researchers from the Bascom Palmer Eye Institute recently completed a retrospective cohort study that revealed an elevated risk of cystoid macular edema (CME) following cataract surgery in eyes with an ocular history of pars plana vitrectomy (PPV).[1]

Using the TriNetX US Network, they identified 615,983 patients who underwent cataract surgery between December 2005 and December 2025—7,422 of whom had a history of PPV at least 6 months before cataract surgery. After propensity score matching (creating 7,318 propensity score–matched pairs), they found that CME occurred in 336 patients with a history of PPV (4.59%) compared with 90 (1.23%) without PPV ($P < .001$). The team noted that the elevated risk persisted in a subgroup analysis of PPV for retinal detachment versus non-retinal detachment indications, as well as after excluding surgical complications of cataract surgery.[1]

Although the study depended on coding-based diagnoses and did not include visual acuity outcomes, it suggests a history of PPV may be associated with a higher risk of postoperative CME after cataract surgery. Surgeons should

closely monitor these patients and consider enhanced antiinflammatory prophylaxis, the authors concluded in their paper.[1]

1. Zhang C, Sandhur BS, Theotoka D, et al. Risk of pseudophakic cystoid macular edema in eyes with previous pars plana vitrectomy [published online ahead of print July 30, 2026]. *JAMA Ophthalmol.* doi:10.1001/jamaophthalmol.2026.2767

TIRZEPATIDE ASSOCIATED WITH LOWER RISK OF WORSE DIABETIC EYE DISEASE

A study published in *Ophthalmology* showed that treatment with tirzepatide led to a reduced risk of diabetic eye disease-related complications such as nonproliferative diabetic retinopathy (NPDR) and proliferative DR (PDR).[1]

In the study, patients with diabetes who were overweight or had obesity and who initiated treatment with tirzepatide were propensity score-matched to patients receiving lifestyle intervention alone with no exposure to weight-loss drugs. After propensity matching for demographic, metabolic, and systemic covariates, 173,846 patients were included in the analysis. Tirzepatide use was found to be associated with reduced 12-month risk of DR incidence and worsening events compared with lifestyle intervention alone, including incident mild NPDR, PDR, DR with macular edema, vitreous hemorrhage, tractional retinal detachment, intravitreal anti-VEGF injection, and panretinal photocoagulation.[1]

The authors concluded that tirzepatide is "unlikely to exacerbate DR or related complications during the first year of therapy"; in fact, it may confer protection for patients with diabetes who are overweight, they wrote in their paper.[1]

1. Shah J, Razavi P, Festok M, at al. Tirzepatide and reduced risk of diabetic retinopathy and related complications: a multicenter US cohort study. *Ophthalmology*. 2026;133(6):728-732. doi:10.1016/j.ophtha.2026.01.013.

IMPLANT FOR GA SHOWS POSITIVE RESULTS IN PHASE 2

Inflammasome Therapeutics reported positive data from a phase 2 clinical trial evaluating its investigational therapy kamuvudine-8 (K8) for geographic atrophy (GA), showing statistically significant reductions in lesion growth and improvement in visual function over 6 months. K8 is a dual inflammasome inhibitor delivered as a bioerodible sustained-release intravitreal implant administered every 3 months. These data were presented at the American Society of Retina Specialists meeting this year in Montreal.[1]

According to the company, the 0.7-mg dose cohort achieved a 54% reduction in the mean rate of GA lesion growth compared with the pooled control group over 6 months using an FDA-preferred linear mixed-effects slope analysis (two-sided $P = .016$). In a prespecified subgroup analysis of eyes with extrafoveal lesions, treatment with K8 was associated with a covariate-adjusted 4-letter gain in BCVA versus control eyes (two-sided $P = .004$).[1]

The study revealed no safety signals during 6 months of follow-up with no drug-related serious adverse events or dose-limiting toxicities and no cases of endophthalmitis, intraocular inflammation, wet AMD, retinal vasculitis, or optic neuropathy. The company plans to initiate a global phase 3 pivotal trial for K8 in patients with GA.[1] ■

1. Inflammasome Therapeutics reports positive phase 2 data for K8 in geographic atrophy [press release]. Eyewire+. July 17, 2026. Accessed August 12, 2026. tinyurl.com/4f7keanc

Eyewire+ Pharma Update

- **Aravind Eye Care System** and **Alcon** launched the Aravind Alcon Global Centre of Excellence for Vitreoretinal Surgery Training in Coimbatore, India, in a collaborative effort to address the global shortage of retina specialists.
- The FDA accepted **Belite Bio's** new drug application for tinlarebant for the once-daily oral treatment of Stargardt disease type 1 with Priority Review; the Prescription Drug User Fee Act date is set for February 12, 2027.
- **Oculis** entered into an agreement to acquire Accure Therapeutics' global development and commercial rights to privosegtor (ACT-01), a neuroprotective drug candidate in development for the treatment of optic neuritis.
- **Science Corporation** commercially launched its PRIMA retinal implant for patients with geographic atrophy in Europe after receiving CE mark approval.
- **Tarsus Pharmaceuticals** entered into an agreement to acquire Alkeus Pharmaceuticals, along with its phase 3 drug candidate, gildeuretinol (ALK-001), in development for the treatment of Stargardt disease.
- **Topcon** received CE mark approval for GAIA, a fully automated ultra-widefield retinal imaging device that can capture a 209° field of view.
- **Vantage Biosciences** completed enrollment of its phase 2 SeeClear trial evaluating an oral AOC3 inhibitor, oruvestat, for the treatment of moderate-to-severe nonproliferative diabetic retinopathy.
- **EyePoint** vorolanib intravitreal insert 2.7 mg (Duravyu) missed the primary noninferiority endpoint versus on-label aflibercept 2 mg (Eylea, Regeneron) in the full phase 3 LUGANO dataset, but an ad hoc analysis excluding 9 of 211 patients (4%) showed noninferiority (nominal $P = .0096$).

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.

SEPTEMBER SPOTLIGHT: VISION CARE FOR UNDERREPRESENTED PATIENTS

In 2006, Rohit Varma, MD, MPH, contributed an article called *Vision Care Interventions Aimed at Latinos are Needed* to one of *Retina Today's* first issues. The article shared findings from the Los Angeles Latino Eye Study (LALES), which revealed that Latinos were not receiving adequate vision care. Two decades later, Dr. Varma reflects on the study's enduring effect on the profession today.

– Rebecca Hepp, MA, Editor-in-Chief

Retina Today (RT): What were the findings from the Los Angeles Latino Eye Study?

Rohit Varma, MD, MPH: The LALES was the largest and most comprehensive population-based study of retinal disease in Latino adults in the United States and provided estimates of the prevalence of diabetic retinopathy (DR) and AMD in one of the nation's fastest-growing populations. The retinal findings were striking: Nearly half of Latino adults with diabetes had DR, and approximately one in five participants with diabetes was first diagnosed during the study examination.[1] More broadly, LALES demonstrated the power of rigorous population-based research to identify opportunities for prevention, early detection, and improved patient care.

RT: How has awareness of retinal disease in underrepresented patients improved?

Dr. Varma: One of the greatest advances has been the recognition that retinal disease is frequently asymptomatic in its earliest stages, making regular examination and systematic screening essential. This lesson carries particular weight for the population studied in the LALES, given the high burden of DR documented among Latino adults.

Equally important, the past 2 decades have seen remarkable therapeutic advances. Anti-VEGF therapy has transformed the management of diabetic macular edema, proliferative DR, and wet AMD, improving visual outcomes.

Population-based research has also expanded across a broader range of communities, and the combination of earlier diagnosis, stronger screening programs, wider adoption of teleophthalmology, advanced retinal imaging, and effective therapy has meaningfully improved care. Important gaps remain, however, in ensuring that every patient receives timely, high-quality eye care.

RT: What are the next steps to ensure underrepresented patients receive the care they need?

Dr. Varma: The next frontier is extending the lessons of LALES to historically understudied populations, particularly those living in rural communities.

Equally important is continued federal investment in long-term population-based cohort studies. Each follow-up examination creates opportunities to answer new scientific questions that could not have been envisioned when the study began.

Longitudinal population-based cohort studies are among our nation's most valuable scientific resources because they allow us to understand who develops disease, why it progresses, and how retinal changes predict future systemic health. Increasingly, these studies also allow us to evaluate retinal biomarkers as indicators of biological aging and systemic vascular health.

This vision is reflected in the recent National Heart, Lung, and Blood Institute roadmap led by Emily Y. Chew, MD, and colleagues. It emphasizes leveraging existing longitudinal cohort studies to investigate retinal biomarkers of cardiovascular disease, stroke, vascular dementia, and other manifestations of systemic vascular aging.[2]

Looking back, the LALES demonstrated how rigorous population-based retinal research can transform our understanding of eye disease and improve patient care. If the first 20 years established the retina as a window to eye disease, the next 20 years will establish it as one of medicine's most powerful windows to systemic health. ■

Acknowledgment: I am deeply grateful to the National Eye Institute and the National Institutes of Health for their continuous strong support of this work.

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FURTHER READING

Vision Care Interventions Aimed at Latinos are Needed
December 2006
By Rohit Varma, MD, MPH

ONE TO WATCH

RT Retina Today

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Alexis Warren, MD

Dr. Warren's advice: If you choose retina, you will always be learning and growing. Early in your career, it is important to make sure you're also having fun, whether that's with great colleagues, new adventures, or personal goals you can finally make a priority. You did it—now it's time to enjoy the rewards of your hard work.

WHERE IT ALL BEGAN

I grew up in Kansas City as the youngest of three siblings. From a young age, I knew I wanted to be a retina specialist—probably because my dad is a retina specialist, and he would take me to work with him. I loved spending time in the clinic, coloring with the same pencils he used for his retinal drawings, and spinning on the clinic stool until I grew dizzy. At the time, I didn't really understand ophthalmology or what a retina was, but I was drawn to the passion I saw in my dad, and I knew that was something I wanted to emulate. It wasn't until medical school that I realized just how remarkable the retina really is, with its connection with the brain and the rest of the body; that early spark has stayed with me ever since.

MY PATH TO RETINA

Having my father as a mentor from such a young age, retina always felt like a natural—almost inevitable—choice. During my residency, I found myself drawn to the retina clinic, the attendings, and the patients. I was happiest in the retina workroom with the team, reviewing images and working through challenging cases.

I still remember being present when one of the first-year fellows performed his first epiretinal membrane peel. He couldn't stop smiling, and the energy and sense of satisfaction in the room were almost electric. The ability to manipulate and peel tissue mere microns thick continues to amaze me and reinforces why the field of retina is so special.

SUPPORT ALONG THE WAY

Some of the first names that come to mind are Jennifer I. Lim, MD; William F. Mieler, MD; and R. V. Paul Chan, MD, MSc, MBA, FACS. I have had many mentors throughout my career, but these three truly helped shape me into the surgeon and clinician I am today. I admire not only their exceptional clinical skills, but also the compassion they show their patients and their humility, despite being giants in the field of retina. They continue to support and advocate for my professional growth, which I am deeply grateful for. It also helps that we live in the same city, so we are able to stay in touch.

AN EXPERIENCE TO REMEMBER

A moment that stands out most was helping one of my residents match into a retina fellowship. Watching her interest and dedication to retina grow, and then seeing her successfully match into her dream fellowship, was incredibly rewarding.

I know firsthand how a mentor can open your eyes to a path you never knew existed. While I was only a small part of her journey, it's exciting to think about the next generation of retina specialists and how, perhaps, I can play a role in someone's journey toward the best job in the world. ■

Alexis Warren, MD, is an assistant professor and vice chair of Diversity and Inclusion at the University of Chicago Ophthalmology and Visual Sciences in Chicago. She can be reached at awarren10@gmail.com.

To read about our other One to Watch honorees, scan the QR code or visit retinatoday.com.

ARDS 2026: EXPERT PERSPECTIVES

Three panels tackled tough surgical and medical topics.

BY CAROLINE C. AWH, MD

The 54th annual Aspen Retinal Detachment Society (ARDS) meeting, held February 28 – March 4, in Snowmass, Colorado, brought together leaders in vitreoretinal surgery, medical retina, ocular oncology, and uveitis for a series of lively panel discussions. As always, these sessions generated thoughtful debate, practical clinical pearls, and valuable perspectives. Here, I summarize the meeting's three engaging panels, which focused on surgical decision making and emerging pharmacologic therapies.

Image courtesy of Kevin Caldwell Photography

Figure 1. The first panel showcased the expertise of Drs. Rachitskaya, Duncan, Murray, Awh, and Ho.

PANEL 1: ADVANCES IN SURGICAL RETINA

The first panel, moderated by Timothy G. Murray, MD, MBA, opened with a case of a patient with a visually significant cataract and a malignant choroidal melanoma. The panelists—including Carl C. Awh, MD; Jacque L. Duncan, MD; Allen C. Ho, MD; and Aleksandra V. Rachitskaya, MD—discussed combined versus staged surgery (Figure 1). They agreed that the approach depends on the pathology, surgeon expertise, and the availability of local cataract surgeons. Dr. Ho noted that if the tumor is growing, it might be preferable to address the malignancy first. Dr. Awh suggested that patients with epiretinal membrane and vitreomacular traction often gain enough improvement from cataract surgery that they do not need macular surgery. The panelists also briefly touched on the use of dyes for macular surgery; most use indocyanine green (ICG) dye and have not had cases of ICG-related phototoxicity.

The second case of a dislocated IOL generated discussion about secondary lens options. The panelists stressed the importance of understanding lens type, capsular support, and patient-specific factors before selecting a surgical approach. The group acknowledged the many surgical techniques available, and surgeons should use the technique that gives them the best surgical outcome based on their own experience and training. Evolving secondary IOL technologies were briefly discussed, including an investigational prosthetic capsular support system.

A case of epiretinal membrane highlighted the variable use of dye, routine internal limiting membrane peeling, and combined phacoemulsification. Finally, Dr. Murray shared a case of iris melanoma with ciliary body extension, in which he completed cataract extraction, IOL implantation, and intraoperative endolaser to the tumor, emphasizing the importance of lifting the hyaloid in these cases.

PANEL 2: DRUG TREATMENTS WE USE AND THE PIPELINE

The second panel, moderated by Donald J. D'Amico, MD, focused on one of retina's most persistent challenges: extending treatment durability while maintaining visual outcomes. The panel included Dr. Duncan; Tarek S. Hassan, MD; Tara A. McCannel, MD, PhD; Lucia Sobrin, MD, MPH; and Robert L. Avery, MD (Figure 2). The discussion opened with the port delivery system (PDS) with ranibizumab (Susvimo, Genentech/Roche), which has demonstrated excellent visual acuity preservation through sustained anti-VEGF delivery. Despite these results, the panelists agreed that widespread adoption has been limited by practical considerations, including surgical implantation, reimbursement challenges, and the growing availability of longer-acting injectable agents. Dr. D'Amico pointed out that our perceptions of the PDS technology might have been different had every-6-month surgical implants preceded monthly intravitreal injections. The panelists then highlighted emerging therapies designed to extend intraocular drug durability through binding to vitreous components, including TH103, an anti-VEGF biologic under development by Kalaris Therapeutics.

Drawing parallels to sustained delivery in other spaces,

Image courtesy of Kevin Caldwell Photography

Figure 2. The second panel focused on pharmacologic therapy, with Drs. Avery, Sobrin, Duncan, Hassan, McCannel, and D'Amico.

Dr. Sobrin shared insights from uveitis management. While longer-acting fluocinolone injectables are available, patients often still require a dexamethasone implant (Ozurdex, Abbvie) every 2 to 3 months because of its superior potency. Consequently, even longer-acting alternatives do not always reduce treatment frequency. The panelists also discussed intravitreal steroids as adjunctive therapy for diabetic macular edema, cystoid macular edema, and wet AMD, particularly in patients with incomplete responses to anti-VEGF treatment. Insurance-mandated step therapy remains a major determinant of treatment selection.

The panelists also discussed the distinction between anatomic and functional outcomes. Although newer agents may achieve greater retinal drying and longer durability, visual acuity gains have remained similar across therapies. Treatment burden, disease control, and durability should also be considered important measures of efficacy, not just visual acuity.

The session concluded with a look toward future therapeutic targets beyond VEGF inhibition, including Wnt signaling and TIE2 activation pathways, as well as the growing role of home OCT monitoring. The panelists envisioned a future in which more durable therapies are paired with remote monitoring technologies, allowing treatment to become more personalized and less burdensome for patients.

PANEL 3: SURGICAL RETINA: TRAUMA, UVEITIS, AND VISUALIZATION

The final panel, moderated by R.V. Paul Chan, MD, MBA, MSc, and including Drs. Avery, McCannel, Sobrin, and David R. Chow, MD, explored the complexities of surgical decision making through a series of challenging cases. The first case involved a zone 1 open globe injury with an intraocular foreign body and retinal detachment (RD). Management strategies varied among the panelists: Some advocated delaying RD repair to allow the cornea to heal, while others favored immediate repair despite the potential need for a combined penetrating keratoplasty to achieve adequate visualization. Panelists also debated whether or not to add a scleral buckle. The discussion underscored the importance of flexibility in ocular trauma surgery and the role of ultrasound in the preoperative assessment.

The panel also discussed an unusual case of pediatric exudative RD that was ultimately diagnosed as uveal melanoma. The discussion served as a reminder that ocular tumors should remain in the differential even in atypical age groups and highlighted the value of multimodal imaging and subspecialty consultation when presentations do not fit classic patterns.

The panel emphasized a stepwise approach to managing uveitis and intraocular lymphoma cases. Using cases of epiretinal membranes with cystoid macular edema in uveitis, Dr. Sobrin explained that macular edema should first be treated medically, with surgery reserved for persistent traction after inflammation is controlled. In cases suspicious for primary vitreoretinal lymphoma, panelists agreed that clinicians should obtain a brain MRI before biopsy, collaborate with neuro-oncology early, and recognize the limited yield of lumbar puncture. Debate centered on diagnostic vitrectomy alone versus in combination with subretinal biopsy to maximize diagnostic yield and avoid repeat surgery.

The session concluded with a debate surrounding pneumatic retinopexy and the increasing effect of OR access on RD management. Experiences from Canada highlighted how resource limitations have driven broader use of pneumatic and temporizing "bubble-and-book" strategies, prompting discussion about how health system constraints increasingly influence surgical decision making in retina practice.

DON'T MISS THE DISCUSSION NEXT YEAR

The open discussion between panelists and attendees regarding the challenges facing retina specialists remains a hallmark of the ARDS meeting. Mark your calendars for next year's meeting, set for February 27 – March 3, 2027, which will deliver another set of outstanding panels. ■

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SAVE THE DATE:
55th Annual Aspen Retinal Detachment Society
February 27 – March 3, 2027
Snowmass Village, Colorado

THE GROWING PIPELINE FOR DIABETIC EYE DISEASES

BY PETER K. KAISER, MD

Welcome to the second installment of this pipeline poster series from *Retina Today*. We kept several foundational elements from the first iteration of the poster, the most important of which is the classification of pipeline candidates by route of administration before subclassifying them by drug class. Keep in mind that this means that some classes of drugs may appear in more than one route. Steroid treatments, for example, may be found under the intravitreal, suprachoroidal, and drops route.

One class of drugs that appears in multiple routes of administration is also one that we should keep an eye on in 2026: tyrosine kinase inhibitors (TKIs), specifically, those that leverage intravitreal injection routes. Two TKIs—Axitinib (Axpaxli, Ocular Therapeutix) and vorolanib (Duravyu, EyePoint Pharmaceuticals)—are in pivotal studies. If those studies demonstrate safety and efficacy deemed sufficient by the US Food and Drug Administration, that may mean that we have new solutions to address diabetic retinopathy (DR) and/or diabetic macular edema (DME).

PIVOTAL STUDY

VEGF INHIBITION

Tarcocimab *(Kodiak Biosciences)*
Ispagratagene *(4D Molecular Therapeutics)*

TYROSINE KINASE INHIBITION

Axitinib | **Axpaxli** *(Ocular Therapeutix)*
Vorolanib | **Duravyu** *(EyePoint Pharmaceuticals)*

WNT/β-CATENIN ACTIVATION

MK-3000 *(EyeBio/Merck)*

FGF INHIBITION

RC-28E *(RemeGen/Santen)* **- anti-VEGF, anti-FGF**

STEROIDS

OCS-01 *(Oculis)*

SURGICAL

Port Delivery System with Zifibancimig *(Roche)*

GENE THERAPY

RGX-314 *(RegenxBio)*

This year's zoom-in illustration is dedicated to an intracellular mechanism of TKIs. Recognizing that the nuances and pharmacodynamics are complex, we nevertheless think a simple schematic depicting the ability of TKIs to block ATP binding sites at the intracellular level communicates TKIs' fundamental value proposition.

There are several other drug candidates moving forward with pivotal studies for DR and DME. Keep an eye out for the blue badge indicating which drug candidates have entered this final phase of research. Similarly, look for the gene therapy badges scattered throughout the pipeline poster, the number of which hints at a possible forthcoming focus for researchers, funding, and conference organizers. ■

GENE THERAPY

VEGF INHIBITION

SKG-0106 *(Skyline Therapeutics)*
FT-003 *(Frontera Therapeutics)*
Ispagratagene *(4D Molecular Therapeutics)* PIVOTAL STUDY
Risuteganib *(Allegro/Senju)*
AXT107 *(Asclepix)*
OCU200 *(Ocugen)* **- Tumstatin and transferrin fusion protein**
AG-73305 *(Allgenesis Biotherapeutics)* **- Anti-VEGF, Anti-integrin**

GENE THERAPY

RGX-314 *(RegenxBio)* PIVOTAL STUDY

If you have any corrections, comments, or requests for additions to this poster, email Cara Deming, Director of Special Projects, at cdeming@bmctoday.com.

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MEDICAL RETINA DEBATES AT VBS 2026


Experts came together to discuss peer review, ROP care, uveitis management, and dry AMD therapies.

BY ALEXANDER SHAER, BS, AND TRISHA ORTIZ, BS

The medical retina debates at the 14th annual Vit-Buckle Society (VBS) meeting, held April 9-11, 2026, in Las Vegas, provided some of the most spirited discussions of the meeting. Debaters dressed in their best Alice in Wonderland-themed costumes to deliver thought-provoking discussions on the peer review process and a range of hot-topic treatment approaches (Figure).

DEBATE 1: PEER REVIEW SHOULD BE...

The first debate tackled a long-standing academic grievance: Should peer review remain unpaid? Katherine E. Talcott, MD, from Cleveland Clinic, presented the argument that peer review is a highly skilled, unpaid labor that helps prop up massively profitable publishing companies, noting Elsevier's reported $1.5 billion profit in 2024. She also pointed out the unspoken pressure of the current system, where many reviewers accept assignments out of a sense of obligation and lingering fear that declining an invitation may jeopardize a journal's faith in their own future submissions.

Durga S. Borkar, MD, MMCi, from Duke University, presented the opposing view: that reviewing is an academic privilege. Introducing financial compensation could dangerously complicate the process and raise additional ethical dilemmas, she argued. She prosed several unanswered questions: Would reviewers prioritize journals that compensate more? Is one reviewer's opinion worth more than another's? Does the amount a journal pays determine the depth of the review you perform? Additionally, the sheer volume of global submissions makes paying every reviewer logistically impossible. Instead, she suggested publishers' profits go toward subsidizing open-access initiatives.

The discussion highlighted a middle ground solution to incentivize reviewers through discounted journal fees rather than direct cash payments, which rewards the labor without compromising the ethics of the review process.

DEBATE 2: HOW TO MANAGE NONINFECTIOUS UVEITIS

The second debate focused on whether noninfectious uveitis should be managed with local corticosteroids or systemic immunomodulatory therapy (IMT). Parisa Emami, MD, from the University of California Davis, debated that while steroids are effective and act quickly, they have a host of ocular complications and don't treat extraocular disease, which is often coexistent. Because conditions such as sarcoidosis often affect several systems, systemic IMT can treat both the underlying disease and control the bilateral ocular uveitis more effectively, she said.

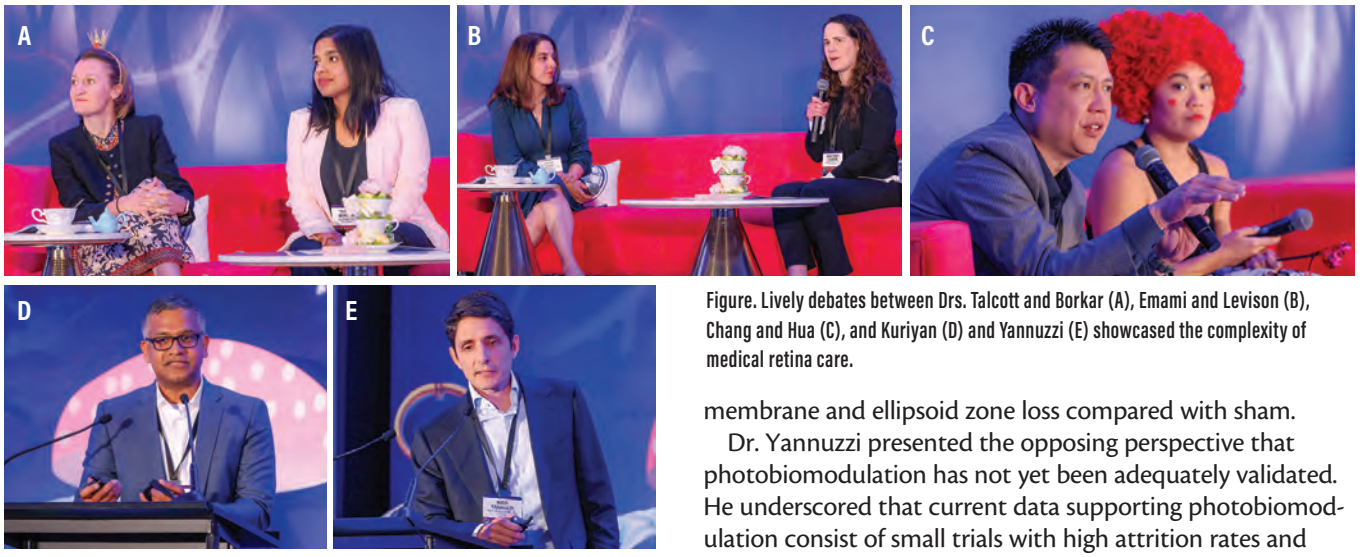
Ashleigh L. Levison, MD, from Colorado Retina Associates, presented the case for local corticosteroids. Many uveitis patients have inflammation confined to the eye, making targeted therapy more practical and safer, she argued. In addition, steroids act rapidly, are familiar to ophthalmologists, and avoid the potentially severe systemic complications seen with IMT, which ophthalmologists may not be fully equipped to manage. Furthermore, she cited the Multicenter Uveitis Steroid Treatment Trial, which showed that steroid implants worked better at controlling inflammation at every time point up to 54 months compared with IMT.

The panel discussion suggested the answer is not black and white and that treatment is often tailored to disease type, systemic involvement, and patient preference.

DEBATE 3: MANAGING MID ZONE II ROP

The third debate addressed the optimal treatment for mid zone II retinopathy of prematurity (ROP). Emmanuel Y. Chang, MD, PhD, of Retina & Vitreous of Texas, presented the argument for laser photocoagulation for ROP, emphasizing long-term anatomic stability. He cited decades of follow-up data and high success rates supporting laser and noted that it offers a more definitive intervention, reducing clinic burden for patients and families. He argued that our focus should be on which treatment best preserves vision

VIT-BUCKLE SOCIETY



Images courtesy of Kevin Caldwell Photography

Figure. Lively debates between Drs. Talcott and Borkar (A), Emami and Levison (B), Chang and Hua (C), and Kuriyan (D) and Yannuzzi (E) showcased the complexity of medical retina care.

through adulthood and cautioned that peripheral avascular retina treated with anti-VEGF alone at infancy may thin out with ocular growth, predisposing these eyes to retinal tractional changes, tears, and detachments.

Hong-Uyen Hua, MD, of Bascom Palmer Eye Institute, discussed the advantages of anti-VEGF therapy, focusing on safety, accessibility, and structural preservation. She noted that laser treatment requires general anesthesia, which may not be suitable for smaller, sicker infants. She highlighted the increased incidence of myopia and strabismus due to laser-related changes. She also stressed the practicality of anti-VEGF therapy as an accessible and safe procedure that can be more reliably employed by pediatric ophthalmologists who may have less experience using lasers. Lastly, she emphasized that first-line anti-VEGF therapy allows for continued retinal vascularization. That said, Dr. Hua acknowledged limitations in the evidence supporting anti-VEGF therapy, noting that many studies have been retrospective and do not control for gestational age or birth weight.

The audience agreed with the practicality of anti-VEGF therapy, leveling the playing field by allowing more ophthalmologists to treat eyes with ROP.

DEBATE 4: PHOTOBIOMODULATION FOR DRY AMD

The session closed with a lively debate between Ajay Kuriyan, MD, of Mid Atlantic Retina and Wills Eye Hospital, and Nicolas A. Yannuzzi, MD, of Bascom Palmer Eye Institute, regarding the use of photobiomodulation.

Dr. Kuriyan summarized the evidence in favor of photobiomodulation, citing its plausible mechanism of action targeting mitochondria, which are known to be largely involved in AMD pathogenesis. He presented small sham-controlled studies showing visual improvement with treatment across all time points and noted an independent reading center study demonstrating less external limiting membrane and ellipsoid zone loss compared with sham.

Dr. Yannuzzi presented the opposing perspective that photobiomodulation has not yet been adequately validated. He underscored that current data supporting photobiomodulation consist of small trials with high attrition rates and imbalanced baseline features that favored the photobiomodulation group. Additionally, he emphasized weak anatomic data lacking baseline incidence rates and functional outcomes likely driven by regression to the mean effect. Finally, Dr. Yannuzzi noted the lack of benefit in other key functional endpoints, such as color and contrast sensitivity, and no visual or anatomic benefits shown in meta-analyses.

The discussion showed overwhelming consensus that larger, better-designed studies with stronger baseline characterization and longer follow-up are still needed to determine the efficacy of photobiomodulation for dry AMD.

THE ART OF FRIENDLY DEBATE

Across all four debates, the clearest takeaways were not necessarily a matter of reaching consensus, but of recognizing the complexity of these highly relevant issues in the field. Each topic exposed meaningful tensions between evidence, practicality, safety, and long-term outcomes. ■

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SAVE THE DATE:
15th Annual Vit-Buckle Society Meeting
April 1-3, 2027, Miami

CHRONIC CME AFTER ARN


Persistent CME may be caused by inflammatory and ischemic mechanisms, even after apparent viral quiescence.

BY COLLIN RICHARDS, MD, AND DAVID FELL, MD

A 36-year-old woman presented with blurred vision in her left eye. The initial examination demonstrated a VA of 20/30 OS with peripheral necrotizing retinitis, arteritis, and vitritis (Figure 1). Anterior chamber paracentesis was positive for varicella zoster virus (VZV), confirming a diagnosis of VZV-associated acute retinal necrosis (ARN).

The patient underwent prompt treatment with intravitreal foscarnet and oral valacyclovir 1 g three times daily. Despite successful stabilization of the retinitis and serial anterior chamber taps, which remained negative for viral DNA, the patient developed a prolonged course of recurrent cystoid macular edema (CME) over the next 2 years.

CLINICAL COURSE

Following induction therapy, the patient's retinitis regressed, and visual acuity initially stabilized. At month 3, the patient's anterior chamber tap was negative for VZV, and systemic antiviral therapy was reduced to valacyclovir 1 g daily. However, over the ensuing months, she experienced recurrent and progressive CME with fluctuating visual acuity.

At month 14, there was concern for recurrent inflammation due to rare cell in the anterior chamber. In addition, we noted worsening CME while on topical prednisolone acetate and ketorolac, and her VA declined to 20/100. The anterior chamber tap was still negative for VZV. By month 20, we noted progressive CME and cataract formation. The patient remained on prophylactic valacyclovir 1 g daily during the entire clinical course after month 3; meanwhile, her VA declined again to 20/200, while the anterior chamber tap remained negative for VZV.

Here, we faced a therapeutic dilemma: Was the persistent CME inflammatory, infectious, ischemic, or multifactorial?

UNDERSTANDING CME IN ARN

CME after ARN is a complex and multifactorial process, with various pathogenic mechanisms. Caution is warranted when considering local steroids, as cases of viral reactivation have been reported with unopposed local steroids.[1]

The differential diagnosis of CME in ARN includes:

- **Inflammatory CME:** Persistent inflammation and blood-retinal barrier breakdown are common contributors to CME following ARN. Even after viral control is achieved, chronic immune activation can sustain vascular leakage and edema.[2]
- **Infectious reactivation:** Reactivation of VZV remains a serious concern for any patient with recurrent inflammation or worsening CME. Maintaining patients on a prophylactic regimen of systemic antiviral therapy is critical long-term, and treatment doses can be reintroduced when there is a concern for reactivation. Repeat aqueous sampling may help guide management decisions, particularly before escalating corticosteroid therapy.
- **Ischemic and VEGF-driven CME:** Peripheral retinal ischemia after necrotizing retinitis can induce VEGF upregulation and chronic vascular permeability. In

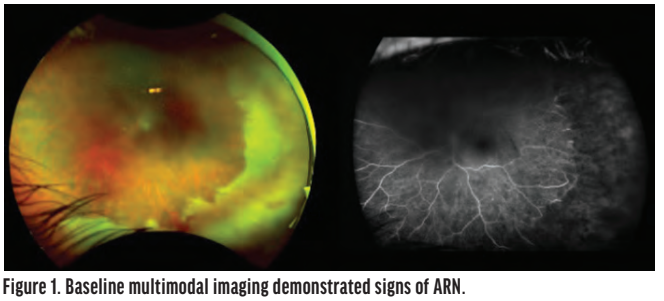

Figure 1. Baseline multimodal imaging demonstrated signs of ARN.

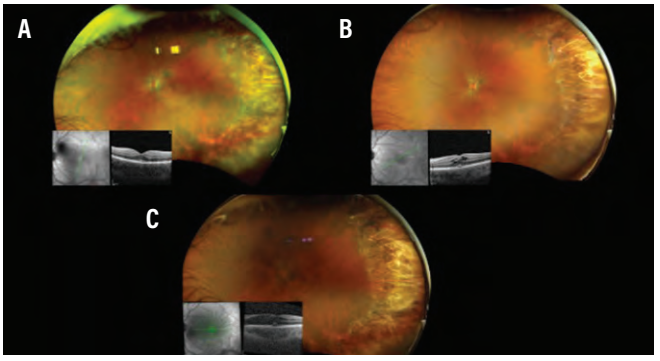

Figure 2. OCT at month 3 demonstrated chorioretinal scarring in the previously affected area without CME (A). At month 14, with no reactivation of ARN, OCT showed new CME (B). At month 20, OCT showed worsening posterior subcapsular cataract and CME despite topical ketorolac and prednisolone acetate (C).

these cases, VEGF-mediated edema may persist despite corticosteroid or antiviral therapy.[3]

Management options for CME following ARN include systemic, periocular, or intravitreal corticosteroids; continued antiviral suppression; intravitreal antiviral injection; intravitreal anti-VEGF injection; and other immunomodulatory agents (eg, tocilizumab or interferon alpha-2a).

In this patient, repeat negative aqueous taps and the absence of clinical signs of inflammation reduced our concern for active viral replication and shifted our attention toward inflammatory and ischemic mechanisms.

ANTI-VEGF THERAPY AS A TURNING POINT

At month 20, the patient received intravitreal aflibercept 8 mg (Eylea HD, Regeneron). Two weeks later, her VA improved from 20/200 to 20/60 with significant reduction in CME (Figure 2). Subsequently, the patient received intravitreal bevacizumab (Avastin, Genentech/Roche), sub-Tenon triamcinolone 40 mg, and cataract extraction with IOL placement. By month 27, her VA improved significantly to 20/25 with substantial restoration of macular architecture. Her vision remained stable without CME recurrence (Figure 3).

This case highlights several important lessons in the management of chronic CME after ARN, including:

- **CME in ARN is often multifactorial.** Although inflammation is typically emphasized, VEGF-driven vascular permeability from peripheral ischemia may play a substantial role in persistent edema.
- **Repeat viral testing can guide steroid escalation.** In this patient, serial negative aqueous taps helped support escalation of antiinflammatory therapy, while reducing concern for active viral replication.
- **Anti-VEGF therapy may be underused.** The patient's dramatic response to anti-VEGF therapy suggests VEGF-mediated vascular dysfunction may be an important therapeutic target in select patients with chronic CME after ARN.

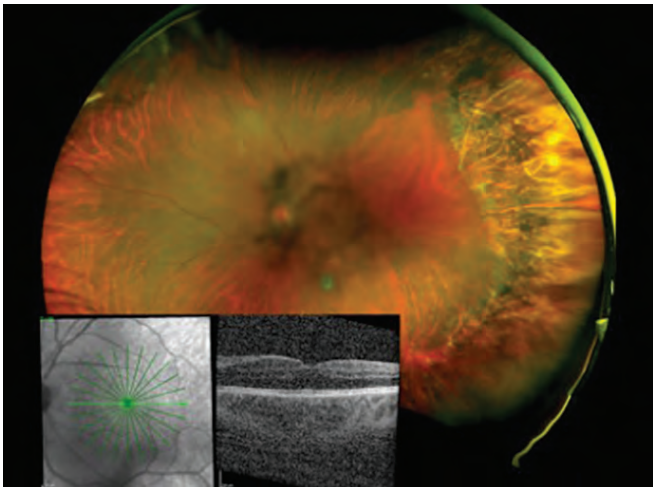

Figure 3. Two weeks after the initiation of intravitreal anti-VEGF therapy, OCT demonstrated resolution of CME.

- **Long-term management requires flexibility.** Patients with ARN frequently require individualized and evolving treatment over months to years. The balance between antiviral coverage, inflammation control, and management of ischemic complications can be delicate. While some patients may wean off antivirals, it is important to maintain prophylactic dosing in the setting of chronic inflammation, especially with local steroid therapy.

A MULTIFACTORIAL DISEAESE PROCESS

Chronic CME after ARN remains a challenge with limited evidence-based guidance. This case demonstrates how persistent edema may reflect overlapping inflammatory and ischemic mechanisms even after apparent viral quiescence.

Clinicians must maintain a broad differential diagnosis, using repeat viral testing when appropriate and considering anti-VEGF therapy in refractory cases. In select patients, targeting VEGF-mediated vascular leakage may lead to meaningful anatomic and visual recovery. ■

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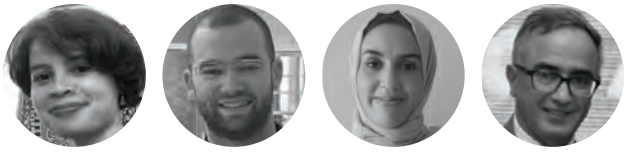
SCLERAL DEHISCENCE FOLLOWING PPV IN A PATIENT WITH MARFAN SYNDROME



Consider a surgical approach that can better accommodate a thin sclera in patients with this connective tissue disorder.

BY SAFI HIND, MD; YOUNES TLEMÇANI, MD, PHD; SARAH BELGHMAIDI, MD, PHD; AND ABDELJALIL MOUTAOUAKIL, MD, PHD

Marfan syndrome (MFS) is an autosomal dominant genetic disease affecting connective tissue. The defect lies in the *FBN1* gene on chromosome 15, encoding fibrillin, an extracellular matrix glycoprotein.[1,2] Broad involvement occurs in MFS, notably with cardiovascular, musculoskeletal, dermatological, and ocular effects.[3,4] Ocular manifestations include ectopia lentis, microspherophakia, myopia, glaucoma, retinal tears, and retinal detachment (RD).[5]

In this article, we describe a rare case of scleral dehiscence following 23-gauge pars plana vitrectomy (PPV) for RD repair in a patient with MFS. This case highlights the potential effects of MFS on the scleral tissue following PPV, identifies contributing factors, and offers ways to anticipate them for future surgical interventions.

CASE REPORT

A 34-year-old woman with MFS presented with a sudden decrease in vision in her left eye. She had undergone intracapsular lens extraction and iris clip IOL implantation for bilateral crystalline lens subluxation 2 years earlier. On examination, her BCVA was 20/20 OD and hand motion OS. She was highly myopic with an axial length of 28.72 mm OD and 27.59 mm OS. Her IOP was 14 mm Hg OD and 11 mm Hg OS. She had corneal scarring and localized iris atrophy from her previous anterior segment surgeries. The iris clip IOL was slightly off-center inferiorly in each eye (Figure 1).

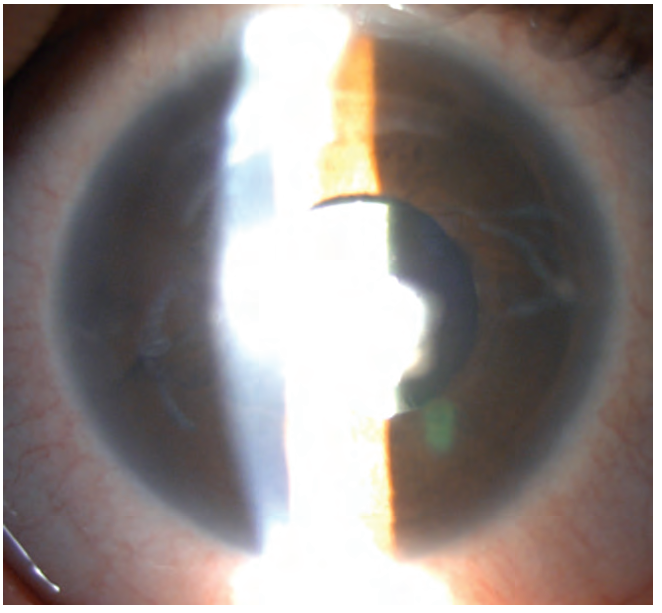


Figure 1. This photograph shows corneal scarring, localized iris atrophy, and slight inferior decentration of the IOL in the left eye.

On fundoscopic examination, we found a total bullous RD in the left eye and a horseshoe tear at the 11:00 clock hour. The retina of the right eye showed signs of multiples peripheral degenerations in the form of palisades.

We opted for a 23-gauge PPV for the repair of the RD in her left eye and a 360° prophylactic laser retinopexy

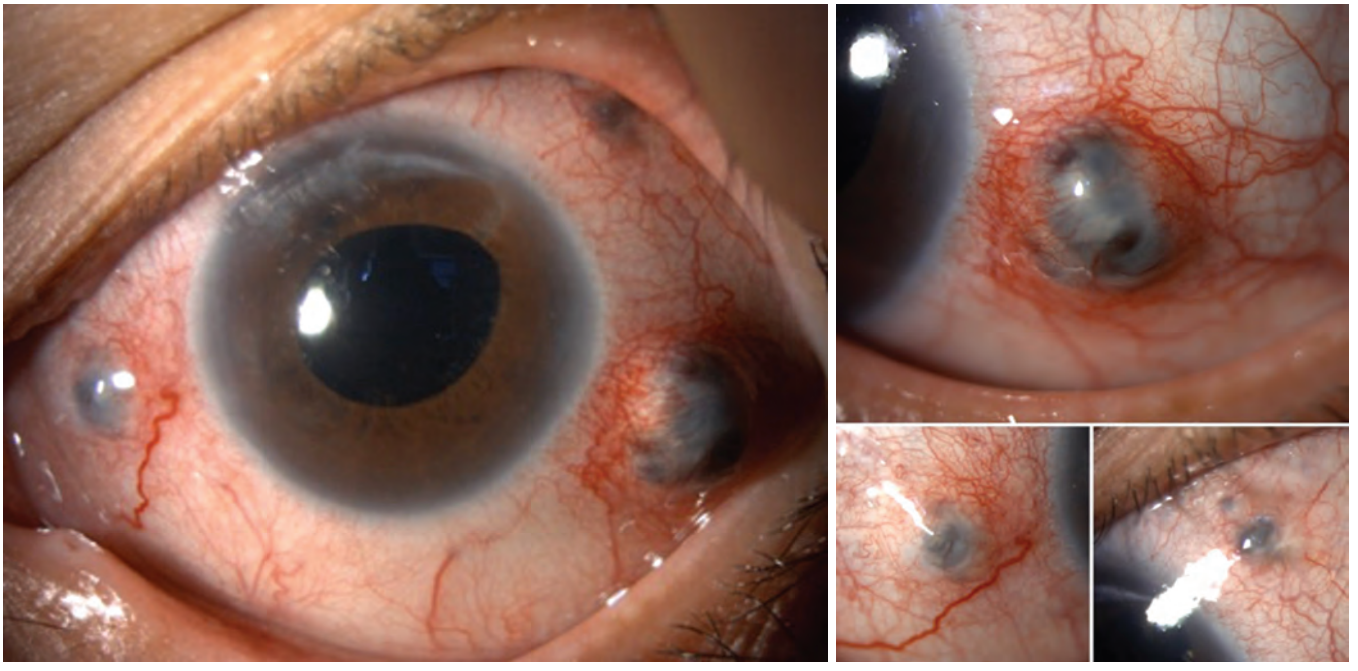


Figure 2. These photographs show the bulging of the choroid through the areas of scleral thinning at the trocar insertion points.

for the right eye. A three-port vitrectomy was performed without incident, and endolaser retinopexy was applied to barricade the tear and for 360° cerclage. C_2F_6 gas was used as an endotamponade with a bubble slipping into the anterior chamber at the moment of exchange. Finally, the sclerotomies were sutured with an 8-0 vicryl, as they were persistently leaking at the end of the surgery.

POSTOPERATIVE COMPLICATIONS

On postoperative day 1, the IOP increased to 45 mm Hg OS. The gas bubble that had slipped into the anterior chamber was pressing on the IOL, causing a narrowing of the inferior angle. The patient was prescribed IOP-lowering medication and instructed to remain in a face-down position to allow the gas bubble to regain the posterior segment. The IOP successfully returned to baseline. The patient was discharged 5 days after surgery, with the maintenance of IOP-lowering medications.

One week postoperatively, we unsuccessfully tried to taper the IOP-lowering medications. The gas bubble in the anterior chamber regressed, but the inferior angle remained narrow. At the 2-month follow-up, her VA was 20/200 OS. We noticed pigmented masses protruding through the sclera at the trocar insertion points (Figure 2). IOP was 42 mm Hg OS despite a combination of IOP-lowering drops.

The anterior chamber was irregular with an inferiorly displaced IOL (Figure 3). On gonioscopy, the inferior angle was fully closed for more than 180° with some localized peripheral anterior synechiae. The retina remained flat.

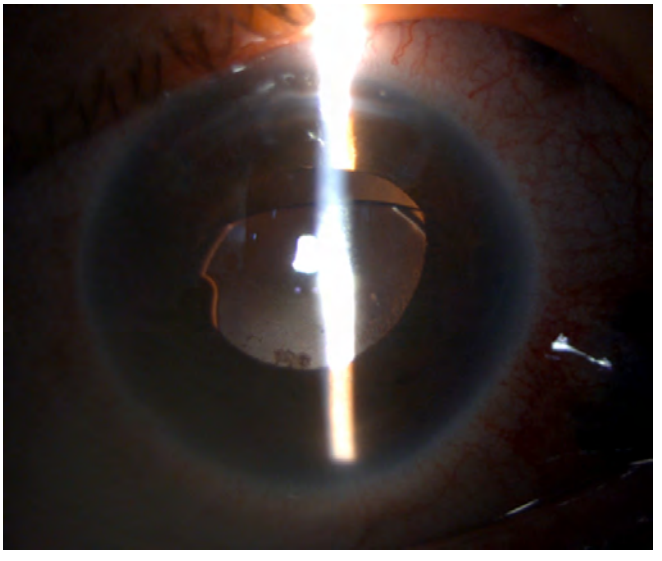


Figure 3. This photograph shows the inferior decentration of the IOL in the left eye.

OCULAR COMPLICATIONS OF MFS

In the setting of ubiquitous pathological connective tissue in MFS, the sclera is also affected, where it is unusually thin and exhibits reduced resistance to mechanical stress. Scleral thinning and perforation can be precipitated by trauma, surgery, or even by centrifugal force emanating from within the eye, such as with elevated IOP.[6,7] Extreme cases of spontaneous scleral rupture have been reported.[8,9] Our patient's case appears to combine multiple risk factors: The surgical insult complicated by increased IOP, which could explain the rapid progression of the choroidal bulge

KEY TAKEAWAYS

- Marfan syndrome (MFS) is a genetic disease affecting connective tissue with autosomal dominant transmission; broad involvement occurs, including cardiovascular, musculoskeletal, dermatological, and ocular complications.
- The authors report a case of a 34-year-old woman with MFS who developed elevated, uncontrolled IOP following 23-gauge pars plana vitrectomy for the repair of a retinal detachment in her left eye and a 360° prophylactic laser retinopexy in her right eye.
- The authors propose that a scleral patch graft may have been more appropriate for closing the compromised thin sclera in this patient with MFS.

through the thinned sclera, instead of the late appearance described in the literature.[10-12]

Given the high risk of RD in MFS, surgeons must contend with pathological tissue that can compromise surgical outcomes and visual prognosis. Deramo et al reported a case of full-thickness scleral erosion in a 33-year-old man with MFS who underwent RD repair with a silicone sponge and silicone encircling band.[7] PPV does not seem safer, as Sridhar et al reported a case of sclerotomy wound dehiscence after 20-gauge PPV and lensectomy for an ectopic lens in a 19-year-old woman.[10] Similarly, Mancino et al reported a case of scleral wound dehiscence in a 34-year-old woman with MFS who underwent lensectomy 20 years prior.[11] However, those cases relied on 20-gauge ports. With the advent of 23-, 25-, and 27-gauge ports, this complication is likely to be significantly reduced; at the time of our research, we found no cases in which scleral dehiscence occurred after a 23-gauge PPV for RD repair.

For repair options of scleral dehiscence, it can be closed with nylon sutures.[7,10] Alternatively, it may require more advanced techniques with an autologous scleral graft or preserved scleral donor patch graft.[8] Rodríguez-Ares et al described another technique that consists of combining a scleral homograft and amniotic membrane transplant as an alternative to autologous scleral and conjunctival grafts.[6] Furthermore, Stanciu et al described a multilayer technique that involves first a direct suture with 10-0 vicryl, the placement of a scleral graft sutured with 8-0 vicryl, and a dried amniotic membrane glued on top.[12]

In our case, we recognize that a scleral patch graft might have been more appropriate for closing the compromised thin sclera in MFS. Furthermore, it was crucial to strictly control IOP to avoid exacerbating this complication in the postoperative period.

ALWAYS PLAN AHEAD

Vitreoretinal specialists must be aware of the risk of scleral dehiscence when treating RD in patients with MFS, even with the advent of new microincisional vitreoretinal surgery techniques. Furthermore, elevated and uncontrolled IOP can exacerbate surgical trauma in these cases, requiring meticulous postoperative management. ■

Acknowledgement: Informed consent was obtained from the patient to use the clinical data in this case report. The principles of the Declaration of Helsinki have been respected.

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GLOBAL DR SCREENING: WHY AREN'T WE THERE YET?

A look at the hope and hurdles of global screening implementation.

By Majda Hadziahmetovic, MD; Michael D. Abramoff, MD, PhD; Abdullah AlQahtani, MD, DES, DISSO, FEBO; Gavin Tan Siew Wei, MBBS, PhD; Sobha Sivaprasad, MBBS, MS, DM, FRCS, FRCOphth; Lloyd C. M. Harrison-Williams, MBChB, MMed(Ophth), FCOphthECSA, FCPSSL; and Jorge C. P. Rocha, MD, PhD

Diabetic retinopathy (DR) remains a leading cause of vision loss among the working-age population worldwide. The numbers are overwhelming; approximately 103 million adults are affected globally, and the burden is projected to exceed 160 million by 2045.[1,2]

Luckily, DR screening programs have expanded substantially over the past 2 decades. Among the most established examples are the United Kingdom's National Diabetic Eye Screening Program and Singapore's Integrated Diabetic Retinopathy Program. Both demonstrate the feasibility of large-scale, systematic DR screening and serve as important models for implementation across diverse health care settings.[3-5]

Recent advances in autonomous AI systems have marked an important step forward in DR screening, expanding the potential for disease detection beyond traditional eye care settings. LumineticsCore (formerly IDx-DR, Digital Diagnostics) was the first autonomous systems introduced

KEY TAKEAWAYS

- Despite recent advances, diabetic retinopathy (DR) screening remains underused and highly variable worldwide, particularly in low- and middle-income countries.
- Experts from Brazil, Saudi Arabia, Sierra Leone, Singapore, United Kingdom, and the United States discuss their experiences with DR screening efforts in their region.
- Barriers to global screening efforts include limited access to specialized care, patient awareness, integration with larger health systems, proper treatment follow-through, and technology constraints.

to detect more-than-mild DR (mtmDR) in adults with diabetes. Subsequent systems, including Eyenuk's EyeArt platform, have expanded automated screening to detect both mtmDR and vision-threatening DR (vtDR). More recently, AEYE Health introduced autonomous mtmDR detection using a portable handheld device, enabling screening across a wider range of clinical and community-based settings. Since then, numerous studies have demonstrated that AI-powered DR screening can match human grading performance and may offer a scalable approach for global screening programs by allowing DR testing for patients in frontline settings where they already receive care (Figure).[6-11]

Despite these advances, DR screening remains underused and highly variable worldwide, particularly in low- and middle-income countries, where the diabetes burden continues to rise. Although successful programs have been implemented in individual countries and regions, few initiatives have established coordinated multinational frameworks that can be widely adapted across diverse resource levels and patient populations. This raises an important question: If DR screening is feasible, effective, and capable of preventing blindness, why has broader global acceptance and implementation remained so difficult? Here, we explore the promise of global DR screening, and the hurdles we have yet to overcome.

THE UNMET NEED

Given the projected rise in DR, we should be concerned that we might be failing this patient population. Despite current and emerging treatments, DR remains a significant issue that affects individuals, families, health care systems, and governments. Evidence-based research links early identification and timely treatment to improved clinical outcomes, but there is still a disconnect with adoption.

MAJDA HADZIAHMETOVIC, MD: IN SAUDI ARABIA, WHAT IS THE SINGLE BIGGEST REASON PATIENTS ARE STILL BEING MISSED?

Abdullah AlQahtani, MD, DES, DISSO, FEBO: Multiple health providers are involved in each patient's care, and we do not have a unified data-sharing system. Without a national program, each service provider has their own costly and inefficient screening program; a lack of centralized data also means we do not have a clear understanding of the national size of the DR burden in our country.

DR. HADZIAHMETOVIC: WHAT IS THE MAIN BARRIER TO PROPER DR SCREENING IN BRAZIL?

Jorge C. P. Rocha, MD, PhD: In Brazil, a country with substantial disparities in health care infrastructure across its regions, we continue to face significant barriers to ensuring that patients receive timely ophthalmic evaluation.

For example, limited access to ophthalmologists—particularly retina specialists—remains a major challenge. Within the public health care system in Brazil, long waiting lists for ophthalmic consultations often delay a patient's diagnosis and treatment.

In addition, patient awareness remains inadequate, and many individuals with diabetes are unaware that the disease can affect the eyes and lead to DR.

Expanding access to retinal examinations through the Brazilian public health care system is essential, particularly in underserved regions where ophthalmologists are scarce. At the same time, continuous efforts to educate patients with diabetes are crucial so that they understand the importance of regular screening, even in the absence of visual symptoms.

DR. HADZIAHMETOVIC: WHERE DO YOU THINK SCREENING FAILS MOST OFTEN?

Sobha Sivaprasad, MBBS, MS, DM, FRCS, FRCOphth: Ensuring treatment follow-through of referred positive cases is the biggest challenge. Over the last decade, we have made significant strides in retinal screening for patients with diabetes. However, most programs are run as independent services, and the link to a secondary care center that offers treatment is nonexistent. Secondary care is usually provided by another health care provider with different reimbursement systems.

This breakdown between the referral of screen-positive patients and treatment defeats the purpose of screening. The referral-to-treatment pathway should be planned and appropriately reimbursed before DR screening programs are established.

Lloyd C. M. Harrison-Williams, MBChB, MMed(Ophth), FCOphthECSA, FCPSSL: It is imperative that screening exercises are not done in isolation; they should be paired with a clear path to further care. First-line treatment should be available at the point of screening, if possible. However, when treatment isn't possible at the screening location, counseling should be mandatory as a crucial first step to ensure patients understand the risk of vtDR, the next line of care, and the financial implications. National eye health programs should commit to implementing this basic tenet and keep a register of screened patients to follow up with their care.

In this way, all are empowered to ensure that screening exercises culminate in adequate action to reduce the complications of diabetic eye disease.

IMPLEMENTATION BARRIERS

DR screening should not be reduced to identifying patients at risk; it should provide an end-to-end system, from image capture at the point of service to closing the loop on referrals and treatments. Successful implementation requires significant effort from the top

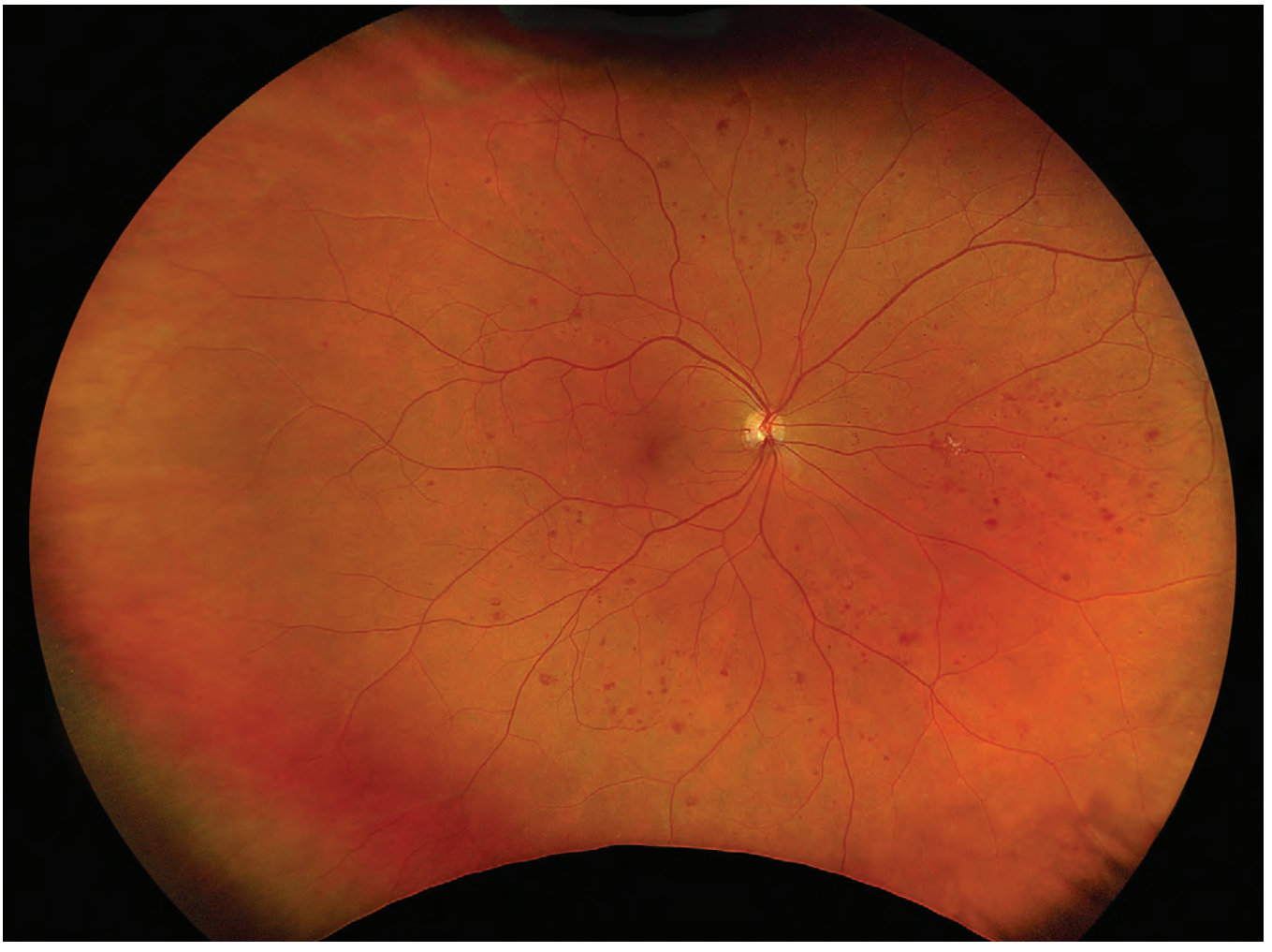

Image courtesy of Retina Rocks (retinarocks.org, @retina.rocks)

Figure. Patients, such as this one with moderate-to-severe nonproliferative DR, can benefit from organized retinal screening.

(eg, stakeholders, IT teams, providers, clinic staff) without disrupting the workflow while ensuring sufficient capture.

DR. HADZIAHMETOVIC: WHAT LESSONS HAVE WE LEARNED FROM SUCCESSFUL PROGRAMS THAT MAY NOT TRANSLATE EASILY TO LOWER-RESOURCE SETTINGS?

Gavin Tan Siew Wei, MBBS, PhD: A successful DR screening program with the goal of reducing blindness and visual impairment must be part of an end-to-end effort to:

- provide comprehensive and regular eye screening (include retinal photography) to patients with diabetes coupled with DR education and awareness regarding the importance of screening and risk factor control (glycemic and other risk factors);
- create a sustainable referral pathway to secondary or tertiary care for those with referrable or worse DR with the provision of affordable treatment options; and
- implement a feedback system to the primary care physician to ensure glycemic control is titrated and optimized in accordance with the disease severity.

The challenges in a low-resource setting are multifactorial. Screening and education may be episodic, and a sustainable referral pathway may be lacking due to a dearth of accessible secondary or tertiary eye care. Patients may be unable to afford treatment, and there is often a lack of a coordinated primary care pathway for diabetes control with a consistent feedback mechanism.

DR. HADZIAHMETOVIC: HOW IMPORTANT IS INTEGRATION WITH OTHER SPECIALTIES SUCH AS PRIMARY CARE, ENDOCRINOLOGY, NEPHROLOGY, AND DIABETES CLINICS?

Michael D. Abramoff, MD, PhD: With DR, we know that early diagnosis and treatment is key, but we also know that it's not happening. Most of these patients with diabetes are not reaching our offices. The only way to solve the problem is to be where the patient is, which is primary care, endocrinology, nephrology, diabetes clinics, and emergency departments—that's where these screening programs must start.

However, other specialties don't have the expertise to examine the retina, which is where AI comes in. We have accurate screening systems we can put into other specialty offices without needing the retina specialist to be there.

These programs help solve the problem of patients not having easy access to screening. The key is ensuring they work for primary care; they need to fit into the workflow and be financially beneficial, in addition to improving the patient/provider experience and patient outcome.

DR. HADZIAHMETOVIC: IN YOUR EXPERIENCE, WHAT CAUSES SCREENING PROGRAMS TO FAIL AFTER THE INITIAL PILOT PHASE?

Dr. Sivaprasad: The initial pilot phase is usually funded by an academic grant or by the government. When the pilot phase is complete and an evidence-based, feasible system is developed, the most common cause of failure to pursue is the lack of funding. However, other reasons exist, such as competing health priorities, lack of initiative or lack of enthusiasm by busy staff to take on more assignments, the lack of trained staff, and the low prevalence of vtDR compared with the total number of patients screened—usually about six in 100 patients. In addition, patients who screen positive may not feel the need to travel to a secondary care office and incur out-of-pocket expenses for an asymptomatic eye condition, as there is a lack of public awareness of the potential for irreversible visual impairment due to diabetic retinal disease.

AI, IMAGING, AND TECHNOLOGY

Imaging and technology are major determinants of successful DR screening. Although advances in AI and automated image interpretation have the potential to transform this field, progress has been insufficient. We need to focus on rigorous validation and clear demonstration of improved clinical outcomes. Current efforts have proven feasibility, but sustainability and wider adoption remain questionable.

DR. HADZIAHMETOVIC: WHAT IS THE PRIMARY BARRIER TO THE ADOPTION OF AI SCREENING PROGRAMS?

Dr. Tan: The main barrier is the need to implement a sustainable photography-based DR screening system. If there is no system to electronically capture retinal photographs on a regular basis, AI can help, but it only provides a small portion of the requirements. If there is a digital telemedicine-based screening program already in place, then the barriers to using AI are regulatory, physician acceptance, and cost.

DR. HADZIAHMETOVIC: WHAT MINIMUM STANDARDS SHOULD BE REQUIRED BEFORE AI-BASED DR SCREENING IS DEPLOYED ON A LARGE SCALE?

Dr. Abramoff: In the primary care clinic or other frontline offices, staff don't have the time or expertise to properly examine the retina, so any automated system we implement must be simple to use. When we sought FDA clearance for LumineticsCore, we ensured the system can be operated by anyone with a high school diploma and minimum training.

In addition to technician training, the system must work in harsh conditions. Low-resource settings don't have a nice dark room with an experienced photographer on hand. Nothing that's designed to work in a traditional ophthalmology or retina lane works in the real-world setting. It all breaks. Whatever system you create must provide clear retina images without an ideal environment with an unskilled photographer.

EQUITY AND GLOBAL HEALTH

Diabetes and DR place a heavy burden on people in underdeveloped and developing areas. Unfortunately, patients most at risk of vision loss are often the least likely to receive timely eye care. Around the world, barriers such as limited access to care, cost, transportation, low health literacy, fragmented referral systems, and competing medical priorities prevent many patients with diabetes from completing recommended retinal screening. As a result, the disease often progresses and leads to irreversible vision loss.

DR. HADZIAHMETOVIC: BASED ON YOUR EXPERIENCE, WHICH MODEL IS MOST EFFECTIVE AT REACHING PATIENTS EARLIER, ESPECIALLY IN UNDERDEVELOPED AND DEVELOPING REGIONS?

Dr. Harrison-Williams: As in all screening programs, there are broadly three models. In the fixed (clinic-based) model, patients travel to the eye facility to access screening.

With the outreach model, eye specialists travel with their equipment to conduct screening within the communities or institutions. This approach, while costly, is effective in optimizing patients access to screening. However, high patient volumes and reduced efficiency may deter some patients.

The mixed (hub-and-spoke) model leverages the advantages and efficiency of the clinic setting with the benefits of meeting patients in their communities; with this approach, a screening team is regularly stationed on specific, well-publicized days in the community.

An ideal model of screening in resource-challenged settings—such as ours in Sierra Leone—is one that uses free online software and common smartphones (if any additional hardware is necessary, it must be economical and readily available). AI-assisted DR screening software could be used by residents to detect early signs of vtDR and then recommend the location and times of nearby screening facilities (spoke-level).

The local screening facility can further assess for vtDR and, if possible, offer first-line treatment. Those with severe complications can be referred to the clinic (hub-level) for surgical intervention.

This model, when well-coordinated with collaboration

THE REFERRAL-TO-TREATMENT PATHWAY SHOULD BE PLANNED AND APPROPRIATELY REIMBURSED BEFORE DR SCREENING PROGRAMS ARE ESTABLISHED.

between key stakeholders, can lead to increased screening at all levels, earlier access to treatment, and reduced prevalence of vtDR.

DR. HADZIAHMETOVIC: HOW SHOULD SCREENING PROGRAMS BE ADAPTED FOR LOW-RESOURCE REGIONS?

Dr. Rocha: Brazil is an upper-middle-income country characterized by marked socioeconomic and regional disparities. Rural areas and small inland cities face significant limitations in health care infrastructure, particularly in eye care. Expanding access to ophthalmic services requires the development of a low-cost, sustainable infrastructure supported by government policies that enable patients to access screening services quickly and easily.

Ideally, every municipality should have a DR screening center where endocrinologists, primary care physicians, and comprehensive ophthalmologists can refer patients without unnecessary bureaucratic barriers. Following retinal imaging and AI-based screening, patients identified as having referable DR or requiring treatment should be automatically referred to a specialized retina center, where they can receive timely evaluation and treatment.

The success of this model depends on three essential pillars: (1) screening centers equipped with retina cameras integrated with AI-based diagnostic systems; (2) an automated and streamlined referral pathway; and (3) retina centers capable of providing prompt treatment.

DR. HADZIAHMETOVIC: WHICH IS MORE IMPORTANT FOR GLOBAL IMPACT: BUILDING HIGH-QUALITY CENTRALIZED READING CENTERS, DEPLOYING AI-SUPPORTED IMAGING, TRAINING LOCAL GRADERS, OR EMBEDDING SCREENING INTO DIABETES VISITS?

Dr. Sivaprasad: Deploying AI-supported retinal imaging in diabetes care visits will have a positive effect on patients. Most diabetes care clinics review patients for all complications of diabetes and have the capability to offer a more holistic approach, especially to identify screen-positive patients. Previously, diabetes care clinics found DR screening challenging due to the lack of specialist staff and the need for costly retina cameras. Now, with automated, AI-integrated, affordable screening, any technician or nurse can capture retinal images. An AI-graded clinical outcome is made instantly available to the patients. This pathway will also ensure personalized health education is provided to screen-positive patients to attend secondary care for treatment.

ECONOMICS AND SUSTAINABILITY

DR screening can prevent costly vision loss by identifying disease earlier, enabling timely treatment and better visual outcomes, but programs must be operationally and financially sustainable. Beyond being affordable and scalable, these efforts must be tailored to local realities that differ on many levels.

DR. HADZIAHMETOVIC: WHICH FINANCIAL MODEL IS NEEDED FOR A SUSTAINABLE DR SCREENING PROGRAM?

Dr. Tan: The financing model depends on the reimbursement system, which varies between countries. Essentially, you need a payer willing to invest in screening based on the strong evidence-based recommendation that it is cost-effective, and it prevents future vision loss.

It's less important if the payer is the government, insurer, non-governmental organization, or another industry partner; what matters is that the program is funded to achieve the complete cycle required to prevent vision loss. Depending on the patients to pay out-of-pocket is often difficult except in higher income countries with extremely good DR education programs. But health systems with good education and awareness programs usually rely on a government payer system in the first place.

DR. HADZIAHMETOVIC: HOW SHOULD WE MEASURE THE VALUE OF SCREENING?

Dr. AlQahtani: We measure the value by documenting earlier detection of disease and a drop in complicated cases, both of which lead to a lower cost of management. Programs can show their value by comparing the number of patients treated after screening with those seen in the clinic, care which is usually delayed because of the waiting list.

In addition, a well-run screening program can allow a more accurate evaluation of the disease burden. Some countries have a high prevalence of patients with diabetes, creating a significant financial burden; early detection and care will decrease that cost burden.

THE FUTURE

Despite tremendous advances in the diagnosis and treatment of DR, more than half of patients with diabetes do not adhere to recommended retinopathy screening, putting them at risk of vision loss.[12] This holds true not only in underdeveloped and developing countries but also

in the United States. We now have the opportunity to close this gap through organized, advanced technology-assisted, equitable screening programs.

DR. HADZIAHMETOVIC: WHAT EVIDENCE DO STAKEHOLDERS STILL NEED BEFORE THEY INVEST MORE SERIOUSLY IN LARGE-SCALE DR SCREENING?

Dr. Abramoff: Currently, only approximately 2% of all people with diabetes in the United States are being diagnosed with diabetic eye disease using an AI system. Given the rising prevalence of DR, that number should be 80% or more. Luckily, we were able to establish reimbursement for AI screening. The reimbursement makes it work for clinics who adopt autonomous AI.

As part of our advocacy with the AAO, we have sought to help US Congress understand that the burden of care for diabetic eye disease is too high for retina specialists to handle alone. With the help of AI, we can take care of all patients who deserve eye examinations because screening positive gets them into our clinics, where we provide the care.

At the end of the day, we need buy-in from all stakeholders, including retina specialists and primary care providers. To get that buy-in, you must solve simple hurdles such as integrated workflow and equipment needs, site support, patient education, and improved outcomes. Research is accumulating, including randomized controlled trials that show the improved outcomes and efficiency and clinician job satisfaction benefits of AI screening for diabetic eye disease. However, population-level outcomes data are still needed to truly understand the lasting effect of AI screening. ■

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A LOOK AT IMPLANTS FOR DIABETIC EYE DISEASE

A review of approved and emerging implant-based treatments for diabetic retinopathy and diabetic macular edema.

By Matthew Pfannenstiel, MD, and Leanne Clevenger, MD

Diabetic eye disease (DED) continues to be a leading cause of vision impairment among working-age adults worldwide, and the burden of diabetic retinopathy (DR) and diabetic macular edema (DME) on patients and health care systems is expected to increase substantially. Conventional treatments—including focal/grid laser photocoagulation, intravitreal anti-VEGF agents, and corticosteroids—have significantly improved visual outcomes over the past 2 decades. However, many patients experience incomplete responses, require frequent injections, or struggle with adherence due to treatment burden or access limitations.[1-3]

Implantable drug-delivery platforms have emerged as an important evolution in the management of DED. By enabling sustained intraocular therapeutic exposure, implants are designed to reduce treatment frequency, improve durability of response, and better match the chronic, relapsing nature of DED. Early corticosteroid implants have now been followed by refillable anti-VEGF reservoirs and investigational gene-based and biomaterial-driven approaches, reshaping long-term treatment strategies. Here, we summarize currently approved implants, emerging technologies, and future directions in sustained therapy for DED (Table).

APPROVED IMPLANT OPTIONS

Several intravitreal implants are currently available for the treatment of DME, primarily using corticosteroid or anti-VEGF delivery to target inflammatory and vascular permeability pathways known to contribute to DME. These devices differ in biodegradability, duration of drug release, and suitability for specific patient populations.[1,4]

Intravitreal Corticosteroid Implants

Corticosteroids exert beneficial effects in DME by inhibiting inflammatory cytokines, stabilizing the blood-retinal barrier, and downregulating VEGF expression.[1] The dexamethasone intravitreal implant 0.7 mg (Ozurdex, Abbvie) is a biodegradable polymer-based implant that delivers sustained corticosteroid exposure for approximately 3 to 4 months. Multiple randomized and real-world studies have demonstrated significant improvements in BCVA and reductions in central retinal thickness in patients with DME, including those previously treated with anti-VEGF agents.[5-7]

The dexamethasone implant has shown utility in pseudophakic eyes, vitrectomized eyes, and patients with inflammatory-predominant DME or suboptimal anti-VEGF response (Figure).[1,6] Adverse effects such as IOP elevation and cataract progression are well characterized and generally manageable with appropriate monitoring.[5-7]

TABLE. COMPARISON OF IMPLANT-BASED THERAPIES FOR DIABETIC EYE DISEASE

Name (Manufacturer)	Delivery Method	Treatment Duration	FDA Approval Status
Dexamethasone intravitreal implant 0.7 mg (Ozurdex, Abbvie)	Office-based intravitreal injection of biodegradable implant	Approximately 3 to 4 months	FDA approved for DME
Fluocinolone acetonide intravitreal implant 0.19 mg (Iluvian, ANI Pharmaceuticals)	Office-based intravitreal injection of non-biodegradable implant	Up to 36 months	FDA approved for DME in previously steroid-treated patients without clinically significant IOP rise
Port delivery system with ranibizumab (Susvimo, Genentech/Roche)	Surgically implanted refillable ocular reservoir with office-based refill-exchange	Continuous delivery; refill approximately every 6 months for DME and every 9 months for DR	FDA approved for DME and DR in previously anti-VEGF-responsive patients
OTX-TKI (Axpaxli, Ocular Therapeutix)	Axitinib hydrogel administered by intravitreal injection	Intended for injections 1 to 2 times per year	Investigational
EYP-1901 (Duravyu, EyePoint)	Bioerodible vorolanib intravitreal insert administered by intravitreal injection	Designed for sustained release for approximately 6 to 9 months	Investigational
Surabgene lomparvovec (sura-vec/ ABBV-RGX-314, Abbvie/Regenxbio)	Suprachoroidal AAV8 gene therapy administered as a single in-office injection	Intended as a one-time treatment with multi-year expression/ durability	Investigational
4D-150 (4D Molecular Therapeutics)	Single intravitreal AAV gene therapy injection	Intended for multi-year sustained expression after one administration	Investigational

Abbreviations: AAV, adeno associated viral; DME, diabetic macular edema; DR, diabetic retinopathy

The fluocinolone acetonide intravitreal implant 0.19 mg (Iluvien, ANI Pharmaceuticals) represents a longer-acting, non-biodegradable corticosteroid platform approved for chronic DME insufficiently responsive to other treatments. This implant delivers low-dose fluocinolone acetonide continuously for up to 36 months. The pivotal FAME trials demonstrated sustained visual improvement and edema control over 3 years, with durable anatomic benefits and meaningful reductions in treatment burden.[8]

Long-term real-world studies, including the PALADIN study, have confirmed sustained efficacy and a favorable safety profile in carefully selected patients who have demonstrated steroid tolerance.[9] Cataract formation and IOP elevation remain common, underscoring the importance of patient selection and pre-implant steroid challenge.[8,9]

Intravitreal Reservoir

The port delivery system (PDS) with ranibizumab (Susvimo, Genentech/Roche) is a refillable, surgically implanted reservoir that continuously releases ranibizumab into the vitreous cavity and is periodically refilled via a minimally invasive office-based procedure.

Clinical studies of the PDS have demonstrated the feasibility of extended anti-VEGF delivery with reduced treatment frequency in retinal disease, supporting the broader concept of durable refillable intraocular biologic therapy. However, disease-specific evidence in DME is still evolving, and safety considerations such as conjunctival complications, implant-related adverse events, and endophthalmitis remain important for patient counseling and long-term monitoring.[10,11]

KEY TAKEAWAYS

- Currently approved implants for diabetic eye disease include the dexamethasone intravitreal implant 0.7 mg (Ozurdex, Abbvie), fluocinolone acetonide intravitreal implant 0.19 mg (Iluvien, ANI Pharmaceuticals), and port delivery system with ranibizumab (Susvimo, Genentech/Roche).
- Several biodegradable polymer implants, sustained-release intraocular delivery systems, and combination antiinflammatory strategies remain under investigation.
- Surabgene lomparvovec (sura-vec/ABBV-RGX-314, Abbvie/Regenxbio) and 4D-150 (4D Molecular Therapeutics) are both in phase 2 for diabetic macular edema.

INVESTIGATIONAL IMPLANTS

The future of implant therapy for DED is increasingly focused on long-term disease modification and novel biologic approaches to address both the vascular and neurodegenerative aspects of DED.[4,12] Hydrogel-based systems and nanotechnology-enabled platforms are being explored to improve drug stability, prolong release, and enhance tissue targeting in retinal disease.[12,13,16] Additional innovation is occurring in platforms designed for controlled release, improved ocular bioavailability, and multimodal treatment delivery. As these technologies mature, cost-effectiveness analyses and real-world durability studies will be critical to define their role alongside established treatment paradigms.[12,13,16]

Tyrosine Kinase Inhibitors

Sustained-release tyrosine kinase inhibitor (TKI) implants are an investigational strategy for DR and DME. Unlike extracellular anti-VEGF agents, TKIs act intracellularly to inhibit VEGF receptor signaling and may also affect related angiogenic and inflammatory pathways implicated in vascular leakage and neovascularization.

OTX-TKI (Axpaxli, Ocular Therapeutix), an axitinib-containing bioresorbable hydrogel implant, is being evaluated in phase 3 for nonproliferative DR, with dosing strategies that include single or repeat administration at 24 weeks.

EYP-1901 (Duravyu, EyePoint), a bioerodible intravitreal insert containing vorolanib, is under investigation in two phase 3 trials for the treatment of DME. These platforms are intended to reduce injection burden while maintaining durable suppression of VEGF-driven permeability and disease progression.[19-21]

For more on TKIs, see *The Potential of Tyrosine Kinase Inhibitors*.

Gene Therapy

Gene-based delivery systems represent a rapidly evolving investigational category. These treatments typically use viral vectors to promote sustained intraocular expression of therapeutic proteins after a single administration. Contemporary reviews highlight the promise of ocular gene therapy while also emphasizing manufacturing, durability, and inflammatory safety challenges that must be addressed before broader clinical adoption.[14,15]

In DED, most clinical gene therapy strategies have focused on sustained intraocular suppression of VEGF signaling. Adeno-associated viral (AAV) vectors are the predominant platform used, as they can drive prolonged retinal expression after a single administration. These gene therapies largely target VEGF-A directly through viral-mediated expression of anti-VEGF proteins; however, newer therapies are also investigating inhibition of VEGF-C, placental growth factor, and other mediators of vascular permeability and inflammation. Routes of delivery vary by platform and include intravitreal, suprachoroidal, and subretinal administration, each with tradeoffs in transduction efficiency, procedural complexity, and inflammatory risk.[14-16]

Surabgene lomparvovec (sura-vec/ABBV-RGX-314, Abbvie/Regenxbio) is an AAV8-based therapy encoding an anti-VEGF antibody fragment administered suprachoroidally for DME.[17] Early data from the phase 2 ALTITUDE trial have been encouraging.[17]

Early data from the phase 2 SPECTRA trail of 4D-150 (4D Molecular Therapeutics) is also promising.[18] This intravitreal gene therapy is designed to potentially provide multi-year expression of an aflibercept-like anti-VEGF moiety and an inhibitory RNA molecule that blocks intracellular expression of VEGF-C.

IMPLANTABLE DRUG DELIVERY SYSTEMS REPRESENT A TRANSFORMATIVE ADVANCE IN THE MANAGEMENT OF DR AND DME.

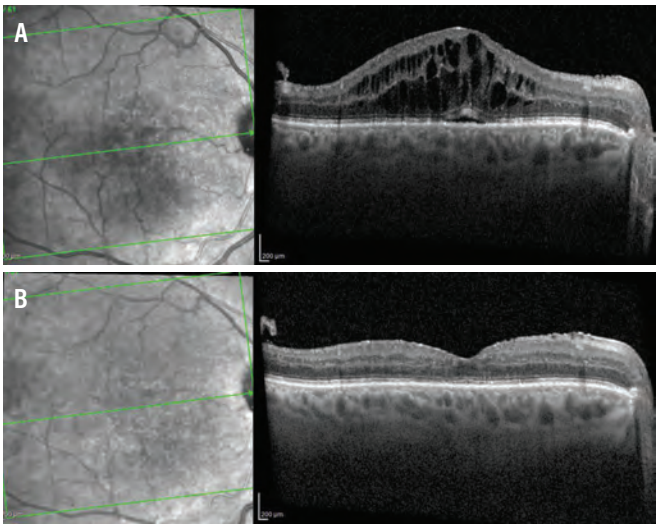

Figure. This patient with DME was not responding well to anti-VEGF therapy (A), necessitating the addition of a dexamethasone implant (B).

ADVANTAGES, LIMITATIONS, AND PATIENT SELECTION

Implant-based therapies offer several advantages over intravitreal injections, including reduced treatment burden, improved adherence potential, and more consistent

BEYOND SUSTAINED DELIVERY: CAN WE MEASURE WHAT'S LEFT?

A noninvasive method for measuring residual drug could lead to pharmacologically guided care.

By Gennady Landa, MD, and Gennady Friedman, PhD

When managing diabetic eye disease, refillable anti-VEGF reservoirs and sustained-release corticosteroid implants can reduce injection frequency and treatment burden while maintaining therapeutic exposure.[1-3] Yet one clinically important question remains unanswered at follow-up visits: How much active drug is left inside the implant?

Currently, retina specialists rely on predetermined retreatment schedules and indirect evidence of declining therapeutic effect, such as recurrent fluid on OCT, worsening visual acuity, or disease progression. This reactive approach may expose some patients to recurrence before retreatment, while subjecting others to retreatment procedures or supplemental therapy despite adequate remaining drug. It can also make it difficult to distinguish drug depletion from other causes of suboptimal response.

A newly developed proprietary technology platform, developed through a collaboration between the Department of Ophthalmology at the Icahn School of Medicine at Mount Sinai and the College of Engineering and Computing at Drexel University, may offer another approach. The concept incorporates engineered magnetic nanoparticles confined within the implant matrix and uses an external reader to obtain a noninvasive signal associated with the amount of drug remaining. In principle, the measurement could be performed during a routine office visit and provide quantitative information to complement OCT, visual acuity, and clinical examination. A low residual drug measurement could favor retreatment, whereas an adequate measurement with disease activity may prompt consideration of an alternative mechanism or adjunctive therapy.

While this is a promising concept, many hurdles to clinical translation remain, including validation of measurement accuracy, signal stability over time, biocompatibility, nanoparticle confinement, compatibility with implant manufacturing, and performance across different therapeutic agents, implant materials, geometries, positions, and tissue overgrowth or fibrosis. Finally, prospective studies must show the benefits of real-time monitoring.

For retina specialists managing diabetic eye disease, the ability to measure what remains inside an implant could represent the next step toward precision dosing and more proactive disease control. ■

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pharmacokinetics.[3,12] These benefits are particularly relevant for patients with limited access to care, poor injection tolerance, or chronic/persistent edema requiring frequent retreatment.

However, implants are not without risk. Surgical implantation, device-specific complications, steroid-related adverse events, and higher upfront costs must all be weighed against expected benefits.[1,4] Thoughtful patient selection remains paramount: Corticosteroid implants may be best suited for pseudophakic patients, those with inflammatory DME phenotypes, or eyes refractory to anti-VEGF therapy while anti-VEGF implants may offer broader applicability across different disease stages.[6,8,10]

UPDATING THE PARADIGM

Implantable drug delivery systems represent a transformative advance in the management of DR and DME. With multiple approved corticosteroid implants and expanding anti-VEGF and investigational platforms, retina specialists

(Continued on page 46)

PEARLS FOR MANAGING COMPLEX DIABETIC VITRECTOMY

Diabetic tractional retinal detachments are challenging for even the most seasoned surgeons. Following these steps can help minimize complications.

By Neil Sheth, MD, MBA, and Dimitra Skondra, MD, PhD, FASRS

Diabetic tractional retinal detachments (TRDs) are some of the most technically demanding cases in vitreoretinal surgery. Each eye presents a unique constellation of posterior hyaloid configuration, vitreoretinal adhesions, fibrovascular proliferation, and neovascular activity. Success demands technical proficiency, systematic preoperative planning, thoughtful selection of instrumentation, and sound intraoperative decision making. In this article, we share our considerations during the key phases of complex diabetic vitrectomy (Table).[1]

PREOPERATIVE PLANNING

Preoperative OCT is invaluable for mapping the extent of the traction, evaluating the foveal contour (including the presence of an epiretinal membrane), identifying focal fibrovascular pegs overlying the macula (and an associated plane for dissection), and identifying any associated tractional-rhegmatogenous component. The integrity of the external limiting membrane and ellipsoid zone can also inform counseling on visual prognosis, which is often limited.

When media clarity is compromised by dense vitreous hemorrhage, B-scan ultrasonography is essential. Key features to assess using this tool include the configuration of the posterior hyaloid, the extent of the subhyaloid hemorrhage, the presence and location of a funnel detachment, and the relationship of fibrovascular tissue to the disc.

While practice patterns vary, preoperative bevacizumab

KEY TAKEAWAYS

- When planning surgery for tractional retina detachments (TRDs), OCT imaging, ultrasound (when needed), possible cataract extraction, and anti-VEGF injection can help map out the extent of the traction, assess the status of the hyaloid, and regress active neovascularization.
- Useful tools in TRD surgery include a delaminating spatula, a high-magnification contact lens, MPC vertical scissors, a lighted pick, a Finesse Flex Loop (Alcon), and dextrose added into the infusion bottle.
- Tamponade selection should favor gas over silicone oil in most complex traction/rhegmatogenous RD cases, as long-acting gas provides 6 to 8 weeks of tamponade and avoids the need for oil removal surgery.

TABLE. TRACTIONAL RETINAL DETACHMENT SURGICAL CHECKLIST

Category	Detail
Preoperative anti-VEGF injection	Administer 3 to 7 days prior to surgery (do not exceed 14 days).
B-scan ultrasound	Assess hyaloid configuration, subhyaloid blood, disc adhesion, and funnel detachment.
OCT	Evaluate foveal traction map, external limiting membrane/ellipsoid zone integrity, and tractional-rhegmatogenous component.
Cataract management	Consider combined or staged cataract extraction/IOL for dense cataract or planned long-acting tamponade.
Corneal clarity	Use Viscoat (Alcon) + 50% dextrose for corneal clarity in phakic eyes.
Infusion fluid additive	Add dextrose to the infusion bottle (~0.1%) for preservation of the lens.
Membrane staining	Use triamcinolone after membrane peeling; stain and remove all residual hyaloid scaffold.
Dissection approach	Consider using the inside-out approach: Start at the disc and avoid abruptly avulsing fibrovascular proliferation over the nerve. You can leave focal pegs, as long as there is no traction and the hyaloid has been removed between other fibrovascular fronds/pegs.
Diathermy	Always have this primed before the first incision; use gently for bleeding combined with IOP elevation.
Segmentation/delamination	Segment first to relieve en bloc traction, and delaminate once a clear plane is confirmed.
Tight-space instruments	Use a delaminating spatula and high-magnification lens in tough cases. For very tight spaces, consider vertical scissors.
Iatrogenic break management	Relieve traction (you can leave small peg if there is no traction and it is disconnected from other fronds), then raise the pressure and apply focal retinectomy, if needed.
End of case	Apply panretinal photocoagulation, intraoperative anti-VEGF injection, and steroid at closure.
Tamponade selection	Favor gas (C_3F_8) over oil; reserve oil for a large inferior retinectomy, proliferative vitreoretinopathy, or hypotony/poor positioners.

(Avastin, Genentech/Roche) administered 3 to 7 days prior to surgery reduces intraoperative bleeding by regressing active neovascularization.[2] Beyond 10 to 14 days, however, the risk of accelerating the contraction of fibrovascular membranes and worsening traction increases. Because these patients often carry significant comorbidities, we recommend confirming transportation, medical clearance, and scheduling requirements (eg, hemodialysis) prior to injection.

If a cataract is present, combined or staged phacoemulsification can be considered, depending on the patient's age, the visual significance of the cataract, the quality of posterior segment visualization, and whether a longer-acting tamponade is planned. Removing a dense lens dramatically improves visualization, maneuverability, and effectiveness of peripheral vitreous base shaving, which can otherwise serve as a nidus for recurrent neovascularization postoperatively.

To ensure corneal clarity, consider using a dispersive viscoelastic applied to the corneal surface, along with 5 cc to 10 cc of topical 50% dextrose solution on the cornea (when available) under the viscoelastic layer to maintain corneal clarity and prevent corneal edema throughout the case.

ESSENTIAL INSTRUMENTATION

We favor 25-gauge instrumentation for most cases, balancing efficient vitreous removal with instrument stability. However, 27-gauge offers a unique advantage with an optimized cutter mouth-to-tip distance for segmentation of adherent membranes. In cases with dense vitreous hemorrhage or thick membranes requiring more aggressive segmentation, 23-gauge provides greater cutting efficiency and instrument rigidity. Know your system and have a plan for conversion.

The following additional instruments are essential to our complex diabetic TRD setup in the OR:

- A delaminating spatula is essential for developing safe planes, which is the cornerstone of success in TRDs.
- A high-magnification contact lens can optimize visualization of the posterior pole during membrane dissection in the macula, especially for plane recognition around retinal vessels, the optic nerve, fovea, and just outside the arcades to prevent breaks.
- MPC vertical scissors allow access to membranes tightly adherent to the arcade vessels and can be used closed for blunt dissection (Figure 1). Vertical scissors are preferred for segmentation perpendicular to the retinal surface in tight spaces that other instruments cannot access. Because they are handled by the foot pedal, they can be very precise. The edges are relatively sharp, so caution is needed to prevent iatrogenic breaks. These scissors can be used alongside the delaminating spatula

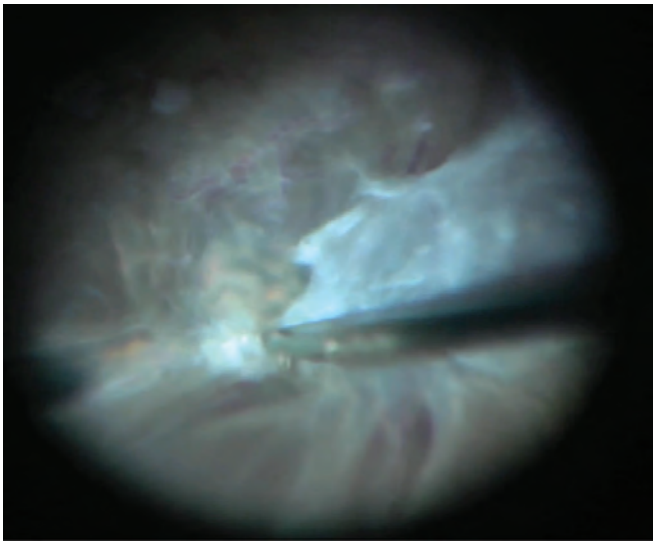

Figure 1. MPC scissors can be useful to access membranes that are tightly adherent to the arcade vessels and can aid in blunt dissection when closed.

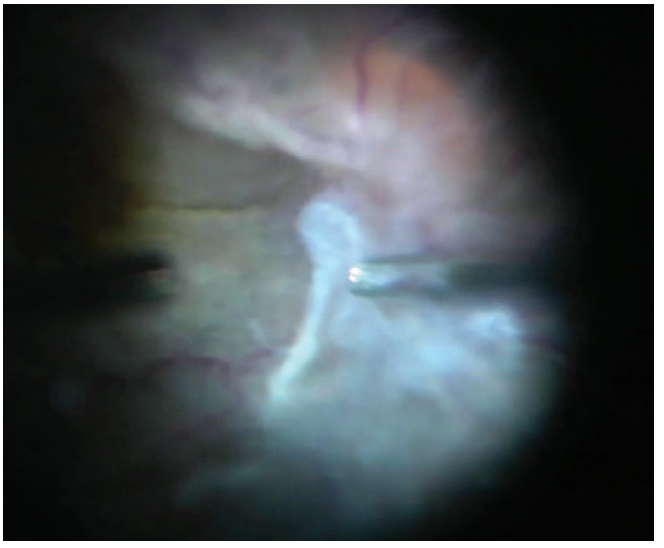

Figure 2. Surgeons can start posteriorly to elevate the fibrovascular tissue and create a plane for dissection.

to ensure a safe plane is created before delamination.

- In select cases, a lighted pick can illuminate the surgical field and function as a dissection instrument for developing tissue planes beneath the hyaloid. The sharp edge can create breaks in the fragile diabetic retina, so exercise extreme caution when using it.
- The Finesse Flex Loop (Alcon) is useful for peeling sticky residual hyaloid membranes, mobilizing preretinal blood clots resistant to aspiration, and atraumatic tissue mobilization in tight anatomical spaces.
- Dextrose in the infusion bottle creates a hyperosmolar environment that helps tamponade neovascular vessels and reduce intraoperative bleeding. Using BSS+ (Alcon) adds dextrose, bicarbonate, and glutathione to the concentrate to preserve corneal endothelial cells and the lens.

After membranes are peeled, intravitreal triamcinolone injected into the vitreous cavity provides invaluable staining of any residual hyaloid scaffold and cortical vitreous. This step is critical because residual vitreous scaffold leaves persistent traction and creates a nidus for fibroglial proliferation. It must be removed before gas or oil tamponade is placed.

SURGICAL APPROACH: INSIDE-OUT VERSUS OUTSIDE-IN

We favor the inside-out (posterior-to-anterior) approach for nearly all TRD cases. Starting at the posterior pole—particularly at the disc, where the hyaloid is often most firmly attached—allows the surgeon to develop a safe working plane under direct visualization before moving peripherally (Figure 2).

The critical principle is to never aggressively avulse fibrovascular proliferation over the optic nerve. The vascular supply to the disc is unforgiving. Instead, use internal limiting membrane forceps to apply gentle, tangential traction to remove the hyaloid/fibrovascular proliferation off the nerve, with diathermy immediately after. The moment you feel resistance at the disc, stop, consider using the soft-tip extrusion cannula on low vacuum, and be patient. Alternatively, stiffen the tissue with viscoelastic, apply diathermy to vessels under tension (while carefully avoiding the nerve itself), and then proceed.

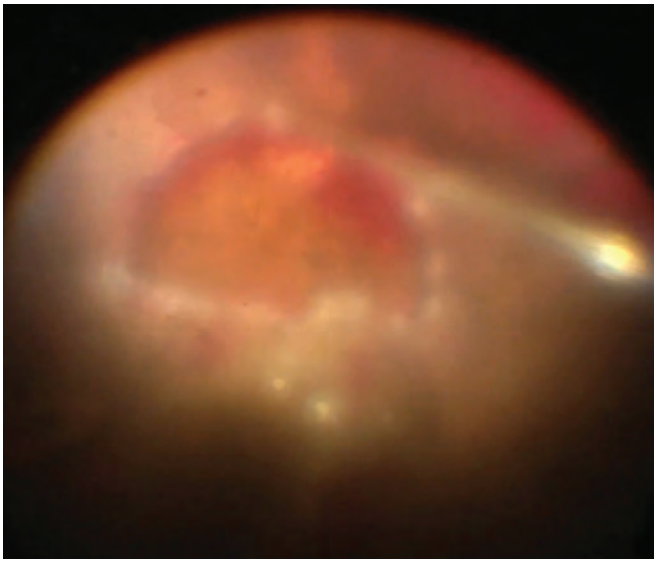

Figure 3. A focal retinectomy can create a manageable edge for tamponade and laser retinopexy.

Segmentation versus delamination is a key intraoperative decision. In general, segment first when en bloc traction is the dominant problem and no clear plane exists. Delaminate (ie, separate the membrane from the retinal surface) only once a clear tissue plane has been established and confirmed under high magnification. Many cases require both: segmentation to relieve global traction, then delamination in

discrete areas of focal adhesion. The limited membranectomy technique, in which carefully selected membranes are intentionally left in situ to minimize dissection trauma and iatrogenic breaks, is increasingly recognized as a viable option for select anatomical configurations.[3]

MANAGING INTRAOPERATIVE BREAKS

Even with the most experienced hands, iatrogenic breaks occur. The key is to stay calm and systematic, following the following steps:

- **Relieve traction first.** Release all residual traction around the break. Attempting to tamponade an open break under active traction is futile.
- **Re-stain with triamcinolone.** Don't forget to re-stain and remove any residual hyaloid on or around the break. This will also help create an edge for separation from other epicenters of traction. Surgeons can leave foci of fibrovascular proliferation, as long as the traction has been removed.
- **Perform a focal retinectomy.** When a break occurs in a zone of stiff, immobile retina under persistent traction that cannot be relieved, consider a focal retinectomy to convert the problem into a manageable edge amenable to tamponade and laser retinopexy (Figure 3).

Once the break is addressed and traction is fully relieved, proceed with fluid-air exchange and laser retinopexy. Do not rush to close without confirming complete retinal apposition under the gas bubble.

MANAGING INTRAOPERATIVE BLEEDING

Bleeding is the most common complication and among the most anxiety-provoking. The approach is straightforward once internalized and includes the following steps:

- **Raise the infusion pressure.** Tamponade first, then immediately identify the source. Increasing IOP through the infusion line will slow most hemorrhages long enough to locate the culprit vessel.
- **Apply diathermy.** Always have bipolar diathermy primed and accessible at the start of every case. When a vessel bleeds, apply diathermy precisely and with minimal energy—just enough to achieve hemostasis.
- **Perform a focal retinectomy.** Rarely, a focal retinectomy may be necessary when there is a break and the subretinal hemorrhage becomes fused with an intraretinal/preretinal hemorrhage and a fibrosis/stiff retina, preventing release of traction from the break.
- **Add perfluorocarbon liquid (PFCL).** Although rarely needed, this can be useful in complex cases involving subretinal hemorrhage or a posterior break encountered while working anteriorly. Surgeons must remove the PFCL fully and ensure it remains in a single large bubble, so it does not enter subretinal space, given the posterior traction if there are any breaks.

END-OF-CASE DECISIONS

Once the membranes are cleared and the retina is flat, end-of-case decision making remains critical to durable anatomic success. Laser retinopexy should be applied to all breaks and in zones of peripheral ischemia. Additional panretinal photocoagulation delivered at the time of surgery is important in patients with limited follow-up compliance.

An intraoperative anti-VEGF injection should be strongly considered at case completion, particularly when residual neovascularization is visible or when the preoperative injection window was too short for full regression. This reduces the risk of postoperative hemorrhage and early reactivation.

Intravitreal or periocular steroids at case closure can suppress the postoperative inflammatory cascade, which can be robust in patients with poorly controlled diabetes.

Tamponade selection should favor gas over silicone oil in most complex cases. Long-acting gas (eg, C_3F_8 12% to 14%) provides 6 to 8 weeks of tamponade, avoids the need for oil removal surgery, and is associated with lower rates of secondary glaucoma and band keratopathy.[4] Eyes receiving C_3F_8 may have a higher likelihood of visual improvement compared with those receiving silicone oil.[5] Reserve silicone oil for cases involving a giant retinal tear, inferior retinectomy, poor patient positioning compliance, or when simultaneous bilateral surgery is planned.

PLAN CAREFULLY, BUT STAY FLEXIBLE

Complex diabetic vitrectomy requires a disciplined framework applied consistently from the preoperative evaluation through the final tamponade decision. By approaching each case with structured planning, a well-prepared instrument setup, and clear contingency protocols for bleeding and iatrogenic breaks, surgeons can navigate even the most advanced diabetic eyes with confidence and consistency. ■

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AI IN DME: FROM PROMISE TO CLINICAL PRACTICE

New data show the growing utility of AI-assisted screening, referrals, and treatment response prediction.

By Scott Song, BA, and T. Y. Alvin Liu, MD

As AI continues to creep into nearly every aspect of our daily lives, many of us wonder whether AI in diabetic macular edema (DME) is an emerging clinical tool or simply another wave of promising algorithms unlikely to translate into practice. AI has been applied to detect DME from color fundus photographs (CFPs) and OCT, estimate visual acuity, quantify OCT biomarkers, and predict response to anti-VEGF therapy. Thus, the central question is not whether AI can perform these tasks, but which applications will ultimately change clinical practice. Three recent studies illustrate how AI may address practical problems along the DME care pathway by expanding screening, improving referral efficiency, and personalizing treatment.

EXPANDING ACCESS: AUTONOMOUS DME SCREENING

One of the clearest opportunities to improve outcomes in diabetic eye disease remains expanding access to DME screening (Figure). Bressler et al evaluated whether deep learning could identify DME using CFPs, which are already widely used for diabetic retinopathy (DR) screening.[1] Unlike many earlier CFP-based DME studies, this work emphasized extensive external validation across independent datasets, representing an important step toward real-world deployment rather than another proof-of-concept algorithm. The model was trained on a large, diverse dataset of more than 32,000 CFPs from nearly 16,000 patients. Performance was then evaluated at the image, eye, and patient levels.

Internal validation demonstrated strong performance, with a patient-level area under the curve of 0.962 and sensitivity and specificity of approximately 90%. Results also remained favorable across several external datasets. On Messidor-2, for example, the patient-level area under the curve was 0.964, with sensitivity of 0.897 and specificity of 0.932. External validation is particularly important for screening tools, which must perform across different populations, cameras, and image-acquisition conditions.[1]

Because CFPs do not directly visualize retinal fluid, the

KEY TAKEAWAYS

- Color fundus photography-based AI models may extend diabetic macular edema (DME) screening to patients who lack access to OCT.
- AI-assisted OCT screening may reduce unnecessary referrals while preserving access to specialist care for patients with DME most likely to benefit.
- Multimodal prediction models of anti-VEGF treatment response may eventually support more personalized treatment decisions.

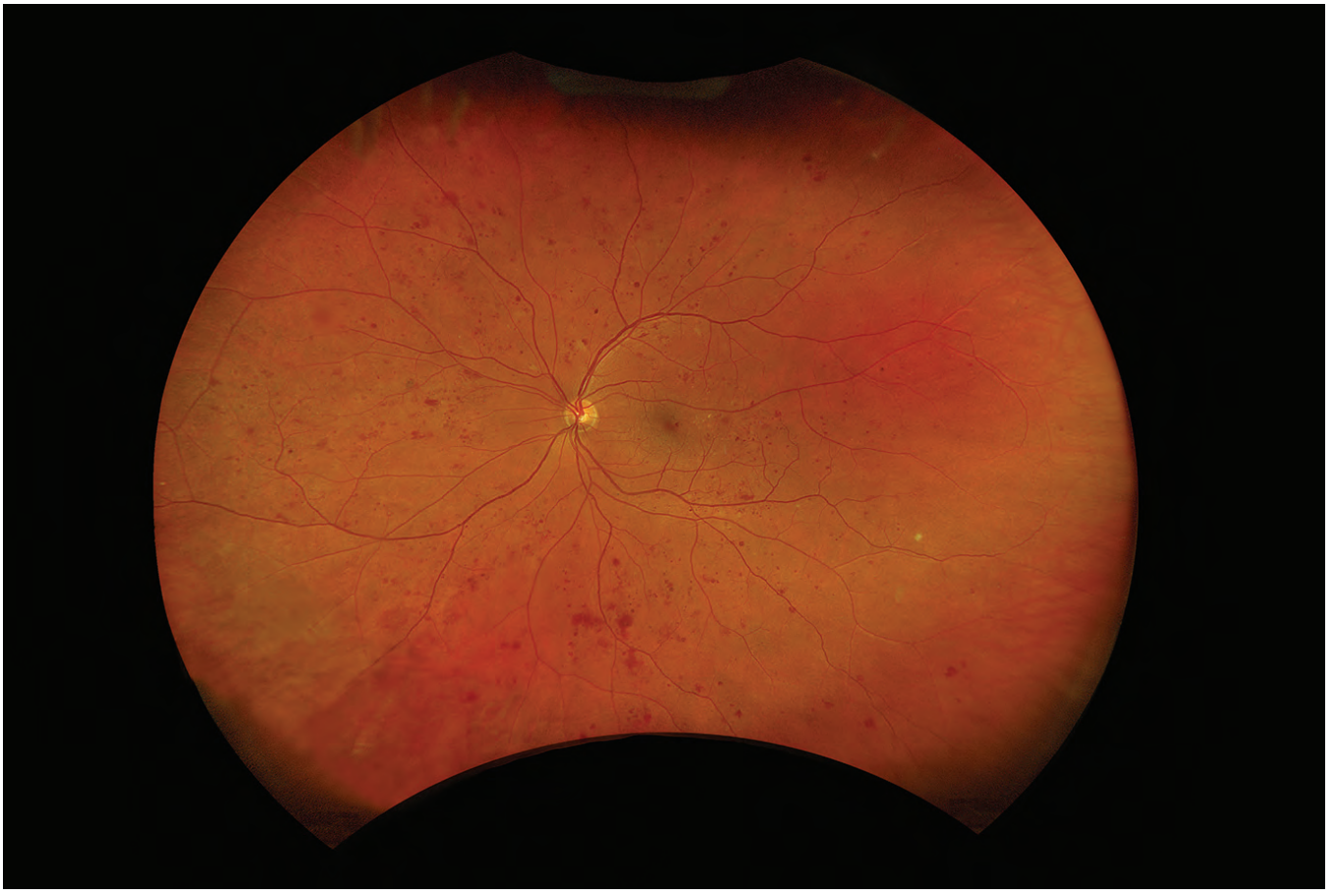

Image courtesy of Retina Rocks (retinarocks.org, @retina.rocks)

Figure. AI-assisted screening may be able to identify patients such as this one with severe nonproliferative DR with DME.

model instead identifies DME likely based on the presence of hard exudates in the fundus photographs. Its role is therefore not to replace OCT-based diagnosis but to identify patients who warrant further evaluation. A scalable CFP-based system could extend DME screening into primary care and teleophthalmology settings where OCT is unavailable, potentially reaching patients who might otherwise never see a retina specialist. Prospective studies are needed to determine how such systems perform in real-world screening workflows and whether they improve access to care and patient outcomes.

IMPROVING CLINICAL WORKFLOW: AI-ASSISTED OCT REFERRAL

Once patients enter a screening program, the challenge shifts from identifying possible disease to determining who truly requires specialist evaluation. CFP-based programs frequently rely on surrogate signs of DME and consequently generate many false-positive referrals. Zhang et al addressed this problem by evaluating an AI-based OCT system within a territory-wide DR screening pathway in Hong Kong.[2]

The investigators conducted a multicenter randomized clinical trial involving 276 patients whose CFP-based screening reports suggested possible DME. In the conventional pathway, all patients meeting the existing screening criteria were automatically referred for specialist DME evaluation based on their CFP screening reports, reflecting standard practice. In the AI-assisted pathway, patients also underwent OCT imaging, and ophthalmologists reviewed both the CFP screening report and the AI-generated OCT analysis report, which included DME probability scores to determine whether referral for specialist evaluation was warranted.

For ethical reasons, all participants ultimately underwent specialist evaluation, so the referral decisions in the AI-assisted pathway were effectively hypothetical. The false-positive referral rate decreased from 69.1% in the conventional pathway to 24.1% with the AI-assisted pathway, while referral sensitivity remained 100% in both groups. Importantly, there were no false negatives in the AI-assisted pathway.

Together, these findings suggest incorporation of AI-assisted OCT analysis has the potential to substantially reduce unnecessary referrals without compromising patient safety. The AI-assisted pathway also incorporated image-quality assessment, uncertainty flagging, and clinician

THE MOST USEFUL AI APPLICATIONS WILL BE THOSE THAT SOLVE PRACTICAL PROBLEMS FOR PATIENTS, CLINICIANS, AND HEALTH CARE SYSTEMS.

oversight, illustrating that the most effective implementation of AI may not be full autonomy, but a carefully designed human-AI workflow in which the algorithm supports routine triage while clinicians retain responsibility for uncertain or complex cases.

Because all participants ultimately underwent specialist evaluation, the study did not directly assess the effect of this workflow on real-world clinic use. Future implementation studies must determine whether these improvements translate into meaningful reductions in specialist workload and improvements in health care delivery.

TOWARD PRECISION MEDICINE: PREDICTING ANTI-VEGF RESPONSE

The next frontier extends beyond diagnosis and triage. Ideally, AI should not only identify patients with DME but also help predict how they will respond to treatment. Unlike prior AI models that relied primarily on OCT images alone, Yoon et al developed a multimodal deep-learning model that combined baseline OCT images, quantified lesion features, and clinical variables. Including age, diabetes history, prior ocular treatments, and systemic comorbidities helped the model predict anatomic response after three monthly anti-VEGF injections, reflecting a shift toward more individualized prediction of treatment response.[3]

The retrospective study included 107 patients, of whom 65 were classified as good responders and 42 as poor responders. During internal validation, the model achieved an area under the receiver operating characteristic of 0.962, accuracy of 0.953, sensitivity of 0.969, and specificity of 0.928. It also outperformed retina specialists and fellows in an experimental comparison, in which clinician accuracies ranged from 0.571 to 0.857.[3]

However, performance declined when the model was tested on two independent validation cohorts: a temporally separate holdout cohort from the same internal institution and an external cohort from a different hospital, with area under the receiver operating characteristics of 0.764 and 0.728, respectively. This drop illustrates the gap between promising internal results and reliable real-world generalization. Before such a model could influence treatment selection, it would require larger prospective multicenter validation and evidence that acting on its predictions improves outcomes.

Even so, the clinical use case is compelling. Earlier identification of patients unlikely to respond adequately to initial anti-VEGF therapy could support closer monitoring, earlier consideration of alternative treatment, and more realistic counseling, while potentially reducing prolonged exposure to an ineffective initial treatment strategy.

AI ACROSS THE DME CARE CONTINUUM

Together, these studies illustrate how AI in DME is beginning to mature across the continuum of care: from identifying patients who need evaluation and improving referral efficiency to personalizing treatment decisions. The most useful AI applications will be those that solve practical problems for patients, clinicians, and health care systems. Future progress depends on prospective validation, performance across diverse populations and devices, thoughtful workflow integration, cost-effectiveness, and sustainable reimbursement. Ultimately, success will be measured not by how well an algorithm performs in isolation, but by whether its use meaningfully improves access, efficiency, treatment decisions, and visual outcomes for patients with DME. ■

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CAN OCTA HELP PREDICT DR PROGRESSION?

Quantitative biomarkers may add a new dimension to the assessment and risk stratification of diabetic retinopathy.

By Kallista Zhuang, BA; Shinji Kakihara, MD, PhD; and Amani A. Fawzi, MD

The current staging framework for diabetic retinopathy (DR) triages patients to broad severity categories; however, within a given severity category, the framework does not necessarily identify eyes with greater risk of progression to vision-threatening complications.[1,2]

Retinal ischemia is central to DR pathophysiology, with ischemic burden being an important key in defining risk of progression in diabetic eyes.[3]

Classically, ultra-widefield fluorescein angiography (UWF-FA) is used to document the extent of retinal nonperfusion, but this dye-based tool does not lend itself to routine or frequent imaging.[1,4]

In contrast, OCT angiography (OCTA) enables noninvasive, depth-resolved quantification of retinal capillary perfusion at the microvascular level, without impedance related to dye or leakage artifacts. Although OCTA images may capture only a portion of the total retinal area accessible to UWF-FA, the technology is rapidly evolving in speed and precision, allowing clinicians to image wider areas of the retina.

Furthermore, emerging evidence suggests that OCTA biomarkers may complement conventional DR staging in terms of the retinal ischemic burden.[5]

QUANTIFYING ISCHEMIA WITH OCTA

OCTA has the advantage of enabling layer-specific evaluation of retinal capillary perfusion. Its depth-resolved capability is particularly relevant, as diabetic capillary damage may not occur uniformly across retinal layers.[6] Quantitative metrics of OCTA-based capillary perfusion

KEY TAKEAWAYS

- Geometric perfusion deficit (GPD) on OCT angiography (OCTA) defines nonperfused retinal tissue based on the distance threshold from the nearest perfused capillary.
- In a prospective study, GPD in the deep capillary plexus was the only OCTA metric to detect significant microvascular changes in eyes with referable diabetic retinopathy (DR) at 6 months, ahead of other metrics that became significant only at 12 months.
- Higher baseline deep capillary plexus GPD predicted earlier onset of DR complications.
- OCTA-derived GPD-deep capillary plexus may complement conventional DR grading.

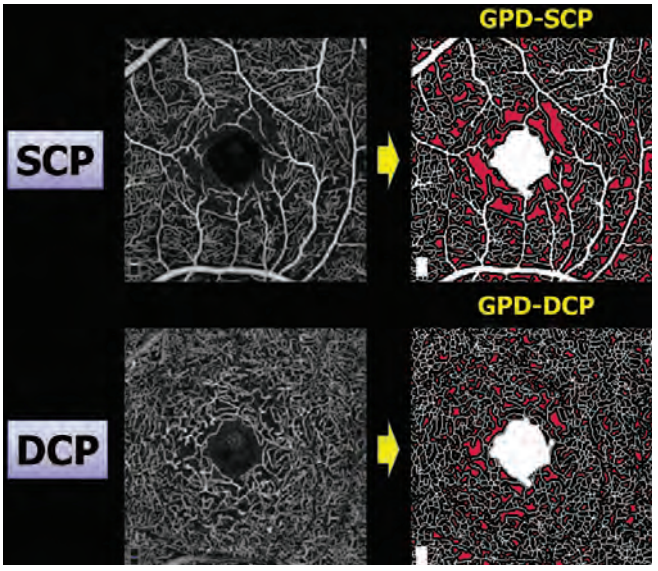

Figure 1. Representative en face OCTA images and corresponding GPD maps in the superficial and DCPs. GPD can be calculated in individual retinal capillary plexuses to quantify layer-specific ischemic burden.

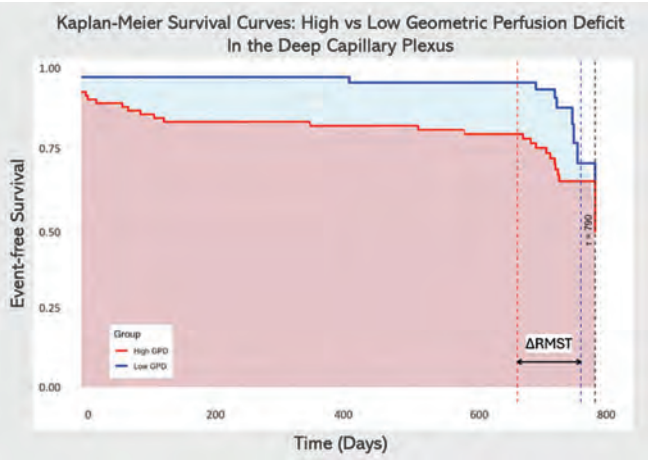

Figure 2. This Kaplan-Meier curve depicts the survival rates of eyes with high GPD-DCP versus eyes with low GPD-DCP. Event-free survival probability is illustrated on the vertical axis. Time in days is depicted on the horizontal axis. The dotted vertical lines represent the unadjusted restricted mean survival time (red for high GPD group, blue for low GPD group). The difference between the survival times is represented by the arrow labeled ΔRMST.

have emerged as a useful approach to characterize diabetic retinal ischemia.[7,8]

One such metric is geometric perfusion deficit (GPD), which defines the proportion of ischemic retinal tissue farther than 30 µm from the nearest perfused capillary (Figure 1), or the theoretical oxygen diffusion limit (excluding the physiologic foveal avascular zone).[9,10] By using this threshold-based approach at the different retinal capillary plexuses, GPD provides a physiologically grounded estimate of layer-specific ischemic burden.

Cross-sectional studies from our group have shown that GPD in the deep capillary plexus (GPD-DCP) captures clinically meaningful ischemic burden in DR. Among several OCTA-derived metrics, GPD-DCP provided the strongest discrimination of referable DR.[11] It also has been associated with vision function, where greater perfusion deficits correlated with worse BCVA, even after accounting for other clinical and ischemic parameters.[12] Importantly, macular GPD-DCP may also provide information about ischemic burden beyond the macula. When compared with UWF-FA, greater GPD-DCP was independently associated with greater posterior, peripheral, and total retinal nonperfusion.[13]

Thus, although GPD-DCP is derived from a small macular OCTA scan, it may function as an indicator of more widespread retinal vascular compromise. Together, these cross-sectional studies provided the rationale for evaluating whether baseline GPD-DCP could also predict future progression and DR-related complications.

RATE OF MICROVASCULAR PROGRESSION ON OCTA

The clinical value of a biomarker depends on whether it can identify eyes at risk for future worsening, rather than simply describe disease at a single point in time. We therefore pursued two complementary longitudinal questions:

1. Can OCTA parameters detect short-term progression of microvascular dysfunction in DR?
2. Can baseline GPD-DCP on OCTA predict clinically relevant complications?

To address the first question, we conducted a 1-year prospective study of 320 eyes (208 patients), evaluating longitudinal changes in multiple OCTA metrics at baseline, 6 months, and 12 months, stratified by DR severity: non-referable versus referable DR.[14] In eyes with referable DR (moderate nonproliferative DR or worse), GPD-DCP showed significant worsening as early as 6 months, whereas no other OCTA metric showed a significant change.[14] In eyes with nonreferable DR, no metric changed significantly at 6 months, and only vessel density in the superficial capillary plexus declined at 12 months. These findings demonstrate how OCTA can capture time-varying microvascular damage across different plexuses; moreover, GPD-DCP was more sensitive than other metrics to microvascular progression in eyes with referable DR.[14]

We next wanted to understand whether baseline GPD-DCP could predict progression of retinal nonperfusion beyond the macula. In a prospective longitudinal study, greater baseline GPD-DCP was independently associated with retinal nonperfusion progression on UWF-FA over 2 years. Although baseline UWF-FA nonperfusion remained the strongest predictor of subsequent progression, GPD-DCP provided independent prognostic information using macular OCTA scan. Thus, when serial FA is not practical or desirable, OCTA may help identify eyes at greater risk of progressive retinal nonperfusion.[15]

WHILE OCTA CANNOT REPLACE ESTABLISHED METHODS OF DR ASSESSMENT, IT OFFERS A COMPLEMENTARY ADVANTAGE: NONINVASIVE, LAYER-SPECIFIC QUANTIFICATION OF MACULAR CAPILLARY ISCHEMIA.

PREDICTING CLINICALLY RELEVANT COMPLICATIONS

We then investigated whether baseline GPD-DCP could predict the onset of clinically relevant DR complications, defined as worsening DR severity on UWF-FA, loss of vision, vitreous hemorrhage, initiation of anti-VEGF therapy, or need for panretinal photocoagulation.[16] In a 2-year prospective study of 175 patients (265 eyes), 48 eyes (18.1%) from 41 patients (23.4%) experienced a complication. We found that higher baseline GPD-DCP was associated with an increased risk and earlier onset of complications.[16] Each standard deviation increase in GPD-DCP was associated with a 77% higher hazard of complications and a 70-day reduction in complication-free survival. When eyes were dichotomized using a Youden's J-derived threshold of 3.41%, those with GPD-DCP above this threshold developed complications approximately 4 months earlier than those below the threshold (Figure 2).[16] These results suggest that GPD-DCP may serve as an objective metric for prognosticating and individualized care in DR.

CAN OCTA PROVIDE THE ANSWER?

While OCTA cannot replace established methods of DR assessment, it offers a complementary advantage: noninvasive, layer-specific quantification of macular capillary ischemia. Across our studies, GPD-DCP is consistently associated with clinically important features of DR. Further validation is needed before GPD-DCP can be incorporated into routine clinical decision making. Additional studies are needed to calibrate this metric across different imaging devices, acquisition protocols, and diverse patient populations.

Nevertheless, current evidence suggests that OCTA-derived GPD-DCP may complement conventional DR grading, providing a quantitative, noninvasive measure of retinal ischemic burden. ■

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RISING STARS IN RETINA

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

Jonathan Lin, MD, PhD

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

As an MD/PhD student at Washington University in St. Louis, I had the privilege of working in the lab of vitreoretinal surgeon-scientist Rajendra Apte, MD, PhD, for my thesis research. In his lab, I investigated the cellular and molecular mechanisms that contribute to blindness in retinal diseases. After seeing the (beautiful) retina in the clinic and witnessing the technical intricacies of vitreoretinal surgery for the first time, I knew that I wanted to become a retina specialist.

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

I am incredibly fortunate to have trained under a team of world-class mentors at Stanford. My fellowship director, Prithvi Mruthyunjaya, MD, MHS, has been instrumental in shaping my professional growth, constantly pushing me to evolve as a clinician, surgeon, and human. I owe a debt of gratitude to the entire Stanford retina family for their relentless support: Darius Moshfeghi, MD; Loh-Shan Leung, MD; Steven Sanislo, MD; Stephen Smith, MD; Theodore Leng, MD, MS; Diana Do, MD; Quan Dong Nguyen, MD, MSc; Carolyn Pan, MD; Ramsudha Narala, MD; Atma Vemulakonda, MD; Ehsan Rahimy, MD; Chase Ludwig, MD; Charles DeBoer, MD, PhD; Ahmad Al-Moujahed, MD, PhD, MPH; Karen Wai, MD; Mary Elizabeth Hartnett, MD; and Natalia Callaway, MD.

Additionally, I am grateful to Vinit Mahajan, MD, PhD, for welcoming me into his research lab during fellowship, and to my mentors during residency at Harvard/Mass Eye and Ear—Demetrios Vavvas, MD, PhD; Dean Eliott, MD; John Miller, MD; and Nimesh Patel, MD—who expertly guided me through my first intravitreal injections and vitrectomies and laid the groundwork for fellowship training.

***RT*: Can you tell us about a memorable experience from your fellowship?**

My most memorable experience was repairing a retinal detachment that occurred after a traumatic open globe injury. Having performed the initial injury repair, I found it deeply rewarding to provide this continuity of care. Both cases were technically challenging, but what was truly memorable was seeing the patient through the entire journey from trauma to recovery.

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

Although I am biased, I believe retina is the best field in ophthalmology, and maybe even in all of medicine. We save vision in vitreoretinal emergencies and can identify systemic diseases through a clinical examination of the retina. Embrace the steep learning curve. It is normal to feel overwhelmed at the start, but if you treat every clinic and OR day as an opportunity to grow, your dedication will be recognized. ■

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RISING STARS IN RETINA
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THE POTENTIAL OF TYROSINE KINASE INHIBITORS

This novel class of drug may one day help to address the growing burden of diabetic eye disease.

By Shawn Kavoussi, MD

Retina specialists caring for patients with diabetic macular edema (DME) currently have three main pharmacologic approaches: anti-VEGF injections, steroids, or a combination of both. Next-generation therapies—such as faricimab (Vabysmo, Genentech/Roche), aflibercept 8 mg (Eylea HD, Regeneron), and the port delivery system with ranibizumab (Susvimo, Genentech/Roche)—now offer more choices, but the limitations remain the same. For example, the Protocol T early analysis showed that up to 35% of patients with DME experience suboptimal responses, gaining fewer than 5 letters at 12 weeks, following monthly aflibercept 2 mg (Eylea, Regeneron) therapy.[1]

Treatment with intraocular steroids, such as the dexamethasone intravitreal implant (Ozurdex, Abbvie) and fluocinolone acetonide intravitreal implant (Iluvien, ANI Pharmaceuticals), comes with the risk for increased IOP and cataract formation.[2,3]

These limitations have led researchers to seek novel mechanisms of action to address DME, several of which are showing promise, including tyrosine kinase inhibitors (TKIs). Here is a look at what TKIs are, where they are in the pipeline, and how they might fit into our treatment paradigm.

A NOVEL MECHANISM OF ACTION

TKIs work by blocking cellular communication and downstream processes through phosphorylation and inhibiting the function of the tyrosine kinase enzyme, which activates cellular signals such as VEGF. When the retina is deprived of oxygen through damage to the vasculature or decreased blood flow, such as in diabetic retinopathy and AMD, VEGF promotes the growth of new, leaky blood vessels. Unlike anti-VEGF medications, which bind to VEGF outside the cell, TKIs block this signaling process within the cell itself. The intracellular mechanism of action blocks all VEGF isoforms, offering the potential for increased durability.[4]

In addition, research shows that retinal thickness

KEY TAKEAWAYS

- The intracellular mechanism of action for tyrosine kinase inhibitors (TKIs) blocks all VEGF isoforms, offering the potential for increased durability.
- Promising TKIs under investigation include EYP-1901 (EyePoint), OTX-TKI (Ocular Therapeutix), and D-4517.2 (Ashvattha Therapeutics).
- TKIs offer the ability to reduce patients' treatment and office visit burden. However, some patients may still require monitoring between injections.

fluctuations with bolus therapy lead to overall worse long-term outcomes and gradual vision decline.[5] Thus, sustained maintenance of consistent drug levels with TKI implants could potentially lead to better visual outcomes.

PROMISING PIPELINE OPTIONS

The vorolanib intravitreal insert (EYP-1901/Duravyu, EyePoint) inhibits VEGFR-1, VEGFR-2, VEGFR-3, and PDGFR-β. Recent radiometric and in vitro assays also demonstrated potent inhibition of JAK1, which tranduces interleukin-6–mediated proinflammatory signaling through the interleukin-6R/gp130 receptor complex.[6]

In the phase 2 VERONA trial, both the 1.34 mg and 2.7 mg doses met the primary endpoint of extended time to first supplemental injection versus aflibercept 2 mg. With the higher dose, BCVA improved by 7.1 letters compared with baseline and central subfield thickness (CST) improved by 75.9 µm compared with baseline—74% more drying in study eyes versus controls.[7] In addition, 73% of eyes in the higher-dose EYP-1901 group were supplement-free versus 50% in the aflibercept group up to week 24. As for safety, the trial reported no treatment-related ocular or systemic serious adverse events.[7]

The company completed enrollment for the phase 3 COMO and CAPRI clinical trials of EYP-1901 for the treatment of DME.[8]

The axitinib intravitreal insert (OTX-TKI/Axpaxli, Ocular Therapeutix) embeds axitinib within a bioresorbable polyethylene glycol hydrogel depot that is injected intravitreally. The hydrogel gradually dissolves while the medication is released over the course of several months, targeting all VEGF receptors and PDGFR. The phase 1/2a clinical study demonstrated sustained intraocular axitinib delivery with an approximately 89% to 90% reduction in annualized anti-VEGF injection burden compared with each patient's historical pre-enrollment treatment frequency. Approximately one-third of patients required no rescue injections through 12 months while maintaining stable BCVA and CST.[9]

The phase 3 Helios-3 trial is evaluating OTX-TKI dosed every 12 months in patients with nonproliferative diabetic retinopathy versus sham. In the phase 3 SOL-1 trial in patients with wet AMD, treatment with OTX-TKI demonstrated superiority over aflibercept for a durability-based endpoint for wet AMD.[10]

Migaldendranib (D-4517.2, Ashvattha Therapeutics) is delivered subcutaneously through a nanoparticle hydroxyl dendrimer carrier. Early phase 1 studies demonstrated favorable safety and biological activity.[11] The TEJAS phase 2 trial was the first randomized clinical study evaluating subcutaneous D-4517.2 in patients with neovascular AMD and DME. The study was designed to assess the safety, tolerability, pharmacokinetics, and preliminary efficacy of repeated subcutaneous dosing compared with intravitreal aflibercept. Multiple subcutaneous doses were safe and well-tolerated and provided a > 69% reduction in treatment burden in study eyes and a > 67% reduction in fellow eye treatment in patients with bilateral disease.[12]

TKI UPDATE IN THE NEWS

EyePoint recently announced the results from the phase 3 LUGANO study in wet AMD. While the primary endpoint was not achieved in the full dataset, the vorolanib intravitreal insert (EYP-1901/Duravyu) was noninferior to on-label aflibercept (Eylea, Regeneron) control (nominal *P*-value = .0096) in an ad hoc analysis excluding 9 of 211 patients who experienced ≥ 15-letter vision loss unrelated to wet AMD.[1]

In the trial, key secondary endpoints were met, including a reduction in treatment burden, increased supplement-free rates, safety with redosing, and strong anatomic control through week 56 compared with aflibercept.[1]

EYP-1901 continued to be safe and well tolerated with repeat dosing, including no observed events of insert migration, anterior chamber opacities, free-floating drug particles, retinal vasculitis, or severe intraocular inflammation.[1]

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GIVEN THEIR NOVEL APPROACH, TKIS HOLD PROMISE AS ADJUNCTS TO OUR CURRENT THERAPEUTIC APPROACHES, OR, FOR SELECT PATIENTS, FIRST-LINE TREATMENT.

FITTING INTO THE TREATMENT PARADIGM

Given their novel approach, TKIs hold promise as adjuncts to our current therapeutic approaches, or, for select patients, first-line treatment. For example, patients newly diagnosed with mild-to-moderate DME might respond to a primary monotherapy with a TKI, significantly minimizing the treatment burden compared with anti-VEGF monotherapy. For more severe disease

where the CST is greater than 400 µm, patients may benefit from a loading phase of anti-VEGF therapy followed by combination therapy. Overall, TKIs offer the ability to reduce treatment and office-visit burden. However, these patients may still require monitoring between injections.

In addition to monitoring concerns, each of the TKIs under investigation come with potential complications due to their sustained delivery method as implants.

For example, the implant procedures will introduce an initial learning curve, as each one has it's own unique injection technique and applicator. In addition, clinicians must educate patients on the potential for visual floaters and set that expectation. Residual material in the vitreous cavity may also affect the treatment decisions to redose patients after 6 to 9 months for some implants.

IMPROVING DME CARE

As the prevalence of diabetes continues to rise, clinicians must seek novel approaches to care for patients presenting with DME. Investigational TKIs may soon provide a novel approach with the promise of reduced treatment burden. Phase 3 trial data and real-world experience will eventually determine the safety and efficacy of TKIs, in addition to clarifying their role in managing our patients with DME. ■

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(Continued from page 31)

now have unprecedented opportunities to individualize therapy and reduce treatment burden. Careful patient selection, vigilant monitoring, and continued evaluation of long-term outcomes remain essential as emerging technologies further reshape the therapeutic landscape of DED.[3,4,6] ■

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DEFINING EARLY GEOGRAPHIC ATROPHY REQUIRES MORE THAN LESION SIZE

Imaging, progression, and patient-specific risk all inform treatment timing.

By Sean Adrean, MD, FAAO

Geographic atrophy (GA) is increasingly recognized as a progressive disease that warrants intervention before central vision is irreversibly compromised. However, defining "early" GA remains a clinical challenge. In my clinic, GA lesions that are smaller than 1 disc diameter of total atrophy are considered early disease. However, diagnosing by lesion size alone is insufficient. Lesion location progression, and the presence of multifocal lesions also inform decision-making, as real-world treatment decisions often require a more nuanced assessment of disease trajectory and functional risk.

Defining Early GA: More Than Lesion Size

Although literature supporting treatment at very early stages remains limited, the inclusion criteria used in the pivotal OAKS/DERBY and GATHER 1 and 2 clinical trial programs provide a framework for identifying patients who will likely benefit from treatment.[1-3] In these trials, enrollment included patients with at least 1 disc area of GA, or approximately 2.5 mm² with a maximum lesion size of 17.5 mm², while excluding those patients with contiguous peripapillary atrophy. Multifocal lesions that added up to 2.5 mm² were also allowed if one GA lesion was at least 1.25 mm² and the other lesions totaled 2.5 mm². Smaller lesions may present challenges for treatment decisions; larger lesions or those that have peripapillary atrophy, not involving the fovea, do not present as much of a therapeutic challenge.

Recognizing Early Disease Through Imaging

In addition to the clinical examination, I collect OCT images, which serve as a practical baseline tool for identifying early atrophic changes. When reviewing these images, I look for complete or incomplete retinal pigment epithelium and outer retinal atrophy, hyperreflective foci, and ellipsoid zone disruption. Often on the SD-OCT, there are hypertransmission defects that alert the clinician to problematic areas. Fundus autofluorescence typically defines GA more clearly than color photography and is the basis of measurement for the pivotal GA trials.

Deciding When to Treat: Progression, Risk, and Functional Impact

Treatment discussions may be reasonable when small lesions threaten central vision. Beyond lesion size, I also consider several factors before making treatment decisions:

- Evidence of progression over time
- Foveal proximity or threat
- Fellow-eye vision loss from GA
- Patient-reported visual symptoms
- Functional limitations during reading or daily activities

In my experience, a strong patient candidate for receiving treatment for early disease is someone with vision loss in the fellow eye from end-stage wet AMD or foveal GA, with early atrophy developing in the functional eye. Patients who are experiencing noticeable visual changes are also strong candidates for treatment. While AREDS supplementation remains part of management discussions, I also discuss the possible benefits of photobiomodulation (PBM), which may be considered in select patients with intermediate AMD or even early atrophic changes.[4] One study showed that GA incidence decreased from 24.0% in sham eyes to 6.8% in PBM-treated eyes ($P = .007$).

Unlike wet AMD, GA generally allows time for observation and shared decision-making between doctor and patient. To this end, repeat imaging at 3- to 6-month intervals may aid decision-making for borderline cases.

Preserving Vision Over Time

There has been some resistance in the retina community when it comes to treating GA, with some doubting how much benefit we are truly providing. For patients who are anxious about treatment, I reference one recent study with long-term data demonstrating that, at 5 years, treatment preserved approximately a year and a half's worth of retinal tissue.[5] Ultimately, long-term treatment for GA should be viewed similarly to the management of other chronic diseases, with the goal of preserving retinal tissue and visual function over time rather than restoring lost vision. ■

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WHAT PATHOGEN TYPE REVEALS ABOUT ENDOPHTHALMITIS

Certain types of bacteria may be linked to a more aggressive disease course post-procedure.

BY SAAGAR PATEL, MD; CHRISTOPHER CONRADY, MD, PHD; AND TALISA E. DE CARLO FOREST, MD

Post-procedure endophthalmitis is an emergency, and visual outcomes can vary tremendously.[1,2] Retina specialists have long recognized that some cases follow a far more aggressive course than others, not only because of timing, host factors, and treatment decisions, but potentially because of the organism itself.

We recently designed a multicenter study to examine this factor more closely: In patients with acute endophthalmitis after an intraocular procedure, does pathogen type meaningfully affect visual and anatomic outcomes? In this retrospective interventional case series, we reviewed 240 adults diagnosed with postprocedural acute endophthalmitis between 2012 and 2022 at four tertiary university-based centers.[3] Of this group, 208 had sufficient follow-up for comparative analysis. Organisms were grouped into surface commensals, primarily coagulase-negative *Staphylococcus*, and nonsurface commensals, such as *Streptococcus* and *Enterococcus*.

The purpose of the study was to determine whether differences in pathogen type translated into measurable differences in vision, need for intervention, and eye survival.

STUDY FINDINGS

The clearest finding was that pathogen type matters. Among culture-positive cases, infections caused by nonsurface commensal organisms were associated with a significantly worse final visual acuity compared with infections caused by coagulase-negative *Staphylococcus* (mean logMAR 2.14 vs 0.77). These infections were also associated with higher rates of third interventions (27.5% vs 10.1%), phthisis (15.4% vs 1.1%), and enucleation/evisceration (12.8% vs 0%).[3]

Importantly, in the postinjection subgroup, nonsurface commensal organisms remained independently associated with poorer outcomes, even after multivariable adjustment.[3]

IMPLEMENTING THESE FINDINGS INTO PRACTICE

The study helps explain why outcomes can vary so dramatically even among patients who appear, at first glance, to have the same diagnosis. For years, more aggressive pathogens have been linked anecdotally and in smaller series to worse outcomes.[4-8] This larger multicenter cohort strengthens that association, suggesting some of the damage may reflect the biology of the organism itself, not just delays in presentation or differences in management.

Although this study does not establish a mechanism, it supports the idea that certain pathogens may be inherently more aggressive once infection occurs. Post-procedure endophthalmitis is not a single entity, but a spectrum in which organism type shapes prognosis in meaningful ways.

STUDY LIMITATIONS

This study does not establish a new treatment algorithm or show that clinicians can reliably identify the causative organism early enough to tailor initial management. It also does not conclude that primary vitrectomy improves outcomes in this setting. In fact, most patients were initially treated with intravitreal injections (92.1%), while initial vitrectomy was uncommon and not significantly associated with better visual outcomes.[3]

However, the results of this study do support a more focused clinical conclusion: If more virulent pathogens are associated with worse vision, more interventions, and higher rates of eye loss, then earlier organism identification becomes more than a microbiology goal.

IMPLICATIONS FOR COUNSELING AND FOLLOW-UP

When a patient develops post-procedure

(Continued on page 53)

OPTIMIZING FUNCTIONAL OUTCOMES IN PVR


Practical strategies and decision making for proliferative vitreoretinopathy surgery.

BY NEIL SHAH, MBBS, FRCOPHTH, AND RODRIGO ANGUITA, MBBS, MD, FEBO, FICO

Proliferative vitreoretinopathy (PVR) remains a leading cause of surgical complications in rhegmatogenous retinal detachment (RRD) repair and an independent risk factor for poor visual prognosis (Figure 1).[1,2] Even if anatomic reattachment is achieved, visual recovery often lags, limited by complications such as macular edema (ME), epiretinal membrane (ERM), macular folds, and photoreceptor loss from recurrent detachment.[3,4] For vitreoretinal surgeons, the challenge is not simply to reattach the retina, but to protect the macula at every step, from preoperative imaging to tamponade selection and removal.

This article details practical, evidence-based strategies to optimize macular outcomes in PVR-RRD.

MACULAR BIOMARKERS OF VISUAL PROGNOSIS

Preoperative macular status should be documented with OCT and should be mandatory in the postoperative period. Subfoveal fluid, photoreceptor integrity and ERM or ME guide patient counselling and predict recovery.[5,6]

OCT biomarkers play an increasingly important role in predicting visual outcomes. In a post hoc longitudinal analysis of a randomized controlled trial of patients who underwent surgery for PVR-C RRD, early postoperative OCT findings, including retinal pigment epithelium and outer retinal layer thickness as well as qualitative markers (eg, gross retinal layer disruption, absence of foveal bulge) were significantly associated with poorer visual outcomes.[7]

Patient-reported outcome data add useful perspectives. Baseline and early postoperative BCVA are among the strongest predictors of 12-month visual function and vision-related quality of life.[2,8] In PVR-RRD cohorts, final BCVA correlates most strongly with Visual Function Questionnaire-25 and Short Form Health Survey-36 scores, rather than the number of surgeries or anatomic reattachment rate.[8]

INTRAOPERATIVE MACULAR STRATEGY: TIPS AND TRICKS

Broad Internal Limiting Membrane (ILM) Peeling

In a large multicenter analysis (370 eyes with PVR-C RRD), ILM peeling[1]:

- significantly improved single-surgery anatomic success compared with no peeling at 3 months (86.6% vs 73.2%) and 6 months (75.2% vs 65.3%);
- raised the retina-attached-under-fluid rate at the final follow-up visit (84.7% vs 75.6%);

KEY TAKEAWAYS

- For surgeons managing proliferative vitreoretinopathy (PVR) following rhegmatogenous retinal detachment (RRD) repair, the challenge is not simply to reattach the retina, but to protect the macula at every step.
- Internal limiting membrane (ILM) peeling has been shown to significantly improve single-surgery anatomic success compared with no ILM peeling and reduce the need for persistent silicone oil as well as the rate of secondary epiretinal membrane surgery.
- Heavy silicone oil is a useful adjunct for inferior PVR-RRD, as it provides a superior tamponade to the inferior retina versus standard silicone oil and negates the need for strict postoperative posturing.

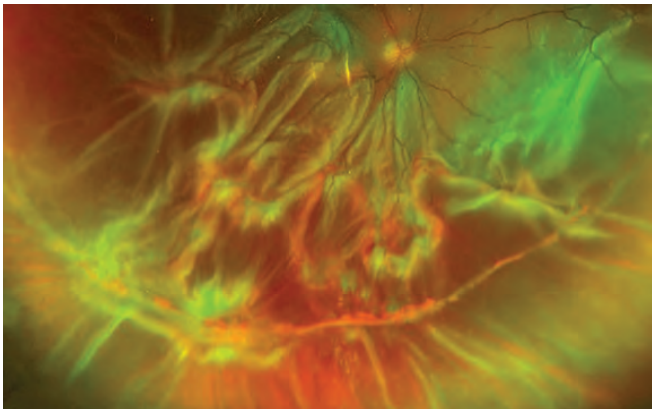

Figure 1. Recurrent RD secondary to PVR.

- reduced the need for persistent silicone oil; and
- halved the rate of secondary ERM surgery (8.9% vs 17.8%).[1]

In addition, extended ILM peeling beyond the vascular arcades was independently associated with better final visual acuity and with reattachment without oil tamponade.[1] The rationale for these results is both mechanical and biological. The ILM is the scaffold on which proliferative membranes grow; removing it denies recurrent PVR its substrate.[1,9] Peeling also confirms complete removal of overlying preretinal tissue and disconnects peripheral traction from the posterior pole.[1,10]

Practical Tips

- Stain with brilliant blue G or indocyanine green.
- Peeling under perfluorocarbon liquid (PFCL) is a good option when the retina is mobile; approximately 60% of ILM peels in the multicenter cohort used PFCL for counter-traction and improved visualization of the peeled edge.[1]
- Extend peeling as close as possible to any retinectomy margin (Figure 2), as that edge is the most common site of PVR proliferation and stretched breaks.[1]

Redetachments in eyes without ILM peeling frequently involve posterior breaks, including macular holes from tangential contraction.[1] Broad ILM peeling reduces this risk by eliminating the posterior scaffold. When a fold is identified intraoperatively, PFCL-assisted flattening, meticulous removal of the posterior hyaloid and epiretinal tissue, and ILM peeling across the fold minimize persistent distortion.

Subretinal PVR

Subretinal bands are part of the PVR-C spectrum and contribute to posterior tractional tethering.[11] They should be removed only when they are clearly preventing reattachment, while small, non-contracting strands can be left alone if the retina flattens. When extensive, a nonmacular retinotomy is preferable to risking direct foveal manipulation.

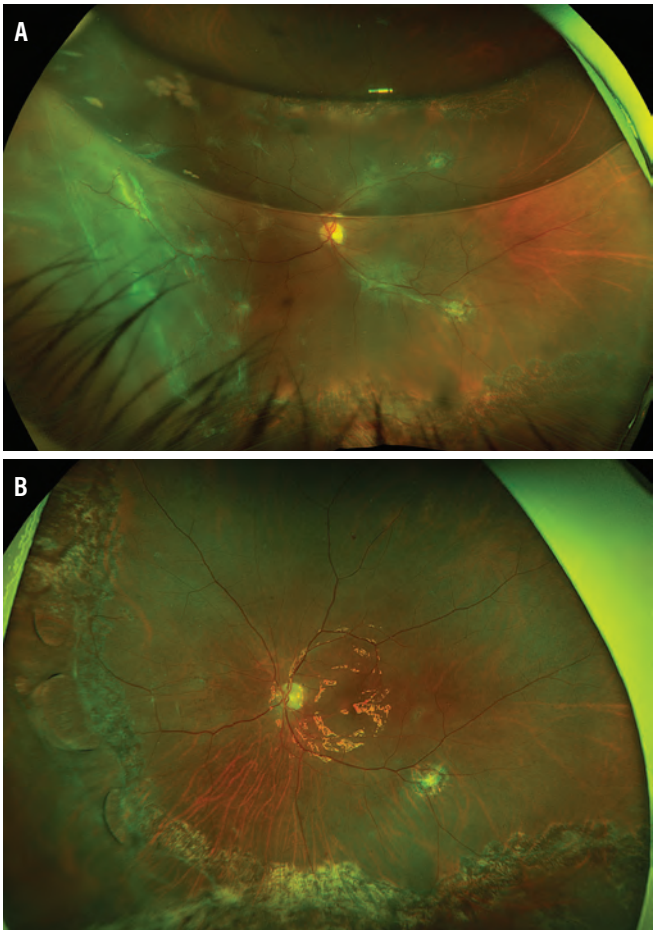

Figure 2. Preoperative fundus photography shows PVR redetachment under gas tamponade (A). Postoperatively, the retina is attached following ILM peeling, retinectomy, and silicone oil tamponade (B).

CHOOSING THE RIGHT TAMPONADE

Tamponade with silicone oil or a long-acting gas (eg, C_3F_8) remains the standard approach for managing PVR. The Silicone Study demonstrated broadly comparable anatomic outcomes between the two types of tamponades for PVR-C RRD cases, while shorter-acting SF_6 has consistently been associated with higher redetachment risk.[12,13]

Silicone oil remains the most common tamponade for PVR-C but is not benign to the macula. It can induce ME through both macrophage-driven inflammation and mechanical traction at the oil-retina interface.[14] Moreover, longer oil duration correlates with worse visual outcomes.[2,15] To facilitate earlier silicone oil removal, peel the ILM up to the retinectomy margin to reduce PVR proliferation and stretched breaks, thus protecting the macula.[1]

Heavy silicone oil is also a useful adjunct for inferior PVR-RRD, as it provides a superior tamponade to the inferior retina versus standard silicone oil and negates the need for strict posture.[16] It should also be removed early (approximately 8 weeks postoperatively) and requires close

monitoring for IOP and lens-related complications in the postoperative period.[17]

Gas tamponade should be considered in cases with a low risk of reproliferation, no active inflammation, and in which membranes have been fully removed.

MANAGEMENT OF MACULAR CONSEQUENCES AND EDEMA

Postoperative increase in ERM and cystoid ME (CME), along with early retinal layer disruptions, are important predictors of long-term visual outcomes.

Disrupted ellipsoid zone and external limiting membrane can be associated with poorer visual outcomes, supporting a hypothesis that external limiting membrane disruption may represent a shift from a protective to a detrimental glial response.[15,18,19]

Postoperative CME should be approached with a stepwise, inflammation-focused strategy. Topical nonsteroidal antiinflammatory drugs or steroids alone or in combination remain first-line therapies.[4]

For recalcitrant or chronic ME, an intravitreal dexamethasone implant (Ozurdex, Abbvie) is an option; in a randomized trial of PVR-C, a dexamethasone implant reduced 6-month CME incidence versus placebo (42.7% vs. 67.2%).[19]

However, ME recurrence is common, and most eyes require repeat implantation. Early intervention (within 4 months of ME diagnosis) has been found to reduce the total number of injections needed.[4,20] IOP elevation and cataract progression are the main risks and must be monitored.[4] ERM formation is strongly linked to persistent ME, and removal is likely to improve visual outcomes.

IMPROVE OUTCOMES WITH PVR

The trends in PVR surgery are clear: more complete mechanical removal of inflammatory scaffolds, earlier antiinflammatory pharmacotherapy, and shorter silicone oil duration. As we move forward, revision of the current classification of PVR is necessary to standardize care, provide a decision-making guide, identify high-risk cases, and improve outcomes. Large, randomized clinical trials are required to assess the effectiveness of adjunctive treatment options in combination with surgery for the management of PVR. ■

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CSCR SECONDARY TO SINUS SURGERY


Be aware of this potential complication after functional endoscopic sinus surgery.

BY AMOL GANVIR, MBBS, DO, DNB (OPHTH), AND CHEKITAAN SINGH, MBBS, DNB, FMRF

Central serous chorioretinopathy (CSCR) is a pachychoroid spectrum of disease characterized by localized serous detachments of the neurosensory retina due to increased choroidal vessel permeability.[1] The condition typically affects middle-aged men; the annual incidence rate of CSCR in men is one per 10,000. Although the pathophysiology of CSCR is unclear, it is associated with stress, elevated corticosteroid levels, and a hyperactive sympathetic nervous system.[2] There is a hypothetical framework of venous overload choroidopathy, which explains a new concept in CSCR: Choroidal venous overload results in remodeling and intervortex venous anastomoses.[3]

CSCR IN A YOUNGER PATIENT

A 27-year-old man presented to our ophthalmology clinic with distorted vision in his right eye. He reported no history of diabetes, hypertension, or cardiac disease, nor any history of drug allergy, smoking, alcohol, antipsychotic medication, sleep disorders, chronic dyspepsia, stress, or steroid intake.

The patient informed us that he had undergone functional endoscopic sinus surgery (FESS) 1 week prior for nasal polyposis and chronic pansinusitis. His surgical records indicated the proper steps, including bilateral nasal polypectomy, maxillary antrostomy, uncinectomy, and anterior ethmoidectomy under general anesthesia.

Six days after his sinus surgery, he developed sudden distortion of vision and a black spot in the central visual field of his right eye. His VA was 20/30 OU. Slit-lamp examination revealed a normal anterior segment in each eye. The retinal examination showed a large serous detachment in his right macula without hemorrhage and extrafoveal retinal pigment epithelium (RPE) changes in his left eye (Figure 1). OCT of his right eye showed a subfoveal neurosensory retinal detachment; the left eye showed a small area of pigment epithelium detachment nasal to the fovea (Figure 2). Based on these findings, he was diagnosed with CSCR of his right eye.

His symptoms began to resolve gradually with observation. Full recovery of vision and resolution of symptoms were achieved 1 month after surgery.

PEARLS FOR POSTOPERATIVE CSCR

Theories explaining the pathophysiology of CSCR suggest that corticosteroids and epinephrine can potentiate choroidal vasoconstriction and relative ischemia, which can then lead to hyperpermeability in the choroidal vasculature as a result of changes in oncotic pressure and disruption of the RPE pump.[4]

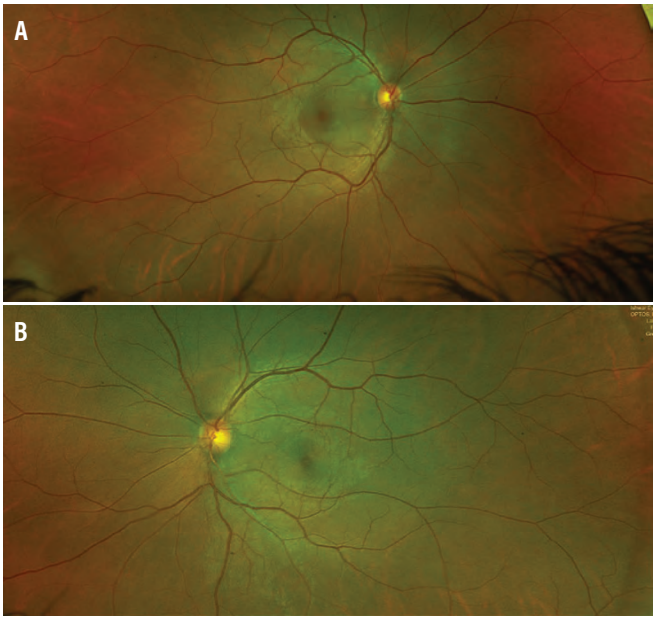

Figure 1. Fundus imaging of the right eye (A) showed serous macular detachment, while the left eye (B) showed a few RPE alterations.

To our knowledge, there have been no prior reports of this complication following FESS. In our case, there was no use of corticosteroids during the procedure or postoperatively. However, the surgeon used a 1:1000 epinephrine-soaked cotton swab intraoperatively during nasal packing.

CSCR may develop after FESS due to psychological stress associated with pain or postoperative difficulty; epinephrine used during nasal packing (ie, retrograde flow of epinephrine into the sinus, traveling backward through systemic valveless venous or arterial circulation, and entering the retinal artery); or sudden onset of orbital hematoma from anterior ethmoidectomy.

In our case, psychological stress or epinephrine use during the procedure could be possible causes for the development of CSCR. CSCR has also been reported to occur after rhinoplasty, orbital blowout fracture, or lacrimal surgery.

If the disease does not spontaneously resolve after

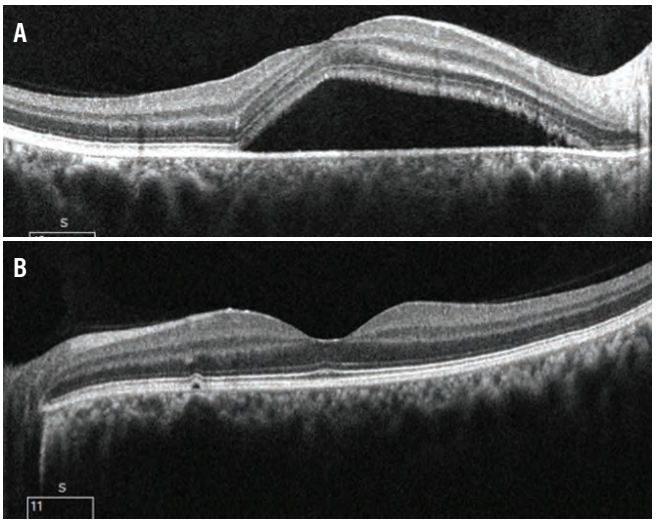

Figure 2. OCT of the right eye (A) showed serous subfoveal neurosensory detachment, while the left eye (B) showed a small pigment epithelium detachment nasal to the fovea.

4 to 6 months, treatment options include focal laser photocoagulation and photodynamic therapy.[5] Ear, nose, and throat surgeons should be aware that CSCR can occur as a result of FESS or epinephrine use during nasal packing. If CSCR is suspected in a patient after FESS, corticosteroids should be discontinued.

AWARNESS OF FESS

In this case, intraoperative use of topical epinephrine during nasal packing may have increased the risk of CSCR development. Topical spray containing another vasoconstrictor can be used before nasal packing. To prevent this potentially serious complication, efforts should also be made to alleviate any psychological stress. ■

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(Continued from page 48)
endophthalmitis, the initial conversation is necessarily urgent and broad. However, once microbiologic information becomes available, pathogen type may help frame prognosis more accurately. In some eyes, the clinical concern is not simply slower recovery or incomplete visual improvement but may include a higher likelihood of repeat intervention, phthisis, or enucleation.

Many retina specialists have felt for years that certain organisms, especially noncommensal pathogens, such as *Streptococcus* and *Enterococcus*, tend to produce a more fulminant and aggressive course.

If pathogen virulence is linked to outcome, then future advances in rapid identification may help clinicians determine earlier which eyes may require more aggressive monitoring, additional intervention, or more guarded counseling.

LOOKING AHEAD

The central conclusion from this study is straightforward: Pathogen type appears to matter in post-procedure endophthalmitis. More virulent nonsurface commensal organisms were associated with worse visual outcomes, more third interventions, higher rates of phthisis, and greater risk of enucleation or evisceration. Our findings give us stronger evidence that the organism itself is an important driver of what happens next, and that future efforts to identify the pathogen earlier may have real clinical value. ■

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CANCER-ASSOCIATED RETINOPATHY WITH THYMIC CARCINOMA

A multimodal approach to treatment led to meaningful visual improvement despite poor prognostic signs on OCT.

BY MENA KOZMAN, MD; AARON SHI, MD; NYAARI KOTHIYA; SAMI DAHR, MD; AND RABIA KARANI, MD, MPH

Cancer-associated retinopathy (CAR) is a rare paraneoplastic autoimmune retinopathy characterized by progressive vision loss. It develops from the cross-reactivity of tumor antigens and retinal proteins, leading to photoreceptor and bipolar cell damage.[1-3] First described in association with small-cell lung cancer, CAR has since been reported with gynecologic, hematologic, breast, prostate, and hepatocellular cancers.[4] The diagnosis remains challenging, however, as many patients exhibit minimal fundoscopic abnormalities; thus, the combination of imaging and antibody testing can aid in accurate diagnosis. There is no standardized treatment strategy for CAR due to its rarity and heterogeneous presentation.

Here, we present a case of CAR in thymic carcinoma treated with a multimodal approach, highlighting the value of aggressive intervention despite profound vision loss.

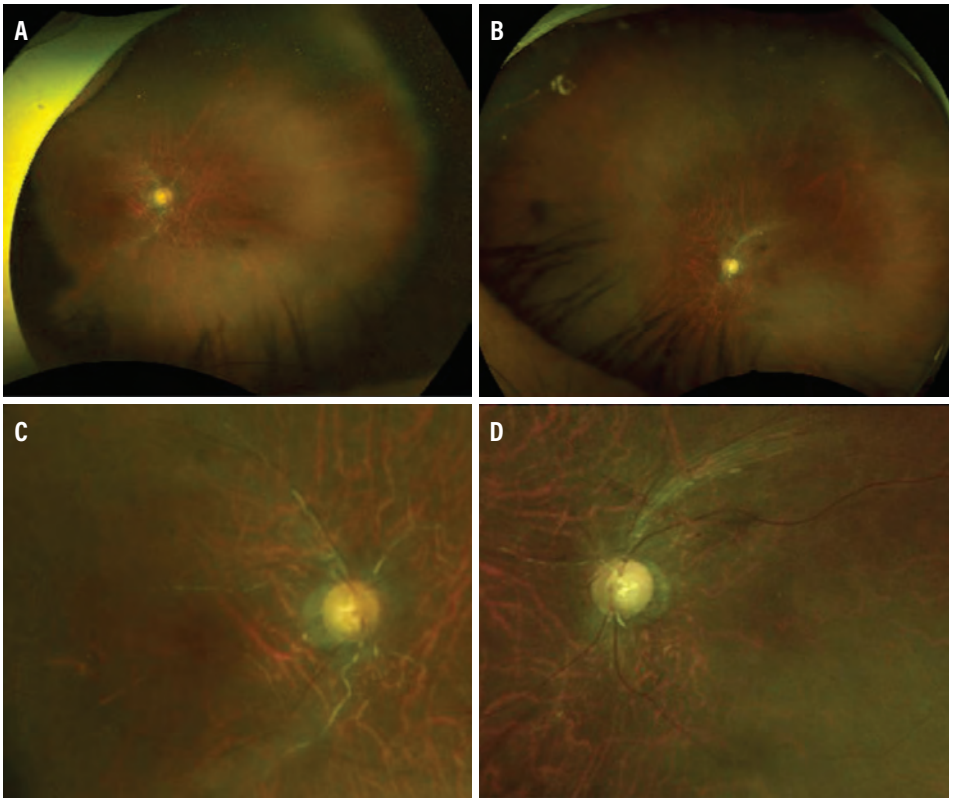

Figure 1. Fundus photography of the right (A) and left (B) eye revealed attenuated, sclerotic ghost vessels. The optic disc of the right (C) and left (D) eye demonstrated temporal pallor.

CASE REPORT

A 54-year-old man presented to an outside facility with rapidly progressive, painless, bilateral vision loss over 1 week. His VA was hand motion OU and IOP was 8 mm Hg OU with no relative afferent pupillary defect. The anterior segment examination was unremarkable, while the fundus examination revealed attenuated, sclerotic ghost vessels and temporal optic disc pallor in each eye. Neuroimaging

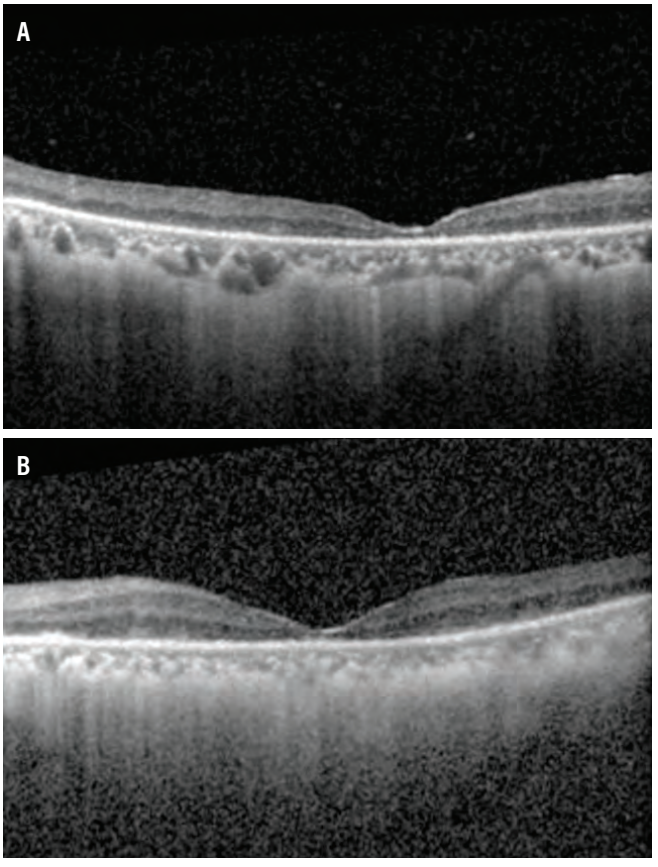

Figure 2. OCT of the right (A) and left (B) eye demonstrated significant bilateral EZ loss, severe photoreceptor and outer retinal atrophy, and diffuse retinal thinning.

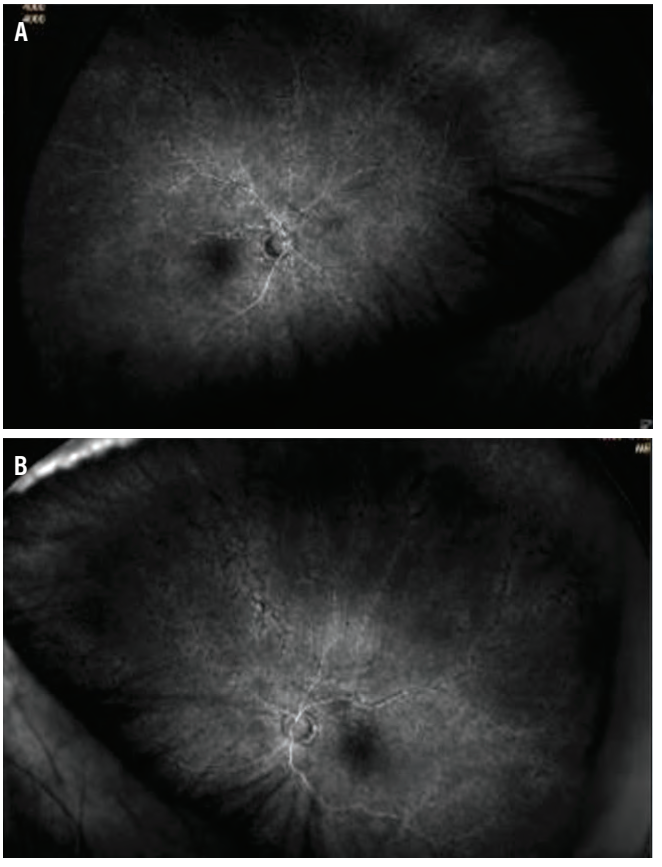

Figure 3. Fluorescein angiography of the right (A) and left (B) eye revealed late phase macular staining and focal filling defects in the superior and inferior arcades.

revealed an acute posterior left temporal white matter infarct, which did not adequately explain his vision loss. Testing for syphilis, tuberculosis, Lyme disease, and Bartonella were each negative. Angiotensin-converting enzyme, lysozyme, homocysteine, methylmalonic acid, vitamin B_9 and B_{12}, lupus anticoagulant, beta-2-glycoprotein, and cardiolipin were also unremarkable.

The patient was treated empirically with high-dose intravenous methylprednisolone (IVMP) 1 g daily for 5 days and underwent paraneoplastic panel testing as well as CT imaging of the chest, abdomen, and pelvis. Imaging revealed a large anterior mediastinal mass measuring 8.2 x 8.5 x 8 cm with areas of necrosis adjacent to enlarged lymph nodes; biopsy confirmed thymic carcinoma. The patient completed 5 days of IVMP with subjective improvement of vision but was lost to follow-up due to insurance issues.

He presented to our clinic 2 months later with decreased VA to light perception OU. Anterior segment and fundus examination remained unchanged (Figure 1). OCT showed significant ellipsoid zone (EZ) loss, severe photoreceptor and outer retinal atrophy, and diffuse retinal thinning in each eye (Figure 2). Fundus autofluorescence showed punctate areas of hypoautofluorescence in the macula and patchy hyperautofluorescent changes along the retinal vessels in each eye. Fluorescein angiography showed late punctate macular staining and focal filling defects surrounding vessels in each eye (Figure 3).

Given a strong suspicion of CAR and the decline in vision, a CAR panel was obtained, which was positive for recoverin, Rab6, aldolase, and enolase. He was reinitiated on IVMP 1 g daily for 5 days, followed by intravenous immunoglobulin (IVIG) 400 mg/kg/day for 5 days and sub-Tenon triamcinolone injection 40 mg with no changes in vision. Nine weeks after vision loss (10 days after presentation), systemic chemotherapy with seven cycles of paclitaxel and carboplatin was initiated, as the tumor was deemed unresectable due to proximity and possible invasion into the right atrium. Four months after vision loss, his VA remained light perception OU. A repeat sub-Tenon triamcinolone 40 mg injection was administered, followed by three sessions of plasmapheresis and four cycles of rituximab.

Five months after vision loss, the patient's VA improved to hand motion OU. An intravitreal dexamethasone implant 0.7 mg (Ozurdex, Abbvie) was placed into each eye. Eight months after vision loss, he continued to report subjective improvement; his VA was counting fingers at

7 ft eccentrically. Repeat intravitreal dexamethasone implant was placed into each eye, and he was scheduled for external beam radiation therapy as further cancer management.

HOW LATE IS TOO LATE FOR MEANINGFUL VISUAL RECOVERY?

To the best of our knowledge, this is the first reported case of thymic carcinoma with CAR. Among the relevant autoantibodies, the anti-recoverin antibody, which was positive in this patient, is most commonly implicated in CAR and results in the most severe manifestation of the disease, as both rods and cones are targeted.[5] The association with thymic carcinoma in this case broadens the spectrum of malignancies linked to CAR.

This case is also notable for the profound functional and physiologic damage to the patient's vision at the time treatment was initiated. Early treatment is considered critical in autoimmune retinopathies, given the potential irreversible damage caused by photoreceptor apoptosis. However, our methodology of treating CAR so far is largely based on case reports, as it is difficult to conduct large-scale studies with such a rare entity. Moreover, treatment of the cancer itself does not necessarily improve the vision loss associated with CAR.[6-11] The patient in this case had extensive EZ loss and outer retinal atrophy on OCT, considered to be poor prognostic indicators reflecting significant irreversible photoreceptor damage,[3] and experienced a 2-month delay between initial vision loss and therapy. Nevertheless, he received high-dose systemic corticosteroids, IVIG, sub-Tenon corticosteroids, plasmapheresis, rituximab, intravitreal dexamethasone implants, and systemic chemotherapy. All these treatments have been used in case reports of CAR, but to our knowledge, no reported cases describe the use of nearly all available therapeutic interventions in a single patient.[6-11] Despite the absence of a standardized treatment algorithm for CAR, this aggressive, multimodal approach was associated with functional visual improvement in this case.

It is worth noting that patients such as ours tend to experience limited, if any, meaningful recovery; nevertheless, the improvement in VA from light perception to counting fingers at 7 ft highlights a potential dissociation between structural damage and functional capacity. It is possible that OCT findings alone may not fully predict functional recovery even when imaging appears severe, suggesting autoimmune retinopathies may exhibit partial reversibility under aggressive immunomodulation and supporting the potential benefits of offering aggressive therapy, even in advanced cases with delayed presentation.

PEDAL TO THE METAL

In most cases of CAR, vision loss occurs after a malignancy diagnosis. However, in a small subset of patients, ocular findings are the first manifestation. Therefore, prompt evaluation for occult malignancy should be considered in similar cases with rapidly progressive bilateral vision loss associated with EZ and outer retinal atrophy and minimal to no intraocular inflammation.

Due to the rarity and heterogeneity in presentation of CAR, there is currently no standardized treatment strategy. In our case, even with profound vision loss and poor prognostic indicators on multimodal imaging, an aggressive treatment approach with intraocular steroids and immunomodulatory therapy lead to meaningful functional recovery. ■

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A PATCH WITH POTENTIAL

An amniotic membrane transplant was used to treat a patient with chronic, complex macular hole.

BY OSAMA M. AHMED, MD, AND MOHSIN H. ALI, MD

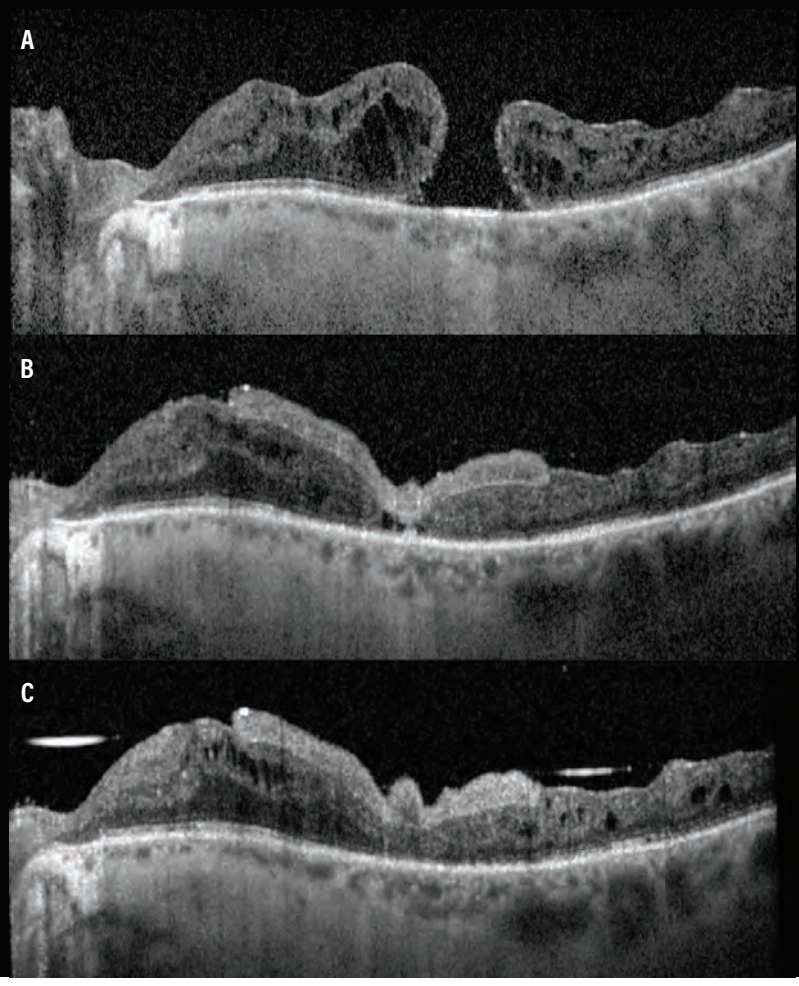

Figure 1. Preoperative OCT imaging shows the MH at presentation (A). Postoperative month 1 shows preretinal AMT without full apposition of the MH edges (B). OCT imaging at postoperative month 2 shows improvement and closure of the MH (C).

A 69-year-old man presented to the retina clinic for consultation of a chronic, refractory macular hole (MH). He had a history of nonproliferative diabetic retinopathy and a rhegmatogenous retinal detachment repaired more than 10 years ago with a scleral buckle, pars plana vitrectomy, and silicone oil tamponade. Despite successful reattachment of the retina, he developed a chronic MH. He later underwent silicone oil removal, and the chronic MH enlarged. His VA was 20/400 in the affected eye.

OCT imaging showed a full-thickness MH, moth-eaten appearance of the MH edges with loss of the ellipsoid and interdigitation zones (indicative of chronicity), cystoid spaces, inner retinal dimpling (from prior membrane peeling), and patchy attenuation of the retinal nerve fiber layer (Figure 1A).

The patient underwent 25-gauge pars plana vitrectomy, brilliant blue-assisted epiretinal membrane and internal limiting membrane peeling, MH massage, and a 4 mm preretinal amniotic membrane transplant (AMT) under perfluorocarbon liquid (PFCL), which was then directly exchanged for 1,000 cS silicone oil (Figure 2).

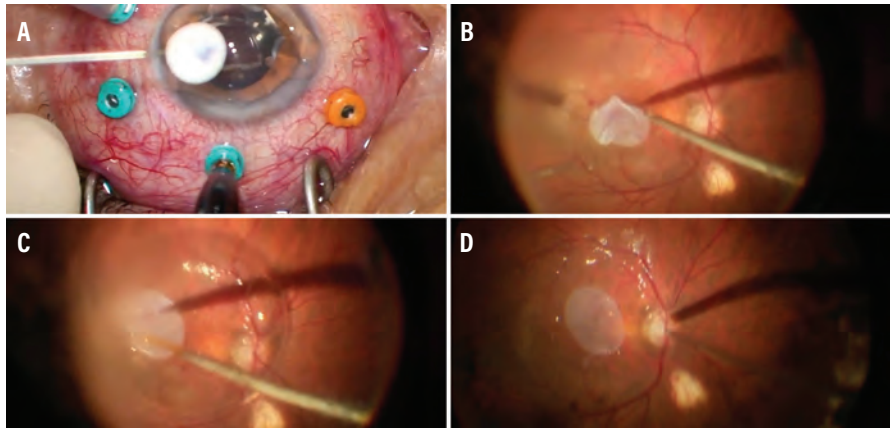

Figure 2. Intraoperative imaging shows a cryopreserved human AMT prepared using a 4 mm circular punch with a gentian violet "F" stamp marking the epithelial side, use of chandelier illumination for bimanual manipulation, and use of 23-gauge cannula for easier insertion of the AMT (A). We unfurled the AMT on the macular surface using a bimanual technique with a Finesse flex loop (Alcon) and internal limiting membrane forceps (B). We then used PFCL to stabilize the AMT (C), followed by direct PFCL-silicone oil exchange (D).

OCT imaging at postoperative months 1 and 2 demonstrated MH closure with a well-positioned preretinal AMT

AMTS MAY BE EFFECTIVE IN REFRACTORY MHS (CLOSURE RATES 85-100%), MYOPIC MH ASSOCIATED WITH POSTERIOR STAPHYLOMA (86-92%), AND COMPLEX RETINAL DETACHMENTS WITH PROLIFERATIVE VITREORETINOPATHY (76-92%).

(Figure 1B and C). The patient's VA improved to 20/200 in the affected eye by postoperative month 7, and he reported a subjective improvement in vision and reduction in central scotoma size. The silicone oil and preretinal amniotic membrane were left in place.

AMT TO THE RESCUE

AMTs may be effective for refractory MHs (closure rates 85-100%), myopic MH associated with posterior staphyloma (86-92%), and complex retinal detachments with proliferative vitreoretinopathy (76-92%).[1] Visual improvement was reported in 81% of cases in a review of 603 eyes; however, the extent of improvement is highly variable.[2] The most common complication is graft dislocation (3.6%).[2] Further large-scale prospective studies are needed to better compare AMT with established techniques for MH repair. ■

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2. Solish D, Gao A, Cheffi N, Mandelcorn E, Felfeli T. Human amniotic membrane (hAM) in macular hole repair: a scoping review [published online ahead of print May 6, 2026]. *Retina*. doi:10.1097/IAE.0000000000004877

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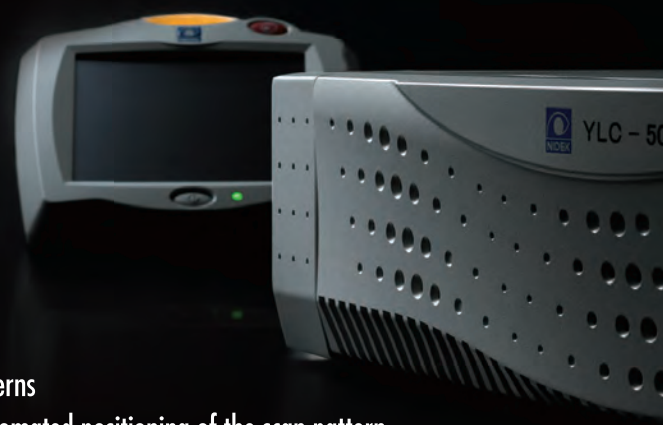

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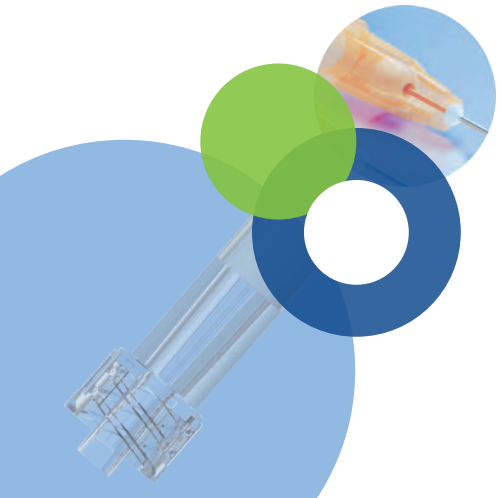

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