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Retina Today

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20TH ANNIVERSARY

SPECIAL EDITION:

AI IN THE RETINA CLINIC

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eyetube

UNLOCKING CLINICAL TRIAL ENROLLMENT WITH AI

A GUIDE TO IMPLEMENTING LLMS IN RETINA

WHAT AVIATION CAN TEACH US ABOUT AI

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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

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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.

CONTRAINDICATIONS

ENCELTO is contraindicated in patients with:

- Active or suspected ocular or periocular infections.
- Known hypersensitivity to Endothelial Serum Free Media (Endo-SFM)

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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

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implant, for intravitreal use

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CAUTION: MAY HALLUCINATE WHEN PROMPTED



There has been plenty of negative press for AI these days. After all, Anthropic's employees just shared a warning that AI could lead to human extinction within the next decade.[1] As is the case with most AI conversations, the current risk of danger is low, but it has the potential to get out of hand quickly.

But sometimes—when implemented carefully—AI really can impress us. For example, researchers at Duke created a deep-learning system that used OCT images to reliably predict when anti-VEGF treatment should be initiated for patients converting to wet AMD, while also measuring changes in outer retinal thickness.[2]

Most of us are already dabbling in AI for certain tasks, such as summarizing research, drafting emails, and finding good restaurants in New Orleans during AAO. Yet, we must remember that HIPAA reigns supreme, and using AI with abandon could put patient privacy and safety at risk. Researchers at Stanford and Harvard collaborated on the NOHARM trial, finding that recommendations from large-language models had the potential for severe harm in up to 22.2% of cases.[3] There remains a gap between our interest in using AI to our advantage, and our ability to do so safely.

This issue is designed to start to fill that gap and help us better understand the potential of AI in our practices—and the pitfalls to avoid. For one thing, there are growing concerns that relying too much on AI in the clinic could be eroding clinical decision-making skills.[4] In one of our featured articles, Andreas Pollreisz, MD, and colleagues address this issue (known as *deskilling* and *never skilling*) by drawing parallels between aviation and the field of retina. He notes that, just as flight automation still requires skilled pilots, automation in retina can augment, but not replace, the skill we bring to our profession.

In keeping with the pilot theme, Daniel Ting, MD, PhD, and Stanley Poh, FRCOphth, explore the future of AI in the OR as a digital copilot. While still theoretical, it may one day enhance surgical planning, intraoperative guidance, training, documentation, and postoperative evaluation.

As for clinical efficiencies, Fares Antaki, MDCM, introduces chatbots—what they are, what they can do—while Fatima Kalabi, MD, and her colleagues show us *how*, exactly, we can prompt them safely. Digging a little deeper, Prashant D. Tailor, MD, and his team summarize their recent research on AI's utility for pre-charting, note-taking, and referral letters. For example, they found that 85% of non-ophthalmology clinicians preferred referral notes that included an AI-generated plain-language summary.

One of the most promising applications of AI is for clinical trial recruitment and data analysis. Sunil Gupta, MD, and Joshua Koo, MS, BS, share their research on an investigational AI model that can automatically flag eligible candidates, potentially improving enrollment rates.

AI has so much potential, and it's already making our lives a little easier in many ways. If we are careful, AI can streamline much of our workflow, too. We just have to implement it with caution. ■

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

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AI in DME: From Promise to Clinical Practice
By Scott Song, BA, and T. Y. Alvin Liu, MD

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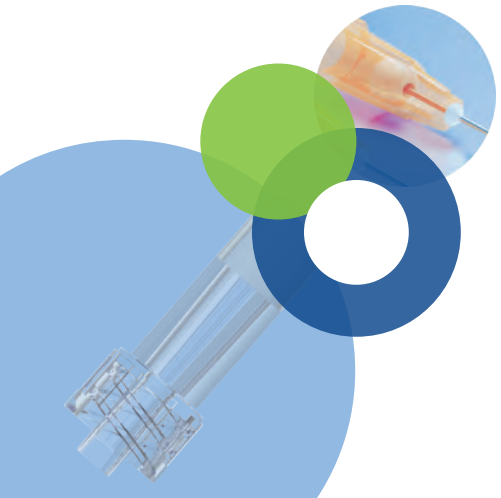
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RETINA MEETINGS: 2027

Ready to present a case, boost your continuing education, or network with colleagues? These conferences are the place to be next year!

JANUARY 2027

51st Annual Atlantic Coast Retina Club (ACRC) and 27th Macula Conference
January 7 – 9
Boston

30th Annual American Uveitis Society Winter Symposium
January 16 – 18
Park City, UT

27th Annual Retina Fellows Forum
January 29 – 30
Chicago

Moorfields Advanced Vitreoretinal Congress (MAVERICK)
January 29 – 30
Westminster, London

FEBRUARY 2027

55th Annual Aspen Retinal Detachment Society Meeting
February 27 – March 3
Snowmass, CO

Angiogenesis, Exudation, and Degeneration
February 6 and 13
Virtual

MARCH 2027

3rd Retina Fellows Business Academy
March 6
Virtual

Business of Retina Meeting
March 12 – 14
Arlington, TX

13th Annual Duke Fellows Advanced Vitreous Surgery (AVS) Course & 24th Duke AVS Course
March 18 – 20
Durham, NC

APRIL 2027

15th Annual VBS Meeting
April 1 – 3
Miami

13th Annual Pacific Retina Club & 14th Annual International Retinal Imaging Symposium
April 15 – 17
Los Angeles

MAY 2027

ARVO
May 2 – 6
San Diego

Retina World Congress
May 13 – 16
Fort Lauderdale, FL

JUNE 2027

50th Anniversary Macula Society Meeting
June 9 – 12
Cannes, France

Clinical Trials at the Summit
June 25 – 26
Las Vegas

JULY 2027

17th Annual Mass Eye and Ear Vitrectomy Course
July 9 – 10
Boston

ASRS
July 28 – 31
San Diego

SEPTEMBER 2027

Euretina
September 16 – 19
Copenhagen, Denmark

Advances in Pediatric Retina
September 18 – 20
Durham, NC

OCTOBER 2027

Retina Society
October 20 – 23
Boston

NOVEMBER 2027

AAO
November 12 – 15
Las Vegas

LOOKING AHEAD: 2028

ARVO – Toronto, Canada
ASRS – Boston
AAO – Chicago

To find more information about these meetings, visit our online conference calendar at **retinatoday.com/calendar/2027.**

RT NEWS

OCTOBER 2026

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FDA ACCEPTS BLA FOR OPTOGENETIC THERAPY FOR RP

Nanoscope Therapeutics' biologics license application (BLA) for sonpiretigene isteparvovec (MCO-010; Mogenry), an investigational gene-agnostic therapy designed to restore vision in patients with retinitis pigmentosa (RP), was accepted by the FDA. The FDA has issued a Prescription Drug User Fee Act date in the first half of 2027.[1]

MCO-010 is designed to improve vision using optogenetics rather than targeting a specific disease-causing mutation. This approach is intended for the treatment of patients who have experienced photoreceptor loss from retinal degeneration, potentially broadening the population eligible for treatment compared with mutation-specific gene therapies, as patients would not need to have a particular genetic variant to receive effective care. The therapy is being developed as a one-time, in-office intravitreal treatment.[1]

"Mogenry does not require genetic testing or administration in a surgical suite, which could enable broad adoption by community retina practices," said Allen C. Ho, MD, Professor of Ophthalmology at Thomas Jefferson University, Director of Retina Research at Wills Eye Hospital, and Chief Medical Advisor for Nanoscope Therapeutics.[1]

The BLA for MCO-010 is supported by safety and efficacy data from a phase 1/2a study (NCT04919473) and the phase 2b/3 RESTORE trial (NCT04945772). According to Nanoscope, the drug met primary and key secondary endpoints in the RESTORE trial, demonstrating improved visual acuity at weeks 52 and 76. It was also well tolerated, with no serious treatment-related adverse events.[1]

1. Nanoscope Therapeutics announces US Food and Drug Administration acceptance of biologics license application for Mogenry for the treatment of retinitis pigmentosa with severe vision loss [press release]. Nanoscope Therapeutics. September 9, 2026. Accessed September 14, 2026. tinyurl.com/mt6vp5aj

FURTHER READING

Optogenetics: Bringing Light to the Blind

By Vinit B. Mahajan, MD, PhD

READ NOW

ROBOTIC-ASSISTED SUBRETINAL INJECTION PERFORMED ACROSS 4,000 KM

A study published in *JAMA Ophthalmology* sought to assess the feasibility and safety of performing an ultra–long-distance robotic-assisted subretinal injection for the treatment of a patient with submacular hemorrhage (SMH).[1]

The proof-of-concept study enrolled one patient with SMH and was conducted between the Zhongshan Ophthalmic Center in Guangzhou, China (the remote control center), and Xinjiang Production and Construction Corps Hospital in Urumqi, China (the patient site)—approximately 4,000 km apart. Pars plana vitrectomy was first performed manually onsite, and while the patient was under general anesthesia, a retinal surgeon remotely teleoperated an ophthalmic robotic system to perform a subretinal injection of recombinant tissue plasminogen activator.[1]

The robotic-assisted procedure was completed without intraoperative complications, with 7 minutes of robotic teleoperation during a total surgical time of 46 minutes. A total of 0.056 mL of recombinant tissue plasminogen activator was delivered remotely. The mean (range) network latency was 77.9 milliseconds (71-90 milliseconds). No serious adverse events occurred during 3 months of follow-up, and OCT demonstrated a progressive reduction of the SMH, with complete absorption by postoperative day 26. Preoperative BCVA measured 1 day before surgery was 20/80; 3 months postoperatively, the patient's vision remained stable at 20/80.[1]

This single-case report provides proof-of-concept evidence that telesurgical robotic systems may have the potential to safely expand access to specialized retinal procedures in geographically remote regions, the authors concluded in their paper.[1]

1. Xu A, Yang B, Liu B, et al. Ultra-long-distance robotic-assisted subretinal injection for submacular hemorrhage [published online ahead of print August 20, 2026]. *Retina*. doi.org/10.1001/jamaophthalmol.2026.3303

POVIDONE-IODINE IRRIGATION ASSOCIATED WITH BETTER VISUAL OUTCOMES IN INFECTIOUS ENDOPHTHALMITIS

A study published in *Retina* found that the use of adjunctive 0.025% povidone-iodine irrigation during pars plana vitrectomy improved ocular morbidity in infectious endophthalmitis compared with standard irrigation.[1]

The multicenter, retrospective, comparative cohort study was conducted across four tertiary referral centers. Sixty-three eyes of 63 patients with presumed infectious endophthalmitis requiring vitrectomy were included. The povidone-iodine group (n = 32) received 0.025% povidone-iodine in a balanced salt solution, while the control group (n = 31) received standard irrigation. The two groups were similar in age, presenting visual acuity (20/2,890 vs 20/4,000), and culture positivity (13/32 [40.6%] vs 13/31 [41.9%]).[1]

The povidone-iodine group experienced significantly better median visual acuity at 3 months (20/138 vs 20/3,000; $P = .017$) and 6 months (20/60 vs 20/400; $P = .010$). In addition, 96.7% of the patients in the povidone-iodine group experienced improved vision compared with 48.3% of the control group at 6 months ($P < .001$). Reoperation rates were statistically similar, although slightly increased in the povidone-iodine group (28.1% vs 16.1%; $P = .365$). No ocular toxicity was attributed to povidone-iodine.[1]

The authors concluded that adjunctive 0.025% povidone-iodine irrigation during vitrectomy was associated with significantly improved visual outcomes without observed ocular toxicity. This simple, cost-effective intervention may thus offer benefits in endophthalmitis management.[1]

1. Yuan M, Pally K, Do B, Ebert JJ, Rahimy E, Adam MK. Adjunct 0.025% povidone-iodine irrigation at time of vitrectomy for management of infectious endophthalmitis: a multicenter single-intervention study [published online ahead of print August 31, 2026]. *Retina*. doi.org/10.1097/IAE.0000000000005006

Eyewire+ Pharma Update

- **Opus Genetics** reports positive phase 1/2 data for OPGx-BEST1 in patients with *BEST1*-related disease, such as Best vitelliform macular dystrophy and autosomal recessive bestrophinopathy. The company aligned with the FDA on a potential pivotal endpoint and expects patient dosing in the phase 3 trial to begin in 2027.
- **Tarsus Pharmaceuticals** completed its acquisition of Alkeus Pharmaceuticals, adding worldwide rights to the investigational gildeuretinol acetate (ALK-001) to its ophthalmic pipeline.
- **Ocugen** has dosed the first patient in a 237-patient global phase 3 trial of OCU410—a *RORA*-based modifier gene therapy—for geographic atrophy secondary to dry AMD.
- **Alcon** recently launched the Unity M surgical microscope, which combines an expanded red reflex zone, color-tunable illumination, and an ophthalmology-optimized depth of field to support visualization during surgery.
- **Ocular Therapeutix** completed its pre-New Drug Application (NDA) meeting with the FDA for Axpaxli (OTX-TKI) in wet AMD and remains on track for a fourth-quarter 2026 NDA submission.

Want more retina news from *Eyewire+*?

HIGH INCIDENCE OF SLEEP APNEA IN PATIENTS WITH RVO

Researchers recently discovered that patients with newly diagnosed retinal vein occlusion (RVO) have a high prevalence of previously undiagnosed obstructive sleep apnea (OSA), suggesting the need for polysomnography (PSG) in patients presenting with RVO.[1]

The team conducted a single-center cohort study of 321 patients with branch (BRVO), hemi-central (HCRVO), or central RVO (CRVO), comparing a retrospective cohort of 272 patients with a prospective cohort of 49 newly diagnosed RVO patients who underwent home or laboratory-based PSG. The study's primary outcomes were PSG-confirmed OSA prevalence and comparison with past medical history (PMH)-based OSA prevalence.[1]

After excluding RVO patients with a prior diagnosis of OSA (5.15% of retrospective cohort patients and 8.16% of prospective cohort patients), they found that PSG identified undiagnosed OSA in 84.44%. Patients undergoing PSG were significantly more likely to be diagnosed with OSA than by PMH alone (85.71% vs 8.16%; risk ratio = 16.65, $P < .001$).[1]

The study authors concluded that RVO may serve as an important clinical indicator warranting routine PSG evaluation in select patients.[1] ■

1. Higgins P, Isaac B, Shmushkevich SB. High incidence of sleep apnea in patients with retinal vein occlusions [published online ahead of print September 10, 2026]. *Retina*. doi.org/10.1097/IAE.0000000000005009

ONE TO WATCH

RT Retina Today

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REGENXBIO



Douglas R. Matsunaga, MD



Dr. Matsunaga's advice: After the last decade of structured training, the "real world" career paths, opportunities, and challenges can be highly varied, and you won't read about them in a textbook. Keep up with your mentors and co-trainees and build your retina community to approach them together.

WHERE IT ALL BEGAN

I was born and raised in Los Angeles and was always interested in science and biology. I attended the University of California Berkeley for undergraduate and studied molecular cell biology. While there, I involved myself in research for cancer and a gene therapy approach to cancer immunology. While I enjoyed the science and discovery of research, I had always been drawn to more direct patient care and went on to study at the University of Southern California (USC) Keck School of Medicine.

MY PATH TO RETINA

Shortly after starting medical school, my interest in ophthalmology was piqued by specialty lunch lectures and increased by elective specialty rotations. When looking into research opportunities, I was quickly drawn to the retina for its complex biology and the rapid expansion of retinal diagnostic technologies and treatments. My research on oxidative stress in retinal pigment epithelium cells and budding OCT angiography technology further cemented my retina interests. Upon starting my residency at Wills Eye Hospital, I should have approached all the specialties with an open mind, but I was fairly set on retina from the start.

SUPPORT ALONG THE WAY

I have been incredibly lucky to have been mentored by many people. The patient guidance and support of my medical school research leaders and counselors made my journey into ophthalmology not only possible but also brighter and more promising than I had thought possible. In residency, the Wills Eye family lived up to its name, and the faculty and my resident class all shared a genuine interest and generosity toward my future. As a fellow at USC and now an attending at Retina Vitreous Associates, I am grateful for the incredible training opportunities and advice from a diverse and elite group of doctors whom I work with and learn from.

AN EXPERIENCE TO REMEMBER

In my first year out of training, I cared for a gentleman who presented with severe bilateral deteriorating vision with no clear anatomic findings or diagnosis after seeing several doctors, including retina.

After the retinal examination, I took a detailed history, during which he mentioned that he had been hospitalized earlier that year for a rare bacterial infection. We investigated further and ran some more tests, ultimately leading to a diagnosis of ethambutol optic neuropathy. He stopped the drug in conjunction with infectious disease, and over the next few months his vision fully recovered (much to everyone's relief).

His case was a reminder that, in the community, a retina specialist is often the first clinician patients turn to with mystery cases, and you must keep your skills—both retina and comprehensive—sharp! ■

Douglas R. Matsunaga, MD, is a vitreoretinal surgeon at Retina Vitreous Associates in Los Angeles and an adjunct clinical professor at the USC Keck School of Medicine. He can be reached at dmatsunaga@laretina.com.

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

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.

OCTOBER SPOTLIGHT: PROGRESS IN RETINAL LASER THERAPY

The PAttern SCAnning Laser (PASCAL, Iridex), like *Retina Today*, debuted in 2006. At the time, Julia A. Haller, MD, authored an article for us, *PASCAL Laser for Retinal Disease Treatment*, to introduce the tool, noting it was the first laser innovation in 35 years. Now, 20 years later, Dr. Haller is back to reminisce about that major update and explore what has changed since that first article.

– *Rebecca Hepp, MA, Editor-in-Chief*

RETINA TODAY (RT): WHAT WAS NEW ABOUT THE PASCAL IN 2006?

Julia A. Haller, MD: When the PAttern SCAnning Laser (PASCAL) was introduced, it represented one of the first truly meaningful advances in retinal photocoagulation in many years. Traditional argon laser treatment relied on relatively long pulse durations—typically 200 milliseconds—which produced effective retinal burns but also resulted in greater collateral thermal spread, more patient discomfort, and longer treatment sessions. PASCAL changed that paradigm by delivering multiple laser spots in rapid, precisely spaced patterns using much shorter pulse durations. The result was faster treatment, improved patient comfort, greater reproducibility, and more controlled energy delivery.

RT: HOW HAVE RETINAL LASERS CHANGED IN 2 DECADES?

Dr. Haller: Over the past 20 years, the biggest story has not been laser technology itself but rather how dramatically the role of laser has changed. In 2006, focal and grid laser photocoagulation remained the standard of care for diabetic macular edema (DME), and panretinal photocoagulation (PRP) was the cornerstone of treatment for proliferative diabetic retinopathy (PDR). Today, intravitreal anti-VEGF therapy has transformed the management of many retinal vascular diseases. For DME, retinal vein occlusions, and wet AMD, pharmacologic therapy has become the first-line treatment because it often preserves or improves vision better than conventional laser alone.

That evolution has changed how retina specialists think about laser. Rather than serving as the primary intervention for many diseases, laser is used more selectively—as an adjunctive treatment, a durable therapy to reduce treatment burden, or the preferred therapy in carefully chosen clinical situations. PRP remains highly effective for PDR, especially when long-term follow-up is uncertain. Laser retinopexy continues to be indispensable for retinal tears, where it has changed remarkably little because it has been highly successful from the beginning. In many ways, laser has matured from a broadly applied technology into a more targeted and strategic tool.

RT: WHAT NOVEL ADVANCES DO YOU THINK WOULD BE BENEFICIAL IN THE LASER SPACE?

Dr. Haller: The greatest opportunities lie in making laser delivery more intelligent and individualized using image-guided systems that integrate real-time OCT, angiography, or AI to identify the tissue that requires treatment while minimizing unnecessary retinal injury. Advances in subthreshold and selectively targeted laser technologies may continue to reduce collateral damage while preserving therapeutic efficacy. Ultimately, the ideal laser would deliver precisely the right amount of energy to exactly the right tissue at exactly the right time, tailored to each patient's unique retinal anatomy and disease activity.

The success of retinal laser therapy over the past 2 decades should not be judged solely by how much the laser itself has changed. Instead, it should be measured by how advances in imaging, pharmacotherapy, and our understanding of retinal disease have allowed us to deploy laser more thoughtfully, selectively, and effectively. PASCAL represented an important technological milestone in 2006, but the greatest advance has been our ability to choose the right treatment—or combination of treatments—for the right patient at the right time. ■

JULIA A. HALLER, MD

- CEO, Ophthalmologist-in-Chief, and William Tasman, MD, Endowed Chair, Wills Eye Hospital, Philadelphia
- Professor and Chair of Ophthalmology, Thomas Jefferson University, Philadelphia
- Emerita Editorial Advisory Board Member, *Retina Today*
- jhaller@willseye.org; @JuliaHallerMD
- Financial disclosure: Board of Directors (Bristol Myers Squibb, Topcon); DSMB, Bionic Sight

READ NOW

FURTHER READING

PASCAL Laser for Retinal Disease Treatment
December 2006
By Julia A. Haller, MD

MASS EYE AND EAR VITRECTOMY COURSE: SHAPING THE NEXT GENERATION OF SURGEONS



Fellows walked away with key didactic teachings and an unforgettable wet-lab experience.

BY LINDSAY KOZEK, MD, PHD
REVIEWED BY JOHN B. MILLER, MD; NIMESH A. PATEL, MD; ELIZABETH ROSSIN, MD, PHD; K. MATTHEW MCKAY, MD; AND JOSE R. DAVILA, MD

The 16th annual Mass Eye and Ear (MEE) Vitrectomy Course, held July 10-11 in Boston, welcomed 60 fellows, eight residents, and 52 faculty from across the country (Figure 1). The course was led by John B. Miller, MD; Nimesh A. Patel, MD; Elizabeth Rossin, MD, PhD; K. Matthew McKay, MD; and Jose R. Davila, MD. Conveniently timed at the beginning of the academic year, the course equips new vitreoretinal surgery fellows with a foundation of core principles, techniques, and decision-making skills essential for successful vitreoretinal surgical training.



Figure 1. The 16th annual MEE Vitrectomy Course welcomed fellows, residents, and top faculty from across the country.

DAY 1: DIDACTIC FOUNDATIONS

The first day consisted of core lectures and panels focused on the fundamentals of vitreoretinal surgery. The morning session introduced the basics of managing retinal detachment (RD), beginning with Ines Lains, MD, PhD, who shared practical pearls for pneumatic retinopexy. Lucy H. Young, MD, PhD, FACS, then reviewed indications and techniques for scleral buckling, followed by Thanos Papakostas, MD, who discussed vitrectomy for primary RD and reviewed the existing literature. Yasha Modi, MD, concluded the session with an overview of intraocular tamponades and perfluorocarbon liquids, followed by an interactive audience question-and-answer discussion.

R. V. Paul Chan, MD, MSc, MBA, FACS, then recognized Donald J. D'Amico, MD, as the Founders' Award recipient (Figure 2). Dr. D'Amico moderated an engaging expert panel on RD repair, in which Steve Charles, MD; John W. Kitchens, MD; Carl D. Regillo, MD; and Christina Y. Weng, MD, MBA, discussed their approaches to various types of RDs. Panelists explored surgical decision making, challenging cases, and technical pearls, providing attendees with a broad perspective on contemporary RD management.

In the afternoon, Robert Bhisitkul, MD, presented on ergonomics, emphasizing crucial techniques to promote surgeon longevity. Dr. Charles followed with an insightful review of vitrectomy fluidics and instrumentation, highlighting advances that improve surgical efficiency and safety. The afternoon continued with focused lectures by Sandra Montezuma, MD, on giant retinal tears, Sophie Bakri, MD, on proliferative vitreoretinopathy, and Maria Berrocal, MD, on the surgical management of diabetic retinopathy. These presentations culminated in a multidisciplinary panel on surgical diabetic retinopathy, led by Dr. Berrocal, in which Raymond Iezzi, MD; Anton Orlin, MD; Archana Seethala, MD; Dimitra Skondra, MD, PhD;



Figure 2. The MEE course recognized Dr. D'Amico as the Founders' Award recipient.

and Nicolas Yannuzzi, MD, shared differing approaches to complex diabetic vitreoretinal disease.

Next, Luis Haddock, MD, reviewed the prevention and management of endophthalmitis, followed by Mario Romano, MD, PhD, who discussed epiretinal membrane surgery and Dr. Weng, who shared on macular hole repair. Dr. Kitchens discussed IOL considerations in vitreoretinal surgery, while Sumit Sharma, MD, introduced vitreous biopsy techniques and the surgical management of uveitis. Eric Nudleman, MD, PhD, concluded the educational program with an overview of special considerations in pediatric retina surgery. The program closed with a networking reception and then a fellows' networking dinner sponsored by YoungMD Connect.

DAY 2: FROM INSIGHT TO IMPLEMENTATION

Saturday began with welcome remarks from Dr. Miller, followed by Yannek I. Leiderman, MD, PhD, who presented a practical framework for preparing for and developing expertise in vitreoretinal surgery. A panel discussion on secondary IOL management, led by Dr. Kitchens, explored strategies for complex IOL scenarios with panelists Dr. Davila, Mohammad Dahrouj, MD, PhD; Miin Roh, MD, PhD; Andre J. Witkin, MD; and Jeremy Wolfe, MD.

The majority of the day was dedicated to wet labs, dry labs, and small-group instruction. Attendees rotated through stations to practice surgical techniques, receive individual instruction and mentorship, and discuss challenging cases with expert faculty in an interactive learning environment.

The wet lab provided one-on-one sessions on essential techniques of vitrectomy, membrane peeling, scleral buckling, and intraocular foreign body removal. Stations introduced fellows to a variety of vitrectomy systems, including Alcon's Unity and Constellation, the Zeiss Eva Nexus, and the Bausch + Lomb Stellaris, and viewing platforms, such as the SeeLuma (Bausch + Lomb), Ngenuity (Alcon), and Biom (Oculus) with the Leica Proveo microscope.

For the dry lab, fellows participated in surgical simulation with the EyeSi (Haag-Streit) and the Genentech Virtual Simulation systems, and became familiar with various injectables, including triamcinolone acetonide injectable suspension (Xipere, Bausch + Lomb), fluocinolone acetonide intravitreal implant (Iluvien, Ani), dexamethasone intravitreal implant (Ozurdex, Abbvie), and pegcetacoplan injection (Syfovre, Apellis). Alcon's Unipexy was also featured along with an overview of intraocular tamponades.

Following lunch, two expert panel discussions addressed complex retinal surgery. The first focused on surgical strategies for proliferative vitreoretinopathy and complex RDs, led by moderator Sharon Fekrat, MD, with Xi Chen, MD, PhD; Karen Jeng-Miller, MD, MPH; Leo Kim, MD, PhD; Szilard Kiss, MD; and Aleksandra Rachitskaya, MD. The second panel explored surgical techniques for epiretinal membranes and macular holes, led by moderator Katherine E. Talcott, MD, with Marisa Tieger, MD; William Foulsham, MD; S. K. Steve Houston, MD; Deeba Husain, MD; Mehnaz Khan, MD; and Ivana K. Kim, MD. Faculty shared their approaches, technical pearls, and management of intraoperative challenges.

The afternoon concluded with hands-on lab sessions, allowing participants to reinforce newly acquired surgical skills before reconvening for a conference survey and a group photograph. In addition to hands-on experience, fellows also learned from surgical cases, where they asked questions and explored complex cases with experienced faculty members, as well as small group career mentoring sessions.

The meeting concluded with a reception and dinner, during which Ronald Gentile, MD, delivered his entertaining and practical presentation on "Top 10 Things to Keep Your Attending AND YOU Happy."

FELLOWS SET FOR SUCCESS

The 16th annual MEE Vitrectomy Course gave fellows a comprehensive introduction to vitreoretinal surgery through didactic lectures and hands-on surgical sessions, with an impressive faculty-to-fellow ratio. The course provides an early foundation for fellows as they begin their new roles and also supports the formation of meaningful and lasting connections with faculty and peers. ■

LINDSAY KOZEK, MD, PHD
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■ Financial disclosure: None

SAVE THE DATE:
17th Annual Mass Eye and Ear Vitrectomy Course
July 9-10, 2027, Boston

ATYPICAL PRESENTATION OF DELAYED-ONSET BILATERAL ARN



Reactivation of the virus in the fellow eye can occur many years after initial presentation.

BY MOHAN BHADRIRAJU, BA; RISHABH GUPTA, MD; AND VEENA R. RAIJI, MD, MPH

Acute retinal necrosis (ARN) is a necrotizing herpetic retinopathy characterized by an aggressive peripheral retinitis that progresses to necrosis and can have devastating clinical outcomes. Bilateral ARN (BARN) is a rare, but well-documented, phenomenon characterized by involvement of the fellow eye shortly after onset of symptoms in the first eye.

In this article, we describe an atypical and delayed presentation of herpes simplex virus-2 (HSV-2)–associated BARN in a monocular immunocompetent individual 30 years after involvement of the first eye. Atypical features of this case include presentation, recurrence of disease despite adequate antiviral therapy, and a morbiliform drug reaction to valacyclovir that changed medical management.

CASE PRESENTATION

A 49-year-old man presented to the emergency department with blurry vision and moderate pain with eye movement. He denied other ocular symptoms. Ocular examination revealed a BCVA of 20/20 OD, eccentrically. He had a VA of light perception OS due to ARN and subsequent total retinal detachment (RD), diagnosed 31 years prior. Slit-lamp examination of his right eye was unremarkable, and posterior examination showed grade 2 papilledema without evidence of vitritis or retinitis. A bedside ultrasound confirmed evidence of chronic RD in the left eye. Initial laboratory workup revealed a mildly elevated erythrocyte sedimentation rate of 34. MRI of the brain and orbits with contrast was unremarkable. The patient was admitted to the neurology service for further workup of suspected optic neuritis, which was negative. Therapy with intravenous (IV) steroids (500 mg solumedrol twice daily) was initiated by the neurology service for empiric treatment of optic neuritis.



Figure 1. Fundus photography demonstrated retinitis in the right eye.

Later that day, the patient reported worsening vision and was brought to the eye center for evaluation. His VA had deteriorated to 20/200 OD. Examination revealed retinal whitening along the superior and inferior arcades with foveal involvement and a peripapillary serous RD (Figure 1). Optic disc edema had worsened to grade 3. OCT confirmed a serous RD with retinitis and scattered macular lesions (Figure 2). A diagnostic anterior chamber (AC) tap and intravitreal injection of foscarnet was performed. Aqueous polymerase chain reaction (PCR) testing was positive for HSV-2. Further immunologic workup showed a CD4 count of 312, raising concerns about potential immunodeficiency, although repeated HIV testing remained negative, and a repeat immunodeficiency profile showed normal CD3 and CD4 counts. Human leukocyte antigen (HLA) typing revealed HLA-DR1 negativity and HLA-DR4 positivity.

The patient received IV acyclovir 10 mg/kg every 8 hours with stabilization of retinitis and was transitioned to

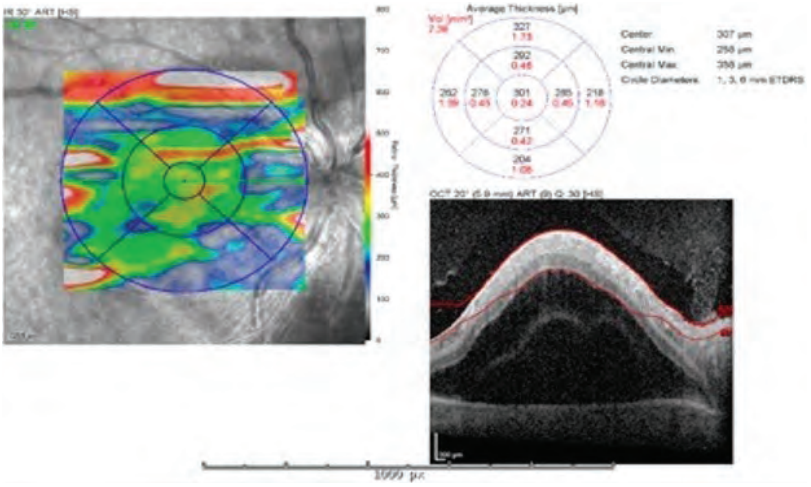


Figure 2. OCT demonstrated a serous RD in the right eye.

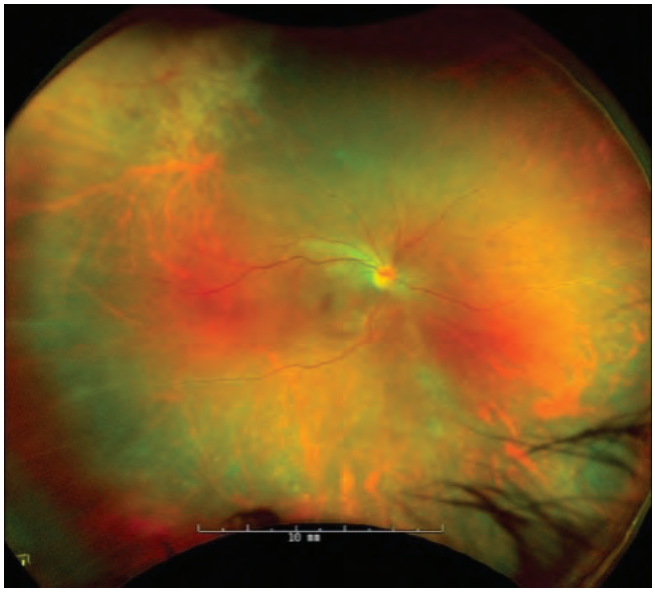


Figure 3. Fundus photography demonstrated the return of peripheral retinitis 4 months after initial presentation.

oral valacyclovir 1,000 mg every 8 hours in anticipation of discharge. Three days after initiation of valacyclovir, the patient developed an erythematous, maculopapular rash on left side of his face that spread to his arms, chest, and upper back. Biopsy revealed necrotic keratinocytes, consistent with a drug reaction. The patient's rash gradually resolved after treatment with topical corticosteroids and cessation of valacyclovir. Due to concerns for recurrence, valganciclovir 450 mg twice daily was initiated. By day 60, the patient's VA improved to 20/50 OD, and ophthalmic examination demonstrated resolution of the serous RD, peripheral granulated retinitis, and mild cystoid macular edema. The patient was discharged with close follow-up.

During outpatient care, the Infectious Diseases service transitioned him from valganciclovir to oral famciclovir 500 mg for lifelong suppression of HSV-2. Approximately 7 weeks after discharge, the patient woke up with redness and blurry vision in his right eye. At the outpatient clinic, his VA was 20/80 OD and his IOP was 55 mm Hg, and the retinitis had returned in the periphery (Figure 3). Given concern for treatment failure of famciclovir, repeat AC tap was performed for HSV-1, HSV-2, varicella zoster virus (VZV), and cytomegalovirus (CMV) DNA quantification and verified the presence of only HSV-2 by reverse transcription-PCR. He was subsequently readmitted for IV ganciclovir treatment.

During admission, antiviral therapy was escalated to combination IV and intravitreal foscarnet, given the potential disease progression on IV ganciclovir. As the retinitis resolved, patchy retinal breaks became apparent and were treated with laser retinopexy.

As the clinical examination stabilized during admission, the Infectious Disease service recommended re-trialing valacyclovir with weekly complete blood count and comprehensive metabolic panel monitoring. The patient tolerated valacyclovir and was discharged with resolving retinitis and a VA of 20/30 OD.

DISCUSSION

ARN is a type of infectious chorioretinitis, which is an inflammatory condition of the retina caused by an infectious pathogen.[1] Common viral pathogens include HSV, VZV, CMV, and Epstein-Barr virus.[1] Classically, VZV affects older individuals, while HSV affects younger patients.[1] Certain genetic predispositions can increase a patient's risk of developing ARN as well.[2] ARN can affect both immunocompetent and immunocompromised patients.[2]

While the presentation of simultaneous BARN occurs in approximately one third of cases of ARN, delayed development of ARN in the initially unaffected eye is relatively low and can occur anywhere between 5 days to 30 years.[3,4] However, reactivation more than 20 years later in the setting of immunocompetency is atypical. One study found the rate of ARN development in the initially unaffected eye while on maintenance antiviral therapy was 3.4%.[5] Antiviral therapy significantly reduces the risk of bilateral involvement, with one study suggesting 87.1% of patients treated with acyclovir had fellow eyes that remained disease-free, compared with 30.4% of untreated patients.[6] In our case, development of ARN in the right eye occurred approximately 30 years after ARN in the contralateral eye. This raises the question of the role of lifelong antiviral therapy in patients with a history of ARN while also considering that a single case cannot be used to generalize conclusions regarding guidelines for prophylaxis.

THE RISK OF ARN RECURRENCE WHILE ON ANTIVIRAL MAINTENANCE THERAPY, WHILE LOW, IS POSSIBLE AND NECESSITATES CLOSE FOLLOW-UP.

Managing ARN

Management of ARN can involve oral antivirals, IV antivirals, or combination therapy. One study demonstrated that visual acuity improvement was highest in patients who received combination therapy compared with oral or IV antivirals alone; however, the results were not statistically significant. Oral antiviral regimens include valacyclovir 1 g to 2 g three times daily until resolution of the retinitis, followed by a maintenance phase of valacyclovir tapered over 2 to 6 months or acyclovir 400 mg five times daily for HSV. Oral famciclovir can be given with a dose of 500 mg three times daily until resolution. Multimodal therapy can include the combination of either foscarnet and ganciclovir, oral famciclovir and intravitreal foscarnet, or intravenous acyclovir and intravitreal foscarnet with induction and maintenance phases.[7]

The risk of ARN recurrence while on antiviral maintenance therapy, while low, is possible and necessitates close follow-up. Resistance to antiviral drugs may contribute to the recurrence of HSV infections.[8] There is no formal data on the recurrence rate of ARN on famciclovir maintenance therapy. The clinical course of our case suggests continued close monitoring of patients with ARN on famciclovir maintenance therapy is important, and adding alternative therapies—such as ganciclovir or foscarnet—in cases of recurrence may be necessary. Additionally, genotyping for HSV-2 resistant mutations was not performed, limiting the understanding of the disease recurrence, and should be considered in future cases of treatment failure.

Atypical Reaction to Valacyclovir

While effective, valacyclovir is not without side effects. The most common adverse reactions include headache, nausea, and abdominal pain, but it can rarely cause an erythematous and pruritic rash, particularly in those with HIV-1 infection.[9] These reactions are generally mild but may require discontinuation of the medication in severe cases. In immunocompromised patients, valacyclovir can cause more severe dermatologic reactions, including symmetrical drug-related intertriginous and flexural exanthema, which typically affects areas such as the axillae and groin.[10] The development of a rash nonresponsive to systemic steroids or antihistamines in an immunocompetent patient highlights the clinical challenge of managing this case.

A LONG HAUL FOR YOU AND THE PATIENT

ARN may present initially with isolated findings of optic nerve edema that may precede retinal findings. Patients with optic disc involvement should be monitored closely for additional findings that suggest an infectious etiology, particularly if they have a history of ocular viral infection. BARN can present in the setting of immunocompetency, and lifelong antiviral suppression may be warranted after an initial presentation of ARN. Side effects should be closely monitored in patients starting new antiviral therapy even in the absence of documented drug reactions. ■

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WHAT AVIATION CAN TEACH US ABOUT AI

Retina specialists looking to integrate new technology should seek a digital copilot, not autopilot.

By Andreas Pollreisz, MD; Ariel Yuhan Ong, MBChB, FRCOphth; and Josef Huemer, MD, FEBO





AI is rapidly transforming medicine, and few specialties illustrate this evolution better than retina.[1] Modern retina care generates enormous quantities of data through OCT imaging (including OCT angiography), fundus photography, and fluorescein angiography. These highly standardized datasets are ideally suited for machine- and deep-learning applications. This has facilitated the development of AI algorithms with remarkable performance in detecting diabetic retinopathy, AMD, glaucoma, and numerous other diseases. Despite these impressive achievements, retina specialists know that clinical decision making rarely depends on imaging alone. Treatment decisions require consideration of symptoms and functional deficits, systemic disease, previous therapeutic responses, patient preferences, and subtle clinical findings that extend beyond image analysis.

AI therefore represents an important complement—not a replacement—for clinical expertise. While AI developments promise substantial improvements in efficiency and patient care, they also raise an important question: How can we safely integrate AI into clinical practice without eroding physician expertise?

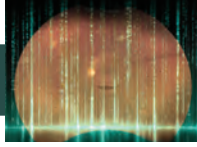
Aviation faced a remarkably similar challenge decades ago. The introduction of increasingly sophisticated automation dramatically improved flight safety and operational efficiency. However, experience also revealed unintended consequences, including reduced manual proficiency, overreliance on automated systems, and diminished situational awareness.[2] These lessons provide valuable guidance as medicine enters the era of AI-assisted health care.

THE AUTOMATION PARADOX

The term *automation paradox*, first defined by cognitive psychologist Lisanne Bainbridge in 1983, describes an unexpected phenomenon: As automation becomes increasingly capable, human operators become progressively

KEY TAKEAWAYS

- In aviation, the introduction of automation improved safety and efficiency but introduced increased reliance on automated systems and diminished situational awareness–and a similar phenomenon is beginning to emerge in medicine.
- To avoid the negative consequences of AI in medicine, the authors recommend viewing AI not as an autopilot capable of independently managing patient care, but as a digital copilot.
- Just as modern aviation combines automation with skilled pilots, the next generation of retina specialists should strive for a partnership in which AI enhances, rather than diminishes, human expertise.



less engaged, leading to a deterioration of manual skills precisely when they are needed most.[3] Paradoxically, more automation then is required to compensate for the skill loss.

Commercial aviation offers several well-known examples of disasters engendered by the automation paradox. Modern aircraft are extraordinarily safe, largely because of automation. However, accident investigations repeatedly demonstrate that pilots who relied excessively on automated flight systems were sometimes slower to recognize unexpected situations or less prepared to take manual control when automation failed.[4]

A similar phenomenon is emerging in medicine. While AI's capabilities undoubtedly improve efficiency, excessive dependence could weaken independent diagnostic reasoning. Recent studies suggest that clinicians exposed to AI assistance may experience declining diagnostic performance once AI support is removed. In gastrointestinal endoscopy, for example, endoscopists regularly using AI-assisted adenoma detection showed reduced detection rates when subsequently performing examinations without AI assistance.[5] Although other longer-term studies are limited, the possibility of AI-induced *deskilling* deserves careful attention.

FROM DESKILLING TO NEVER SKILLING

An equally important concept is *never skilling*, recently discussed in *Nature Medicine* to describe a potential risk for future physicians.[6] Unlike deskilling, which refers to the gradual erosion of established skills in experienced clinicians,[7] never skilling describes a trainee's failure to acquire foundational clinical reasoning skills due to a reliance on AI.

Again, aviation provides an important contrast. Before pilots can rely on autopilot, they must master manual flying, repeatedly demonstrate proficiency under simulated emergency conditions, and undergo repeated training throughout their careers.[8] Automation therefore augments an already established skill set rather than replacing its acquisition.

Medicine currently lacks such safeguards. If ophthalmologists routinely rely on AI during their training to interpret OCT scans or formulate differential diagnoses before developing these competencies independently, they may appear proficient while lacking the expertise required when AI is unavailable or produces incorrect recommendations. Although never skilling remains a theoretical concept that has not yet been demonstrated empirically, it reinforces an important lesson from aviation: Automation is safest when it builds upon, rather than substitutes for, fundamental human expertise.

FROM AUTOPILOT TO DIGITAL CO-PILOT

In our recent perspective article,[2] we examined the lessons medicine could learn from the field of aviation regarding optimized safety in the age of automation. One of the most important lessons was that automation should support and not replace human expertise.

Rather than viewing AI as an autopilot capable of independently managing patient care, a more appropriate model may be that of a digital co-pilot. Just as airline pilots remain ultimately responsible for every flight despite sophisticated automation, physicians should retain responsibility for clinical judgement while AI provides additional information, consistency, and efficiency. This collaborative model is particularly relevant in retinal practice. Although AI may accurately segment retinal layers, quantify intraretinal or subretinal fluid, identify imaging biomarkers, predict disease progression, or generate patient reports, the ophthalmologist remains responsible for integrating these findings into the broader clinical context.

This partnership combines complementary strengths. AI excels at rapid image analysis, consistency, and recognition of subtle pathological patterns. Physicians contribute contextual understanding, clinical reasoning, ethical judgement, communication skills, and the ability to interpret findings based on individual patient circumstances.

The future of retina care lies not in replacing clinicians with algorithms, but creating high performing human-AI teams.

BEYOND IMAGE ANALYSIS: THE NEXT GENERATION OF AI IN RETINA

The role of AI in retina is already expanding beyond image interpretation. Generative AI has the potential to transform clinical workflows by automatically generating structured reports from electronic health records, producing referral letters, drafting scientific documentation, and creating patient-friendly explanations of complex retinal diseases. Such systems could significantly reduce administrative burden while improving communication between specialists, referring physicians, and patients.[9]

At the same time, advances in high-resolution retinal imaging allow entirely new biological information to be extracted from the eye and are reshaping the emerging field of oculomics, which seeks to derive systemic health information from the eye.[10] Coupled with AI, these imaging modalities have the potential to enable earlier disease detection, more accurate patient stratification, and therapy monitoring in a number of diseases. These developments illustrate an important principle: The greatest effect of AI may not simply be faster diagnosis, but enabling clinicians to measure previously inaccessible biological processes.

Equally important is AI literacy. Retina specialists do not need to understand every mathematical detail of neural networks, but they should understand how AI systems are trained, their limitations, and when their outputs require careful scrutiny. Recognizing uncertainty and knowing when to question AI recommendations may become as important as interpreting retinal images themselves.

(Continued on page 24)

AI CHATBOTS IN THE RETINA CLINIC

Large language models are not coming for your job. But they may redefine what your job looks like.

By Fares Antaki, MDCM



AI has been in ophthalmology for years, and most retina specialists are familiar with AI as it relates to image analysis. Algorithms that detect diabetic retinopathy (DR) from fundus photographs or segment fluid on OCT have received the most attention and, in the case of autonomous DR screening, regulatory clearance.[1,2] However, a second wave of AI is reaching the clinic, and this version can read, write, and reason with text. These large language models (LLMs) power the chatbots that are quietly changing how physicians work.[3]

WHAT ARE LARGE-LANGUAGE MODELS?

LLMs are a class of AI designed to understand and generate human language. The technology behind products such as ChatGPT (OpenAI), Gemini (Google), and Claude (Anthropic) is conceptually straightforward. During training, a model is shown massive amounts of text and learns to predict the next word in a sequence.[4] Consider the phrase attributed to Heraclitus: "The only constant in life is change."[5] A model in training would see "The only constant in life is…" and learn to predict "change." This process is repeated billions of times across the entirety of the internet, books, and encyclopedias. The result is a system with a broad representation of human knowledge.

These models can hold multi-turn conversations, interpret nuanced queries, generate structured outputs, and adapt tone and style to context. However, because these inputs contain misinformation, errors, and bias, LLMs must undergo a process called *alignment* to ensure they are helpful, honest, and harmless (3H), aligning with human values.[6] In practice, human evaluators grade thousands of model outputs, and these preferences are used to fine-tune the model toward 3H behavior.[7] Despite alignment, LLMs can still produce confident but incorrect and potentially harmful statements—a limitation critical for clinical applications.

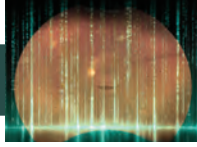
OPHTHALMIC KNOWLEDGE

LLMs have shown impressive performance in medicine, specifically on ophthalmology knowledge assessments.[8] In our research, we tested successive generations of GPT models on a 260-question multiple-choice dataset licensed from the AAO, comparable with the Ophthalmic Knowledge Assessment Program. Each iteration of the AI performed better: GPT-3.5 scored 55.8%, GPT-4 achieved 75.8%, and GPT-5 scored 96.5%.[9-11]

Multiple groups have now demonstrated LLM competence not only on ophthalmic board-style questions

KEY TAKEAWAYS

- Large language models have embedded ophthalmic knowledge that is improving rapidly with each model generation.
- Practical applications for retina specialists span two categories: workflow improvement (electronic health record documentation, report generation) and clinical assistance (triage, decision support).
- Vibe coding allows retina specialists without programming experience to build custom clinical tools using large-language models.



RETINA SPECIALISTS ADOPTING THESE TOOLS MUST DO SO WITH APPROPRIATE CAUTION, TREATING LLM OUTPUTS AS ADVISORY RATHER THAN AUTHORITATIVE.

but also as a clinical assistance tool and for patient education.[12,13] Each model generation embeds deeper medical knowledge and demonstrates stronger clinical reasoning. Most recently, a new class of reasoning LLMs can break down complex clinical problems into step-by-step chains of thought before producing an answer, further narrowing the gap with expert-level performance.[14,15] Thus, LLMs have accumulated enough ophthalmic knowledge to serve as useful tools in the hands of a trained clinician.

PRACTICAL APPLICATIONS IN RETINA

Applying LLM chatbots in the retina clinic falls into two broad categories: workflow improvement and clinical assistance tools.[16]

In workflow improvement, the most immediate use case is documentation. AI scribes that listen to patient encounters and generate structured notes are already in clinical use.[17] Chatbots can also draft referral letters, extract relevant data from lengthy records and summarize the chart, and prepare patient education materials.[18] These tasks consume a significant portion of a retina specialist's day. Offloading them to an LLM does not replace clinical judgment; it reclaims time.

A more forward-looking application is clinical decision support. In daily life, consumers use chatbots to answer health questions. More than 230 million people globally ask health- and wellness-related questions on ChatGPT every week.[19] LLMs can process unstructured patient descriptions, ask targeted follow-up questions, and generate a prioritized differential diagnosis and triage suggestions in real time. Consider the potential utility of a 24/7 triage chatbot where a patient describes acute symptoms after an intravitreal injection, and the system flags concern for endophthalmitis and directs them to the emergency department. Early-stage systems like this are being explored, although regulatory and liability frameworks remain undeveloped.

LLMs can also function as on-demand consultants during clinical decision making. A retina specialist uncertain about a rare presentation can describe the case to the chatbot and receive a differential diagnosis with supporting reasoning. In a recent study, our group partnered with Google to evaluate AMIE, a medically fine-tuned LLM based on Gemini, across 100 ophthalmology vignettes. After reviewing AMIE's output, clinicians improved their accuracy from 83.7% to 87.3%, revised their management plans in 34% of cases, and tended to rank the correct diagnosis higher in their differential.[20] The LLM response is not a substitute for clinical expertise, but it can serve as a cognitive aid, particularly for trainees or in settings with limited specialty access.

VIBE CODING: BUILDING YOUR OWN TOOLS

Perhaps the most underappreciated application of LLMs is their capacity to turn clinicians into software developers. The term *vibe coding* refers to a software development approach where the user describes what they want in plain language and the chatbot writes the code.[21]

For example, I wanted to streamline referrals to my retina practice. I described the requirements to the chatbot in Replit (a vibe coding platform): Build a web application that allows optometrists and other doctors to submit referrals with patient demographics, visual acuity, IOP, examination findings, and suspected diagnosis. Within minutes, I had a functional patient intake form with Snellen notation placeholders, dropdown menus for common diagnoses, and an image upload feature for fundus photographs and OCTs. The entire process required no programming knowledge.

Every retina specialist has inefficiencies in their practice that could be addressed by a simple tool. The barrier to building that tool has effectively been removed.

LIMITATIONS AND GUARDRAILS

Enthusiasm for LLMs must be tempered by an honest assessment of their limitations. LLMs can generate statements that are fluent, internally consistent, and wrong, known as *confabulations* or *hallucinations*.[22] In a clinical context, an incorrect differential or a fabricated management plan could have direct and serious consequences for patients. Any information generated by an LLM must be carefully verified by the clinician before acting on it.

Data privacy is another consideration. Entering protected health information into a commercial chatbot raises compliance concerns under HIPAA and equivalent regulations. Enterprise-grade and on-premises solutions exist, but most retina specialists interacting with chatbots today are using consumer-facing products. Awareness of what information is being shared and with whom is essential.

Finally, the medicolegal landscape is undefined. If a chatbot-assisted triage decision leads to a missed diagnosis, where does liability fall? These questions are being debated but have not been resolved. Retina specialists adopting these

tools must do so with appropriate caution, treating LLM outputs as advisory rather than authoritative.

TIME TO INTEGRATE

Chatbots will never replace retina specialists. The retina clinic requires procedural skill, clinical intuition built from pattern recognition over thousands of cases, and a patient-physician relationship that no AI can replicate. However, the technology is imperfect but improving at a rate outpacing most physicians' awareness of it. The question is no longer whether AI will play a role in the retina clinic; it's whether you will be the one shaping that role or reacting to it. ■

AI disclosure: Claude Haiku 4.5 was used for language editing. All content was reviewed, verified, and revised by the author, who assumes full responsibility for the accuracy and integrity of the manuscript.

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LOOKING AHEAD

Retina is uniquely positioned to lead the safe integration of AI into ophthalmic care. The specialty has embraced digital imaging earlier than most other fields, possesses standardized datasets ideally suited for AI development, and already benefits from a number of clinically validated and regulator-approved algorithms.

The future of ophthalmology will not be defined by algorithms alone. It will be shaped by how effectively clinicians and AI work together. Just as modern aviation combines highly sophisticated automation with skilled pilots, the next generation of retina specialists should strive for a partnership in which AI functions as a trusted digital co-pilot—enhancing, rather than diminishing, human expertise. ■

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RISING STARS IN RETINA

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Yuxi Zheng, MD

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

My interest in vitreoretinal surgery developed throughout my undergraduate education, medical school, and residency, but my earliest exposure came during college. Through a volunteer experience, I met one of the first patients to receive the Argus II retinal prosthesis (Cortigent). Seeing firsthand how emerging technology could meaningfully affect a patient's visual function and quality of life introduced me to the innovation-driven nature of retina and left a lasting impression.

As my training progressed, I became increasingly drawn to the combination of complex decision making, surgical precision, and scientific innovation that defines the field.

***RT:* Who do you look to as mentors?**

I have been fortunate to work with outstanding mentors who have shaped my career path and my approach to surgery, teaching, and lifelong learning. Many of these mentors have become close friends. Durga Borkar, MD, MMCi, and Xi Chen, MD, PhD, guided me through my very first retina surgeries. I have been inspired by Lejla Vajzovic, MD, Dr. Chen, and Cynthia Toth, MD, for their passion and leadership in pediatric retina. Yannek Leiderman, MD, PhD, and Jason Fan, MD, PhD, taught me invaluable lessons about surgical training, encouraging me to refine my skills and explore new techniques. Sharon Fekrat, MD, and Dr. Toth challenged me to think critically and strive for excellence in research, and Glenn Jaffe, MD, and Dilraj Grewal, MD, provided foundational training in uveitis and the management of complex surgical cases.

I am grateful for these mentors who continuously push me to be better, encourage curiosity and critical thinking, and support me in every stage of my professional development.

***RT:* What was one of the most memorable experiences of your fellowship?**

One of the most rewarding aspects of fellowship was teaching residents and medical students. Guiding trainees through their first endolaser treatments, fluid-air exchanges, secondary IOL placements, and scleral-depressed examinations was incredibly meaningful. There is nothing like witnessing the "aha" moment when a resident truly understands a new technique. Teaching has been a defining and fulfilling part of my training, and I look forward to continuing to work with trainees and contributing to surgical education throughout my career.

FIRST CAREER MILESTONE

Dr. Zheng has joined Mid Atlantic Retina, Wills Eye Hospital.

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

First, welcome to the best specialty in all of medicine. Second, start early. Build relationships, get involved in research, and spend as much time as possible in clinic and the OR. Retina is a small world, and the connections you make during residency will follow you throughout your career. Finally, say yes to everything. Be enthusiastic, reliable, and willing to work hard. Take on opportunities, learn from every experience, do a good job, and your efforts will be noticed. ■

YUXI ZHENG, MD

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A GUIDE TO IMPLEMENTING LLMS IN PRACTICE

Retina specialists can use AI to streamline their communication, if they do it carefully. Here's how.

By Fatima Kalabi, MD; Mohammad Hossein Amirhosseini, BSc, MSc, PhD; and Rodrigo Anguita, MBBS, MD, FEBO, FICO







Large language models (LLMs) are not reading OCT scans for us yet, but they are changing how we talk to patients, draft correspondence, and prepare trainees for oral examinations. Understanding what they can and cannot do is now a practical clinical skill. For a broad overview of what LLMs are and their potential uses in the clinic, see *AI Chatbots in the Retina Clinic*.

Here, we explore *how*, exactly, retina specialists can implement these tools safely in their workflow.

DRAFTING PATIENT EDUCATION

Retinal disease can present significant communication challenges. The difference between wet and dry AMD, the rationale for repeated intravitreal injections, or the urgency of a retinal detachment repair may be obvious to the specialist but bewildering to a newly diagnosed patient. LLMs can produce a first draft of a plain-language explanation, adjust reading level, or reformat content for a patient portal.[1,2]

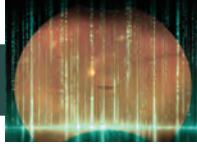
In a cross-sectional study of ChatGPT-4 (OpenAI) responses to common questions about retinal detachment, macular hole, and epiretinal membrane surgery, retina specialists judged most answers to be appropriate. However, the authors cautioned against treating these tools as factual authorities and highlighted persistent concerns about credibility and readability in specialized contexts.[3]

The key phrase is *first draft*. Without careful prompting, models may overstate the likelihood of visual improvement, omit the need for ongoing treatment, or miss return precautions entirely. The clinician is always responsible for the final message.

Patient Education Example Prompt: Draft a [350]-word handout at a sixth-grade reading level for a patient newly diagnosed with [neovascular AMD] who is starting [intravitreal anti-VEGF injections]. Include: what the condition is; that treatment aims to preserve rather than restore vision; that treatment continues alongside monitoring rather than as a fixed course; and a separate list of symptoms needing same-day contact such as increasing pain, worsening redness, sudden reduction in vision, new floaters or flashes. Exclude drug names, treatment intervals, success rates and prognostic figures. Write [CONFIRM] wherever a statement depends on this patient's findings.

Prompt design: Whenever possible, give the model something to write rather than something to avoid. Stating that *treatment aims to preserve rather than restore vision* is more reliable than *do not overstate benefit*. Where a prohibition is unavoidable, make it specific: *no drug names, intervals, or success rates* is quickly checkable, whereas *nothing misleading* is not.

Requiring the red flags be a separate list is a formatting instruction doing safety work. Content requested only by topic tends to be absorbed into the surrounding prose,



where it softens. For example, if you ask for warning symptoms, the LLM may weave them into a closing paragraph of reassurance, phrased as things to raise at the next visit. Instead, ask the LLM to give warning symptoms their own heading or bulleted list to ensure they are a discrete, scannable instruction. This also does clinical work, as a patient scanning a handout reads lists rather than paragraphs. Specify format wherever content must be easy to find, not merely present. The same precision applies to readability. *Sixth-grade reading level* produces consistent output where *simple language* does not.

Finally, the [CONFIRM] placeholder turns silent gap-filling into a visible prompt for the clinician. This is the highest-yield instruction in the set, and one worth reusing across every prompt that follows.

DRAFTING LETTERS

High-volume retina clinics generate large amounts of letters to general practitioners, optometrists, and referring colleagues. A specialist can provide de-identified bullet points and prompt AI to produce a structured letter; specifying diagnosis, visual acuity, key OCT findings, treatments, and management plan. The model is not deciding whether to treat, extend, or observe, but helping to express a decision already made.

Correspondence Example Prompt: Convert the bullet points below into a structured letter to a referring [optometrist]. Use only the information given. Do not add findings, diagnoses, recommendations, or follow-up intervals that are not stated. If a standard letter section cannot be completed from the material provided, write "not stated" rather than filling the gap. Keep to [200] words in a formal clinical tone. [Paste de-identified bullets]

Prompt design: The key instruction here is the gap-handling rule. *Use only the information given* is necessary but weak on its own, because it tells the model what not to do without giving it an alternative action. When a conventional letter section has no input, the model resolves the conflict by completing the pattern. Supplying the fallback output *not stated* gives it a compliant way to leave the gap; it turns an omission you would have to detect into one you can see. Generalize the technique by specifying what to produce whenever you forbid something.

DRAFTING CALL SCRIPTS

LLMs can assist in drafting symptom-based scripts for call handlers, FAQ responses for common queries, and text for clinic websites or appointment reminders. Triage decisions should follow existing clinical protocols; the LLM's role is to make approved guidance clearer, not to replace it.

Call Script Example Prompt: Below is our triage protocol for calls about [flashes and floaters]. Rewrite it as a call-handler script with the questions in the order they should be asked and the resulting action for each answer. Change no threshold, timeframe, or action. Add no new questions. List anything ambiguous under "for clinical review" rather than resolving it. [Paste protocol]

Prompt design: This is a transformation task rather than a generation task, and it is the safest pattern available. The clinician includes the clinical content in the prompt, and the model restructures the language, reducing the review to comparing the output against the source.

Change no threshold, timeframe, or action names the dimensions along which potential drift occurs, which works better than a general instruction to stay faithful to the original. The ambiguity clause matters for a subtler reason: A model asked to rewrite an unclear instruction will clarify it, improving readability while quietly changing clinical meaning. Routing ambiguity to a separate list preserves it as a question for the clinician rather than resolving it silently. Wherever an approved document already exists, prefer this pattern to drafting from scratch.

STUDY TOOLS

Evidence for LLMs as educational tools has improved substantially as models have advanced. Trainees can use them to generate single best-answer questions, Objective Structured Clinical Examination scenarios, viva prompts, and synthetic retina cases, including consent role-plays for intravitreal injection, vitrectomy, scleral buckle, pneumatic retinopexy, or macular hole surgery. The value lies in structuring knowledge and practicing communication; factual claims should always be checked against trusted sources.

KEY TAKEAWAYS

- Large language models are text-generation tools that can help retina specialists draft patient education and correspondences, teach cases, and research documents.
- Without careful prompting, AI models may overstate the likelihood of visual improvement, omit the need for ongoing treatment, or miss return precautions entirely.
- Safe adoption requires no patient-identifiable data, institution-approved platforms, careful prompting, and clinician review of every output.

Study Example Prompt: Write [one] best-answer question at fellowship level on [the management of rhegmatogenous retinal detachment], each question with four distractors and a short explanation. Do not cite papers, trials, or numerical outcomes. Where management is genuinely contested, say so in the explanation rather than presenting one option as definitive.

'GPT-5.6 Thinking' (OpenAI) response: A 62-year-old pseudophakic patient presents with a macula-involving rhegmatogenous retinal detachment. Examination shows multiple retinal breaks in different quadrants, fixed retinal folds, and a circumferential epiretinal membrane causing retinal shortening. What is the most appropriate primary management?

A. Pneumatic retinopexy with cryotherapy
B. Segmental scleral buckle without drainage
C. Pars plana vitrectomy, membrane peeling, retinopexy, and internal tamponade
D. Demarcation laser photocoagulation around the detachment
E. Intravitreal expansile gas followed by delayed laser retinopexy

Answer: C

Explanation: The fixed folds, circumferential membrane, and retinal shortening indicate established proliferative vitreoretinopathy. Successful repair requires removal of vitreoretinal traction, dissection of proliferative membranes, closure of all retinal breaks and internal tamponade. Retinectomy may also be required if the retina remains shortened after membrane removal. Pneumatic retinopexy, laser alone, and an isolated segmental buckle do not adequately address extensive traction or multiple breaks in different quadrants. The choice of gas versus silicone oil, and whether to add an encircling buckle, remains dependent on the detachment configuration, severity of proliferative vitreoretinopathy, patient factors, and surgeon preference.

Prompt design: Exclude by task, not by subject. Models fabricate references and outcome figures readily, but write reliable question stems and plausible distractors, so the prompt avoids the first and asks for the second. The final clause addresses tone rather than accuracy. Explanations read as authoritative whether the evidence supports it or not, so where surgeon techniques differ, AI will present one option as settled unless told otherwise. Specify how the output should read, not only what it should contain.

LIMITATIONS AND MYTHS

LLMs can hallucinate—ie, generate plausible but false statements. In retina, this could mean a wrong dosing interval, an inaccurate trial result, or an invented contraindication. A systematic review of LLMs in ophthalmology found that most studies reported accuracy but few addressed calibration or uncertainty, with substantial heterogeneity in pooled diagnostic performance.[4]

Hallucination Example Prompt: What is the licensed treatment interval for faricimab (Vabysmo, Genentech/Roche) in diabetic macular edema, and how does it differ from the aflibercept 8 mg (Eylea HD, Regeneron) regimen?

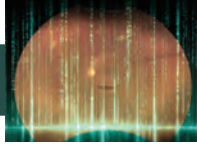
Claude Opus 5 (Anthropic) response, in part: Following 4 monthly loading doses, faricimab may be extended to fixed 16-week dosing in eligible patients, with the YOSEMITE and RHINE protocols permitting extension in 4-week increments based on central subfield thickness and BCVA criteria assessed at weeks 20, 24, and 28.

Hallucination Analysis: The general approach is right, the drug and trials are real, and the mechanism is described with appropriate vocabulary. However, the specifics such as the maximum interval, the increment size, the assessment weeks, and the extension criteria are assembled from the statistical regularities of how anti-VEGF regimens are described; they are not from the protocol or the label. Some of it may be correct, but nothing in the output distinguishes which parts.

Two features make this more dangerous than a fabricated citation. A reference can be checked quickly and its absence is unambiguous. A dosing statement, however, must be checked against a label or protocol by someone who already suspects it may be wrong. In this example, the error is partial rather than total, so the surrounding accurate material lends the invented figures credibility.

Avoiding hallucinations is a matter of task selection rather than prompt wording. No instruction prevents an AI model from producing numbers when numbers are what a question demands. Asking an LLM to flag uncertainty helps only where it is uncertain, and here it is not. The tractable move is to stop asking. Regulatory and dosing facts have authoritative sources, and AI can help interpret those documents, not supply the facts themselves. Where a specific figure is needed, paste the relevant section and ask the LLM to summarize or reformat it, which converts the task from recall, where the model is unreliable, to transformation, where it is reliable.

Data protection deserves particular attention. Removing a patient's name or date of birth does not reliably de-identify clinical notes. Laterality, procedure dates, rare diagnoses, visual acuity history, and unusual treatment sequences can combine to make a patient recognizable, particularly in smaller or highly specialized services. Patient-identifiable or potentially identifiable information should never be entered into public tools.



GETTING STARTED SAFELY

The safest starting point is low-risk, non-identifiable work: generic patient education materials, teaching cases, departmental workflow documents, journal club outlines, and rewriting approved text in simpler language. A practical prompt specifies the audience, task, length, tone, limits, and instructs the model not to invent missing information.

Seven Tips That Make an AI Prompt Work

1. **Task and audience:** clarify who is reading this, and why
2. **Format/length:** specify word count, headings, and tone
3. **Reading level:** name a grade level, not *"simple"*
4. **Source material:** state *"use only what I provide below"*
5. **Prohibitions:** state *"include no invented findings, figures, intervals, or citations"*
6. **Gap handling:** stipulate that the AI *"write 'not stated' rather than filling any gaps"*
7. **Uncertainty:** ask that it *"flag anything I should verify"*

Lines 1–3 determine whether the output is usable, and lines 4–7 determine whether it is safe. Every prohibition should be paired with an alternative action, or the model will resolve the gap on your behalf.

Institution-approved or enterprise deployments should be preferred over public consumer tools, particularly for anything approaching clinical documentation. Platform approval does not remove the need for output review.

Enterprise deployment at scale is already arriving. In June 2026, NHS England announced that Microsoft 365 Copilot would be made available to more than 500,000 clinicians and support staff, following a trial across 90 organizations in which administrative support saved an average of 43 minutes per user per day.[6] Tools embedded in an institutional environment can offer clearer data-governance arrangements than public consumer products, but the same principles apply.

Departments benefit from an internal policy defining appropriate tasks, approved tools, what information must not be entered, how outputs should be reviewed, and whether AI assistance requires disclosure in academic or patient-facing materials.

TOWARD MULTIMODAL RETINA ASSISTANTS

Retina is a high-stakes specialty; small errors in timing, interpretation, or wording can affect vision. Until larger multimodal AI assistants are validated and regulated, LLMs are best understood as textual power tools in today's clinic. They can explain, summarize, draft, and teach. They can also hallucinate, omit, and sound confident when wrong. Used with curiosity and caution, LLMs may become a useful conversational layer around the AI already reshaping, rather than replacing, the human expertise at the center of the specialty. ■

AI disclosure: The authors used Claude Opus 5 (Anthropic) in the preparation of this manuscript for language refinement of specific sections. All content was reviewed, verified, and edited by the author, who takes full responsibility for the accuracy and integrity of the work.

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TACKLING THE DOCUMENTATION BURDEN

AI can synthesize outside records, draft visit notes, and translate retina jargon, but the physician remains responsible for every word.

By Bradley S. Gundlach, MD; Haley S. Garrison, MD, MS; and Prashant D. Tailor, MD





Retina practice is a documentation stress test. A single encounter may require synthesis of outside anti-VEGF history, prior surgery, systemic medications, examination findings, multimodal imaging, and injection details followed by initiating a plan that patients and referring clinicians can understand. In one academic study, ophthalmologists spent a mean of 10.8 minutes in the electronic health record (EHR) per encounter, totaling 3.7 hours during a full clinic day.[1]

Large language models (LLMs), which can organize information quickly, may be able to reduce some of this burden; however, they can also omit crucial facts, reverse laterality, and add unsupported details.

BEFORE THE VISIT

New retina consultations often arrive with fragmented or lengthy notes, imaging reports, operative records, and injection histories. AI can extract a timeline and populate a problem-oriented draft, so the physician has a structured summary. For example, Mayo Clinic's RecordTime, a tool that organizes and summarizes outside records, anecdotally saved one physician 5 to 30 minutes of preparation per patient,[2] although peer-reviewed performance data have not yet been published.

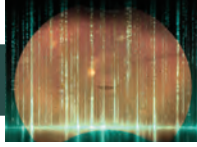
In our study, a locally hosted LLM generated pre-charting drafts for 48 external retina, uveitis, and ocular oncology referrals.[3] AI drafts were rated more complete and organized, whereas physician drafts were clearer and more clinically relevant; overall preference did not significantly favor either source. Physicians spent a median of 5.12 minutes manually summarizing and pre-charting each referral, although the study did not directly compare this time with physician review and editing of AI drafts. Among available AI note-review forms, errors were reported in 20 of 43 and pertinent omissions in 18 of 45, supporting supervised synthesis rather than autonomous record review.[3] These findings suggest AI solutions can accelerate record synthesis but cannot replace clinical prioritization, source verification, or final review.

DURING THE VISIT

Ambient-listening AI scribes convert the patient-clinician conversation into a draft note, but studies show heterogeneous rather than universal benefit. In

KEY TAKEAWAYS

- AI can assist with documentation before, during, and after a retina visit, but efficiency gains vary by product, clinician, and workflow.
- Protected health information should be processed only through approved systems with appropriate contracts, security review, patient disclosure, and clinician oversight.
- Clinicians should use AI to organize and draft and require verification of high-consequence details.



THE SUCCESS OF AI-ENHANCED DOCUMENTATION DEPENDS ON WHETHER IT RETURNS ATTENTION TO THE PATIENT, SHORTENS THE PATH TO AN ACCURATE RECORD, AND FAILS SAFELY WHEN THE WORKFLOW EXCEEDS WHAT IT CAN CAPTURE.

a randomized trial of 238 outpatient physicians across 14 specialties, one solution reduced time-in-note by 9.5% relative to usual care, whereas another product did not affect the documentation time. Both products improved several clinician-reported measures, although clinicians reported occasional clinically significant inaccuracies.[4] Another trial of 66 clinicians across ambulatory practices similarly found improvements in work exhaustion and documentation-related outcomes, while showing that adoption, workflow fit, and baseline documentation habits influenced who benefitted from the AI scribes.[5]

Real-world evidence is broader and mostly observational. In a five-center study of 8,581 clinicians, including 1,809 adopters, AI scribe access was associated with 13.4 fewer minutes of total EHR time and 16 fewer minutes of documentation time per 8 patient hours, no significant change in after-hours EHR time, and 0.49 additional visits per week.[6] Another study of 263 clinicians found that self-reported burnout decreased from 51.9% to 38.8% after 30 days of AI scribe use.[7] Survey data also showed improved documentation-related wellbeing, but individual experiences ranged from major time savings to added editing burden.[8] Although ophthalmologists were included in at least one multispecialty cohort, none of the cited studies reported ophthalmology or retina-specific outcomes.

Retina adds a fundamental limitation: Much of the clinic work occurs outside the recorded conversation or is never verbalized. For example, OCT interpretation and comparison may occur before the patient encounter, and the peripheral retinal examination is often performed silently or only partially narrated. Ambient audio therefore captures only a subset of the information required for a complete retina note. In scripted vitreoretinal encounters, models additionally fabricated information in some cases.[9]

AFTER THE VISIT

AI may be most valuable when it turns a finalized note into a plain-language summary or concise referral letter. In our randomized quality improvement study, 85% (n = 362) of non-ophthalmology clinicians and professionals preferred ophthalmology notes that included an AI-generated plain-language summary. Diagnostic understanding increased by 9% and clarity by 23%. However, ophthalmologist review identified at least one error in 26% of summaries, although most were low risk and none were judged to pose a risk of severe harm or death.[10] Other studies have similarly found major readability gains alongside omissions and inaccuracies requiring review.[11,12] Our group is now evaluating patient comprehension in a randomized controlled trial (NCT06859216).[13]

Automated post-visit summaries could translate the finalized note into a clear explanation of the diagnosis, treatment, follow-up, and return precautions, improving communication with patients, caregivers, and referring clinicians while reducing manual drafting. Their value, however, depends on the physician's initial documentation and careful verification.

NONNEGOTIABLES FOR SAFE IMPLEMENTATION

First, only use an organization-approved platform. When a vendor handles health information on behalf of a covered entity, a business associate agreement is generally required, together with institutional risk assessment and security safeguards.[14] Practices should understand where and how long data are stored; whether they are used for model training or other secondary purposes; which subcontractors can access them; and how access controls, audit logs, breach notification, and data return or destruction are managed. Retention should be minimized, justified, and contractually defined.

Second, be transparent with patients. Recording and consent requirements vary by state and institution. The Ophthalmic Mutual Insurance Company recommends combining general disclosure, periodically updated written consent, and an institutional governance policy.[15] Qualitative research also supports clear education, flexible consent methods, and an accessible opt-out process.[16] At the visit, confirm that the patient agrees and may decline without affecting care.

Third, require clinician review and audit the full workflow. Signing an encounter should remain a hard stop, supported by a retina-specific checklist that focuses on laterality, imaging, medications, procedures, and follow-up. During implementation, measure adoption, editing time, same-day note closure, high-consequence errors, patient opt-outs, and

(Continued on page 34)

A POTENTIAL DIGITAL CO-PILOT IN THE RETINA OR

AI systems may one day augment traditional surgical workflows to improve efficiency and patient outcomes.

By Stanley Poh, MBBS, MMED (OPHTH), FRCOPHTH, FAMS, and Daniel Ting, MD, PhD





Vitreoretinal surgery is a complex discipline involving intricate and highly variable pathology. Many decisions depend on dynamic changes in anatomy and tissue behavior, surgical visualization, and potential complications. As such, vitreoretinal fellows face a steep learning curve. Years of training through residency, fellowship, and independent surgical practice are required to develop the judgement needed to determine whether surgery is warranted, which intervention is most appropriate, and how urgently it should be performed.

As AI tools proliferate and improve, they could advance the evolution of the retina OR. By analyzing large volumes of clinical, imaging, and procedural data, AI could generate timely, clinically meaningful insights to enable more informed decision making across preoperative, intraoperative, and postoperative phases of care (Figure).

In many ORs, digital visualization systems and intraoperative OCT have already broadened what surgeons can see and have influenced surgical decision making. These technologies can provide magnified stereoscopic visualization, digitally enhanced color contrast, and real-time imaging of retinal structures, offering invaluable guidance during surgery.

PREOPERATIVE APPLICATIONS

Every surgical case requires meticulous planning, and many decisions are made before the first trocar is inserted. This process integrates considerable data, including history, patient-specific risk factors, examination findings, and multimodal retinal imaging. For retinal detachments, for example, machine-learning models could integrate ultra-widefield imaging, OCT findings, and other clinical variables to estimate the likelihood of anatomic success. In macular surgery, AI models could help predict anatomic closure or visual outcomes using features such as macular hole dimensions, epiretinal membrane configuration, ellipsoid zone integrity, and other changes.[1,2] Such predictions could improve prognostication and optimize the operative approach.

Large language models may also reduce administrative burden and improve preoperative and perioperative workflows. Studies show that these models can efficiently summarize clinic notes, extract relevant information from electronic health records (EHRs), and draft treatment plans.[3,4] When appropriately integrated into EHR systems, AI could identify high-risk cases and flag factors such as suboptimal glycemic control, anticoagulant use, medical comorbidities, drug

KEY TAKEAWAYS

- By analyzing large volumes of data, AI could generate clinically meaningful insights to enable more informed decision making in the OR.
- AI could identify high-risk cases and flag factors such as suboptimal glycemic control, anticoagulant use, medical comorbidities, drug allergies, and mobility limitations.
- Agentic AI can act as a digital co-pilot by integrating preoperative, intraoperative, and postoperative capabilities.

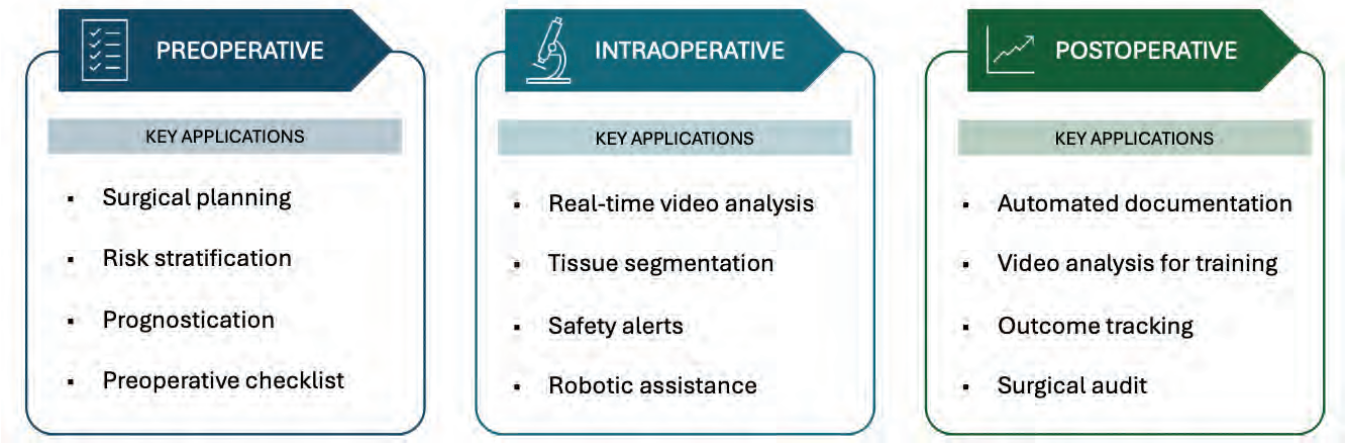


Figure. Potential roles of AI across the vitreoretinal surgical workflow.

allergies, and mobility limitations. These considerations are important not only for perioperative safety but also for tailoring surgical plans to individual patient needs. AI could also generate case-specific equipment checklists based on the pathology, procedure, and surgeon's preference, helping OR nurses and assistants support surgical workflows.

INTRAOPERATIVE APPLICATIONS

One of the most compelling potential applications of AI in the retina OR is the real-time analysis of surgical video. Early proof-of-concept studies demonstrated that deep-learning models can identify, classify, and segment instruments and ocular anatomy in vitreoretinal surgical recordings.[5,6] These models may recognize the instrument being used and its position, movement, depth, and proximity to critical structures such as the macula and optic disc. Future integration with surgical visualization systems could facilitate intraoperative navigation, motion analysis, and collision avoidance.

Real-time anatomic segmentation of intraoperative OCT images could further expand these capabilities. During macular surgery, an AI-assisted system might identify residual epiretinal or internal limiting membrane, persistent traction, or a full-thickness retinal defect following release of vitreomacular traction. Such assistance could be particularly valuable during membrane dissection in proliferative vitreoretinopathy and tractional retinal detachment. Potential applications include identifying safe sites to initiate peeling, highlighting areas at risk of iatrogenic injury, distinguishing fibrovascular proliferation from the underlying retina, and monitoring retinal perfusion during fluctuations in IOP.

Robotics is another rapidly developing field in ophthalmology, as it can eliminate a surgeon's tremor and enable instrument control with micrometer-level precision. These capabilities may be particularly valuable for maneuvers requiring extreme precision, such as subretinal injection, retinal vein cannulation, and targeted delivery of gene or cell therapies.[7-10] AI can potentially enhance these platforms by incorporating preoperative imaging for anatomic localization and establishing virtual safety boundaries to limit excessive instrument movement and improve instrument stability.

POSTOPERATIVE APPLICATIONS

AI has the potential to make surgical documentation more accurate and efficient. An AI assistant could, for example, generate a draft operative note and suggest procedural codes, with surgeon review and approval.[11] In an AI-integrated health system, surgical audit can be done more effectively. Intraoperative events and procedural variables can be correlated with postoperative outcomes and patient satisfaction, supporting complication surveillance, workflow optimization, and institutional quality improvement.

Vitreoretinal surgery is particularly difficult to teach because many aspects of surgical performance are difficult to assess objectively. In cataract surgery, deep-learning models were able to localize key ocular structures and instruments with high accuracy, enabling the derivation of metrics for evaluating surgical skill.[12] Similar approaches can be replicated and applied to vitreoretinal surgical videos. Within each surgical phase, AI can assess instrument trajectories, tremor, proximity to critical structures, ocular centration, image focus, procedural efficiency, and time spent on key steps. For trainees, this can provide objective, actionable feedback that complements traditional assessments and learning through increasing surgical volume.

FROM ASSISTANT TO AGENT

Over the years, AI has evolved from rule-based systems into machine learning, deep learning, generative, multimodal, and now agentic systems. Agentic AI does more than generate an isolated prediction; it supports an entire clinical workflow. In the retina OR, it can act as a digital co-pilot by integrating preoperative, intraoperative, and postoperative capabilities. The digital co-pilot augments but cannot replace a surgeon's judgment, operative decisions, and responsibility.

AUGMENT, NOT REPLACE

The retina OR of the near future is likely to become increasingly digital and interconnected. AI will play an expanding role in enhancing surgical planning, intraoperative guidance, training, documentation, and postoperative evaluation. These technologies should be thoughtfully integrated into clinical workflows, while carefully considering their limitations, risks, and need for appropriate oversight. The surgeon's ultimate responsibility is to align surgical goals with each patient's needs. AI may support and inform these decisions, but it cannot assume responsibility for them.

For now, AI in the retina OR is best understood as an emerging digital co-pilot. Its promise lies not in autonomous surgery but in augmented surgery: more structured planning, improved visualization, greater surgical efficiency and safety, and more effective postoperative learning. The goal is not to make surgery less human, but to provide surgeons with better information the moment it's needed. ■

AI disclosure: GPT-5.6 Sol (OpenAI) was used solely for grammatical refinement. The authors reviewed and approved the final manuscript and take full responsibility for its content.

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(Continued from page 31)

clinician and patient experience. Reassess performance after software updates and in challenging encounters involving interpreters, multiple speakers, or complex surgical histories.

VERIFY, VERIFY, VERIFY

The success of AI-enhanced documentation in retina depends on whether it returns attention to the patient, shortens the path to an accurate record, and fails safely when the workflow exceeds what it can capture. In retina, evidence remains limited, and benefits cannot be assumed from other specialties. Retina specialists should implement AI with caution; use it to organize and draft, require verification of high-consequence details, and retain only workflows that improve accuracy, efficiency, and patient care. The goal is an accurate, timely, understandable record that allows the physician to reserve their attention for the patient. ■

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SUPPORTING PATIENTS THROUGHOUT THEIR GA JOURNEY

Lifestyle and functional strategies can help support patients as geographic atrophy progresses.

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By Priya Vakharia, MD, FASRS

For patients with age-related macular degeneration (AMD), counseling about lifestyle and daily function is not a single conversation. As AMD progresses to geographic atrophy (GA), the focus of that conversation may also evolve. What begins with lifestyle considerations and risk reduction can shift toward preserving function, maintaining independence, and preparing for the practical effects of vision loss.

Tailoring Counseling to Disease Stage

My approach to lifestyle counseling is based on disease stage. In early or intermediate AMD, I recommend UV protection, a healthy lifestyle, smoking avoidance, and vitamin supplementation. As well, patients with AMD may benefit from adopting a Mediterranean-style diet, with the most important foods varying according to disease stage.[1] For intermediate AMD, high fish intake is particularly important, followed by high vegetable intake and low red meat intake.

For patients who have advanced disease, have progressed to GA, or are experiencing visual changes and functional difficulties, the priority shifts from influencing future disease risk to helping them preserve independence. The benefits of a healthy diet are still part of the conversation. In AREDS2, the mean GA enlargement rate was approximately 15% slower among participants with the highest Mediterranean-diet adherence compared with those with the lowest adherence. Additionally, higher whole-fruit intake was associated with 22% slower GA enlargement, while lower red-meat intake was associated with a 23% slower enlargement rate.[1]

Setting Realistic Expectations

Lifestyle counseling should not create the impression that behavioral changes will reverse AMD or eliminate disease progression. I try to temper treatment expectations by explaining that a healthier diet, for example, would not cure their macular degeneration, but it could offer some benefit. I also explain that a large part of their disease and its progression is both genetic and age-related. Framing lifestyle counseling this way can help patients understand what they may be able to influence while maintaining realistic expectations about their disease.

Preparing Early for Functional Changes

I firmly believe counseling should be tailored to the person's lived experience rather than based solely on a visual acuity measurement. Because of this, I find it beneficial to ask patients about their daily challenges, their level of independence, their ability to maneuver safely, and overall, how they feel about their disease. Practical preparation should begin when early visual changes emerge rather than after substantial vision has already been lost. The suggestions I provide most often to patients include installing railings in the shower, using stand and handheld magnifiers, learning to use visual aids before they become essential, and removing tripping hazards, including low decorative furniture.

Involving Clinical Team and Family Members

The role of the physician in educating patients about lifestyle modifications is an important part of the conversation, albeit difficult at times. With an already demanding schedule, I cannot always afford the necessary chair time for comprehensive counseling. For this reason, we cross-train our staff so that they're familiar with relevant lifestyle modifications and answers to the most frequently asked questions from patients.

The effects of GA extend beyond visual function. In my experience, the three most common patient concerns include fear of disease progression, fear of losing independence, and the emotional burden of feeling isolated or misunderstood. I encourage patients to share these types of issues with family members because GA can often be confusing and difficult to manage alone. However, families should understand that the patient's vision could continue to worsen even with treatment; their role is to remain positive and supportive without denying their family member's experience.

Ultimately, lifestyle counseling for GA extends beyond discussing disease progression alone. By adapting these conversations as patients' needs change, clinicians, staff, and family members can help patients prepare for vision loss while continuing to support their function and independence. ■

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UNLOCKING CLINICAL TRIAL ENROLLMENT WITH AI SCREENING

It's not a patient population problem. It's a signal-extraction problem.

By Sunil Gupta, MD, and Joshua Koo, MS, BS





Every practice that runs clinical trials knows a particular kind of frustration. You open a new protocol for geographic atrophy, wet AMD, or diabetic macular edema, confident that patient volume will fill it. And then you watch enrollment crawl. The reflex is to assume the shortfall is a supply problem: not enough patients. However, in a busy retina clinic, the eligible patients are there—the problem isn't patient scarcity, it's patient identification.

On any given clinic day, dozens of patients have the conditions our open protocols were written to study, and the information needed to identify them as trial candidates is already in the record: acuity measurements, medical and treatment histories, laterality notes, and OCT scans. However, we still need a dependable way to identify that information quickly for each patient.

HOW WE SCREEN TODAY

For most sites, pre-screening follows one of two methods, neither of which scales. The first is physician memory or a cheat sheet. The treating specialist must keep the inclusion and exclusion criteria for every active protocol in mind and match against them in real time.

The second method is a manual pre-screener, usually a clinical trial coordinator who reviews charts ahead of clinic. This is more systematic but labor intensive, limited in reach, and vulnerable to fatigue. A coordinator can review part of the schedule carefully, but patients may still go unreviewed. Both approaches, even when staffed by capable people, have the same result: Eligible patients are missed, screen failure rates stay high, and enrollment lags.

AN AUTOMATED APPROACH

Now, an agentic AI can create a structured screening process that runs in the background for every scheduled

KEY TAKEAWAYS

- Current clinical trial screening methods rely on physician memory or a manual pre-screener, often leading to missed eligible patients, high screen failure rates, and lagging trial enrollment.
- An investigational AI model can automatically flag eligible candidates, allowing the physician to initiate the trial conversation and potential formal screening on the same day.
- Using the AI system allowed the Retina Specialty Institute to bring a protocol live in about 4 weeks.



Figure 1. This diagram illustrates the five-stage AI screening funnel that runs automatically in the background for every scheduled patient. Counts shown are illustrative. Abbreviation: LLM, large-language model.

patient. The framework we have been working with organizes screening into five stages (Figure 1).

Stage 1: Intake

Every patient on the day's schedule enters the screening process automatically, and the work begins before the clinic doors open.

Stage 2: Extraction Filter

A broad extraction filter casts a deliberately wide net, comparing structured data such as acuity ranges and prior treatment history against protocol criteria. This stage is fast, rule based, and consistent, built to keep candidates in rather than screen them out prematurely.

Stage 3: AI Deep Filter

The third stage is where the real value lies. A large-language model reads the free text of the clinical note and pulls out diagnosis history, prior treatments, laterality, and disease duration, then maps that language against each protocol's inclusion, exclusion, and study eye requirements. Anything ambiguous is flagged for physician review. In addition, image-analysis models quantify pathology from OCT and retinal images, measuring geographic atrophy lesion size, fluid, and layer integrity, and returning objective values to check against protocol thresholds.

Many such models now exist, and they take much of the subjectivity out of the eligibility question. The system reads every chart and measures every image, for every patient, every day.

Stage 4: Physician Review

Patients who clear the deep filter arrive with a short eligibility summary delivered at the point of care. In our workflow, the candidate list also goes out the evening before clinic as a secure summary to the treating physicians and technicians, and a brief eligibility note is placed in the chart (Figure 2). The physician reads the reasoning and makes the final call. The trial conversation is prompted by evidence, and clinic flow stays intact.

Stage 5: Formal Screening

Confirmed candidates move to formal, pre-qualified screening. Using this process, screen failures drop and coordinators can spend their effort on genuine candidates instead of long shots.

THE TREATMENT-NAIVE CONSULT

Many protocols require a treatment-naive study eye, and those patients arrive as new consults with thin records and a one-visit window. A referral note may be all the chart holds the night before, and if the visit ends with a standard-of-care injection, eligibility is gone. Thus, the system runs a second, faster loop for new patients. Referral packets are parsed the evening before, and consult slots whose visit reason suggests a naive-eligible diagnosis are placed on a watch list. The screening and trial conversation then happen on the day of the visit. OCT and fundus images are quantified within minutes of capture, and the eligibility flag reaches the physician before the treatment decision is made, with a reminder that any same-day injection closes the protocol window.

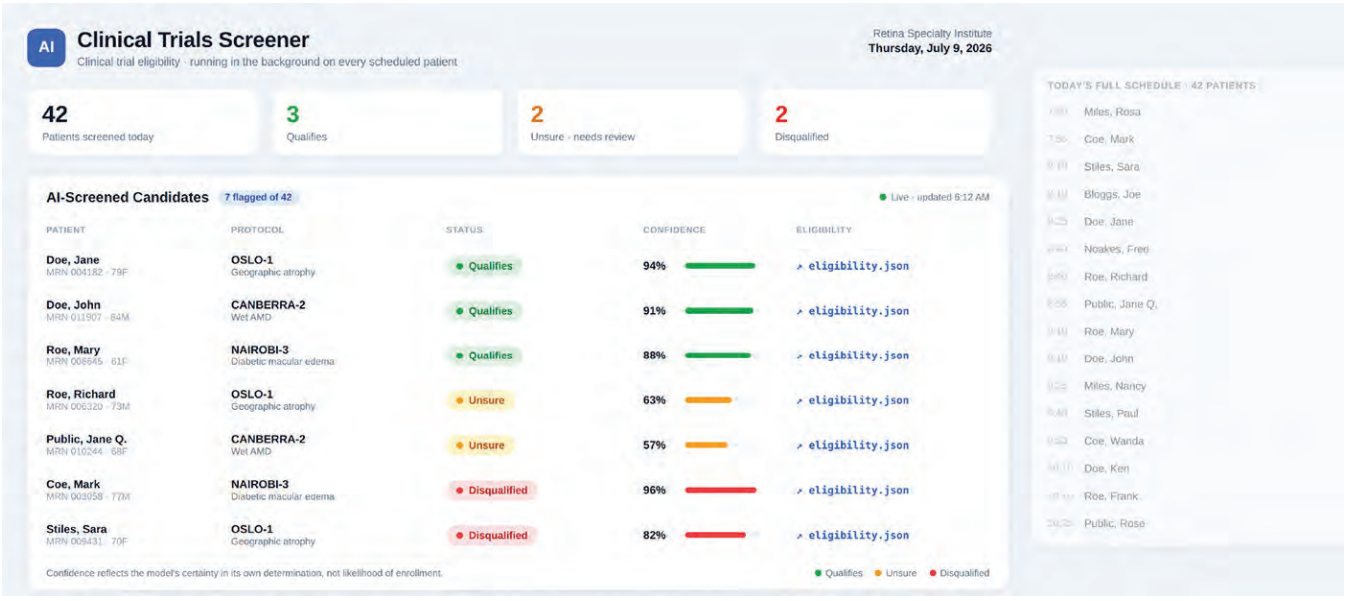


Figure 2. This is an illustrative point-of-care view of the AI pre-screener, which has flagged candidates by eligibility status and model confidence for physician review. All patient names, medical record numbers, and study names shown are fictional and for demonstration only.

COMPLIANCE CONCERNS

Reviewing existing records to identify prospective participants is a well-established recruitment activity that Institutional Review Boards (IRBs) routinely approve, and HIPAA allows it under the preparatory-to-research provision. The review must stay inside the practice, distribution must be secure and limited to the care and research team, and no protocol-specific procedure can happen before informed consent is signed.

With our system, the treating physician makes first contact. The AI's output is a flag for review, never a determination, and the chart language reflects that, as patients often read their own notes. Every pre-screen is logged automatically, which sponsors increasingly expect, and patients who decline are marked so they are not approached again. Sites adopting a similar workflow should confirm that AI-assisted pre-screening is described in their IRB-approved recruitment plan and that any vendor handling patient data operates under a business associate agreement.

WHAT ACTUALLY CHANGES

In practice, systematic extraction flags more eligible candidates than manual review. Deep filtering and image quantification reduce screen failures, because much of the disqualifying information is caught before anyone is consented. In our practice, this structured onboarding process can bring a protocol live in about 4 weeks. These numbers will vary by site and protocol, and every practice should test them against its own data.

The underlying philosophy is simple: AI does the heavy lifting, and physicians make the decisions. Patients get a fair shot at trial enrollment, practices build durable enrollment pipelines, and cleaner candidate selection and lower screen failure rates shorten timelines and improve data quality.

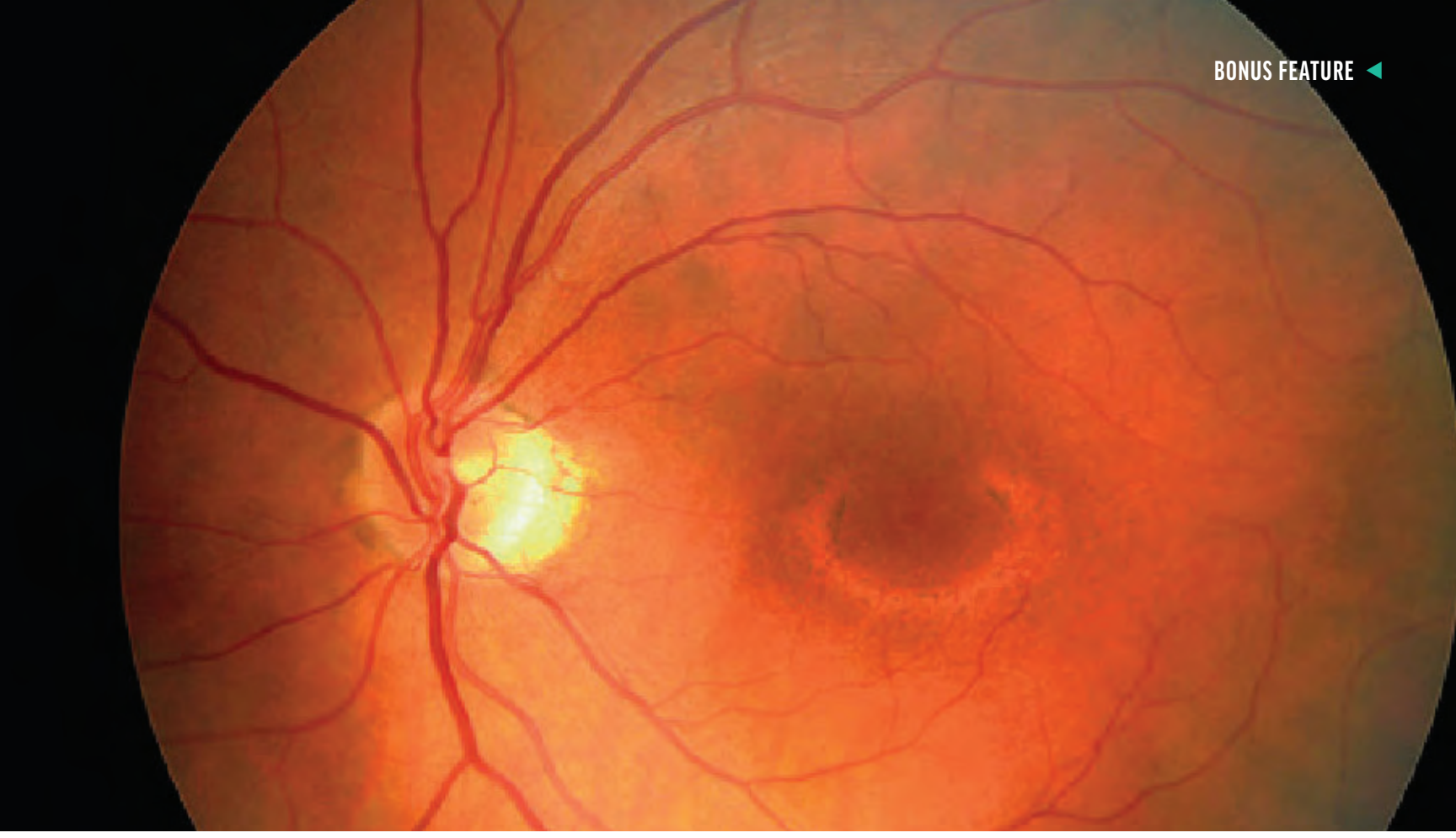
Rather than requiring more patients in the practice, this workflow is designed to identify the patients we already see. Your next enrollee is likely on tomorrow's schedule. Is your process built to recognize them before they walk back out the door? ■

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AN UPDATE ON HYDROXYCHLOROQUINE RETINOPATHY SCREENING





In 2025, the AAO released updated guidelines for screening; Here's what you need to know.

BY BONNIE HUANG, MD, AND NITA VALIKODATH, MD

Hydroxychloroquine is used to treat systemic lupus erythematosus, rheumatoid arthritis, sarcoidosis, and other autoinflammatory and dermatologic conditions.[1] In addition, researchers are investigating its potential use as an adjunct cancer therapy.[1] The recommended dose is < 5 mg/kg/day based on real body weight, which originates from a study by Melles et al showing that the likelihood of toxicity was < 1% within 5 years and < 2% after 10 years of treatment with hydroxychloroquine.[2] High doses, long duration, and risk factors such as age, renal disease, tamoxifen use, or underlying macular disease can cause retinal toxicity with the use of hydroxychloroquine, with damage first occurring in the photoreceptors and outer retina, and eventually the retinal pigment epithelium (RPE).[3] The classic pattern of hydroxychloroquine toxicity is the development of bull's-eye maculopathy caused by parafoveal RPE depigmentation (Figure 1).[4]

However, this is a late manifestation of toxicity, and the goal of the AAO's Screening Guidelines for Hydroxychloroquine Retinopathy is to recognize early evidence of toxicity to prevent vision loss.[5]

In October 2025, the AAO updated its 2016 guidelines on screening for hydroxychloroquine toxicity.[5,6] In this article, we highlight the changes you need to be aware of.

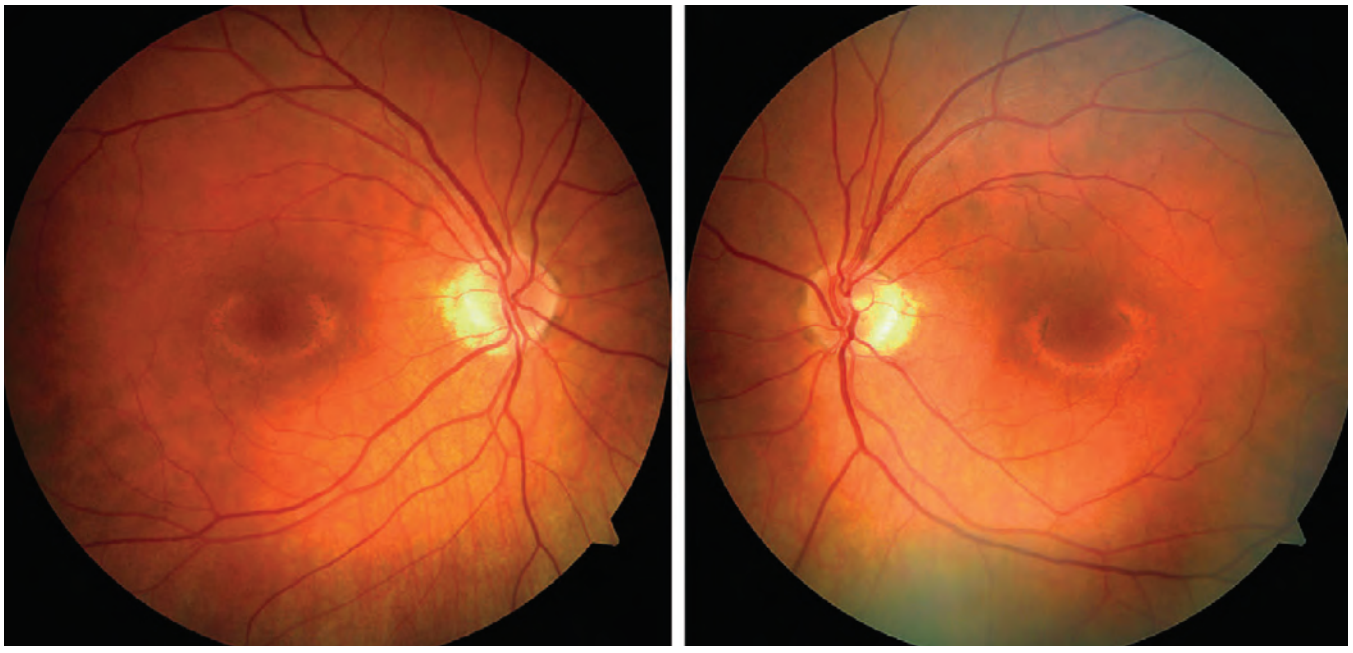


Figure 1. Bull's-eye maculopathy from hydroxychloroquine use. Reprinted with permission from Modi et al.[4]

PRIMARY SCREENING TESTS

The previous 2016 AAO guidelines recommended automated visual fields and spectral-domain OCT (SD-OCT) as the primary tests for routine screening; multifocal electroretinography (mfERG) and fundus autofluorescence (FAF) were recommended as adjunct tests to obtain as needed.[6]

The 2025 guidelines still recommend SD-OCT as one of the primary tests for screening, but they no longer recommend visual fields as a primary screening modality due to its subjectivity and wide variability.[5] Instead, they now recommend widefield FAF in addition to SD-OCT as primary screening tests.[5] SD-OCT can show characteristic retinal changes from hydroxychloroquine damage, including initial outer retinal thinning. It can also document later parafoveal patterns of damage most often seen in European patients, and pericentral patterns of disease most often seen in East Asian patients.[7] For detecting pericentral patterns of damage, widefield FAF is particularly helpful for imaging beyond the central macula. Early signs of toxicity on FAF are represented by areas of increased autofluorescence, while more severe signs of toxicity are visualized as dark areas on FAF due to missing photoreceptors and damaged RPE (Figure 2).[8]

SECONDARY SCREENING TESTS

Visual fields are now recommended as a confirmatory test that can be performed as needed and should include both central and peripheral testing (eg, 24-2C test). Another secondary test is mfERG, which examines responsiveness of the retina to light and can reveal ERG depression in parafoveal or extramacular areas. Tests not recommended for annual screening purposes include fundus examination and photography (visible damage on examination/photography implies an advanced stage of RPE damage), OCT angiography (vascular changes on OCT angiography suggest severe macular damage), and color vision testing (not sensitive or specific for hydroxychloroquine toxicity).[5]

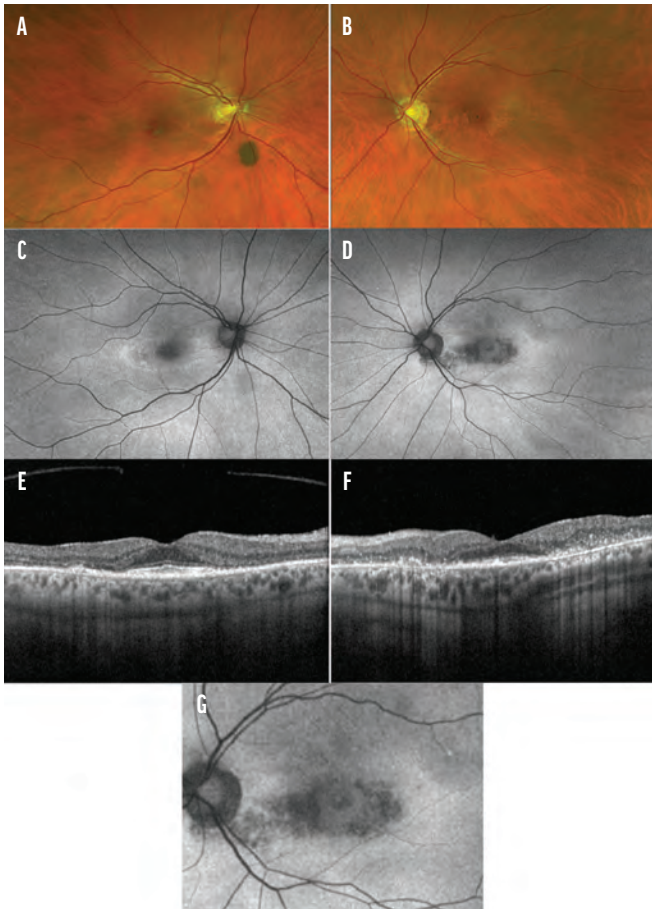
SCREENING TIMELINE RECOMMENDATIONS

The 2016 guidelines recommended a baseline fundus examination to rule out any underlying disease or preexisting retinal damage before starting hydroxychloroquine and only obtaining SD-OCT and visual fields if maculopathy is present.[6]

The 2025 guidelines recommend SD-OCT and widefield FAF in addition to the fundus examination during the baseline screening for comparison with later imaging.[5] The new guidelines also recommend annual screening with SD-OCT and widefield FAF upon initiation of hydroxychloroquine. However, during the first 5 years of hydroxychloroquine use, annual screening can be deferred if there are no significant risk factors for retinopathy, including renal disease, concurrent tamoxifen use, and starting hydroxychloroquine after 45 years of age.[9]

NEW DIAGNOSTIC TECHNOLOGIES

Novel imaging technologies are under investigation for their potential utility in hydroxychloroquine screening, such as adaptive optics (AO), which allows for the visualization of retinal cells in high resolution. Jorge et al compared individuals with no history of hydroxychloroquine use to individuals on hydroxychloroquine who had no



Images courtesy of Anjali Shah, MD, University of Michigan

Figure 2. Multimodal imaging of a patient with hydroxychloroquine toxicity demonstrating asymmetric progression. Color fundus photography demonstrates subtle pericentral pigmentary alterations in the right eye (A) and advanced, confluent pericentral macular depigmentation in the left eye (B). FAF reveals a classic hyperautofluorescent pericentral ring, signaling outer retinal stress and lipofuscin accumulation in the right eye (C) and a well-defined zone of patchy hypoautofluorescence secondary to RPE atrophy, bordered by a hyperautofluorescent transition zone in the left eye (D). SD-OCT of the right eye shows localized parafoveal ellipsoid zone disruption and external limiting membrane with foveal sparing ("flying saucer" sign) in the right eye (E) and severe, widespread outer retinal excavation, extensive ellipsoid zone/external limiting membrane loss, and thinning of the outer nuclear layer in the left eye (F). A magnified FAF image of the left macula highlights the geographic boundaries of RPE atrophy and the surrounding hyperautofluorescent ring of active photoreceptor degeneration (G).

evidence of retinal toxicity on SD-OCT, visual fields, or mfERG.[10] The researchers found that the group taking hydroxychloroquine had lower density and larger spacing of cones on AO imaging, which highlights that AO may have the potential to detect hydroxychloroquine retinal toxicity before other imaging modalities.[10]

Another area of research is in advanced autofluorescence techniques, including fluorescence lifetime imaging ophthalmoscopy (FLIO), which measures how long retinal fluorophores glow after excitation by laser pulses. While Solberg et al did not find a statistically significant difference in fluorescence lifetimes between healthy controls and patients on hydroxychloroquine therapy with no clinical retinopathy,[11] Sauer et al found that clinically normal patients on hydroxychloroquine therapy had prolonged fluorescence lifetimes compared with healthy individuals not on hydroxychloroquine, highlighting that FLIO may be able to detect hydroxychloroquine toxicity at its beginning stages.[12]

SCREEN EARLY, SCREEN OFTEN

As a key long-term treatment option for many systemic conditions, hydroxychloroquine is a relatively common finding on patients' medication lists. Thus, clinicians must be prepared to screen carefully to ensure they catch retinal toxicity early and avoid vision loss whenever possible. ■

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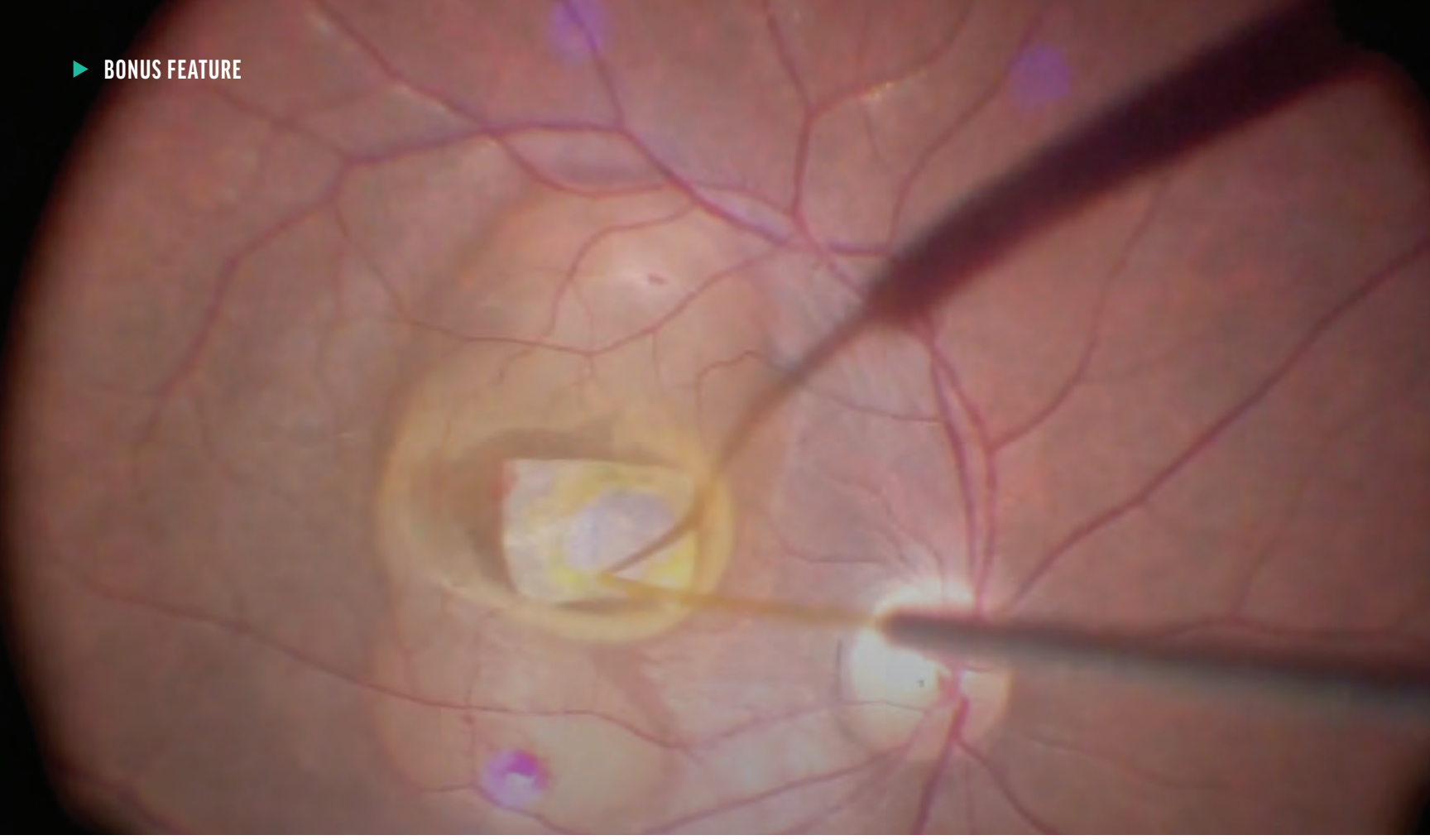
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FURTHER READING

Special AAO Report: Recommendations on Screening for Hydroxychloroquine Retinopathy (2025 Revision)

READ NOW



ADVANCED TECHNIQUES FOR IDIOPATHIC MACULAR HOLE



When internal limiting membrane peeling is not available, autologous retinal transplantation is another option to achieve anatomic closure.

BY YUSUKE OSHIMA, MD, PHD

A 78-year-old woman underwent combined 25-gauge phacoemulsification and pars plana vitrectomy with gas tamponade in a hospital setting for treatment of an idiopathic macular hole. Following surgery, she experienced worsening visual acuity and enlargement of her central scotoma. She was referred to our clinic for further evaluation.

At presentation, her BCVA was 20/25 OD and 20/400 OS. Fundus examination revealed a sheet-like material located beneath the macula (Figure 1). OCT demonstrated that the edge of the sheet was embedded within the inner retinal layers, while the macular hole remained open above the implant.

SECOND SURGERY

The patient was unaware of the nature of the implanted material. Based on its appearance, location, and the presumed surgical technique, the graft was thought to be a dehydrated or cryopreserved human amniotic membrane (HAM) implanted into the submacular space during her previous surgery.[1] Although the graft had been accurately positioned beneath the retina, the macular

hole remained open, and the patient's visual symptoms progressively worsened.

Because the patient strongly requested removal of the HAM, revision surgery was performed after a detailed discussion of the potential risks and benefits. Intraoperatively, extensive internal limiting membrane (ILM) removal from the previous surgery was confirmed. A localized retinal detachment was created around the graft via subretinal injection of balanced salt solution. Additional hydraulic dissection was then performed to separate the adhesion between the macular hole edge and the implanted membrane, allowing successful mobilization of the graft, which was subsequently excised with intraocular scissors and removed using forceps (Video 1).

As the macular hole was relatively small, we anticipated that HAM removal combined with subretinal fluid

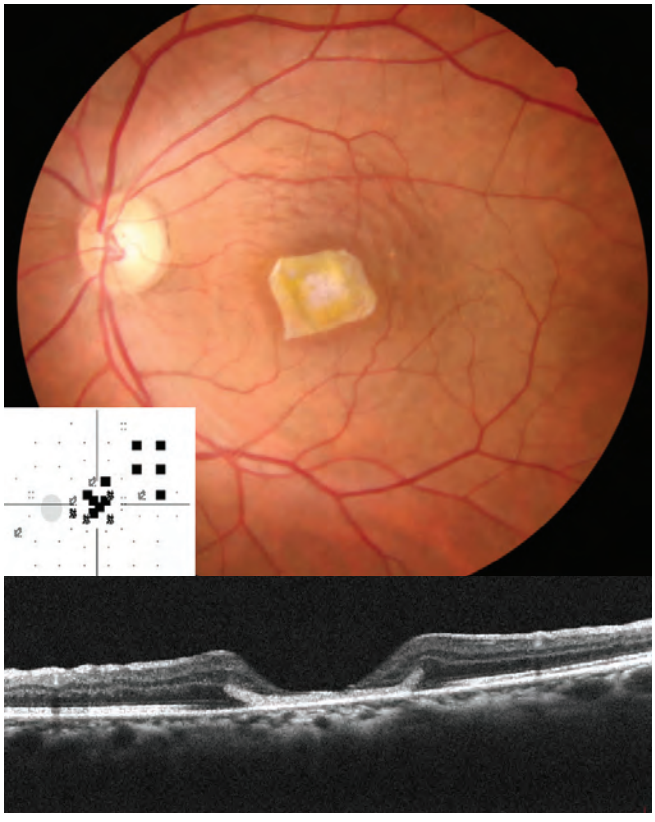


Figure 1. Fundus photography shows a HAM underneath the macula with the edge embedded within the inner retinal layers, as shown on OCT. The macular hole remained open.

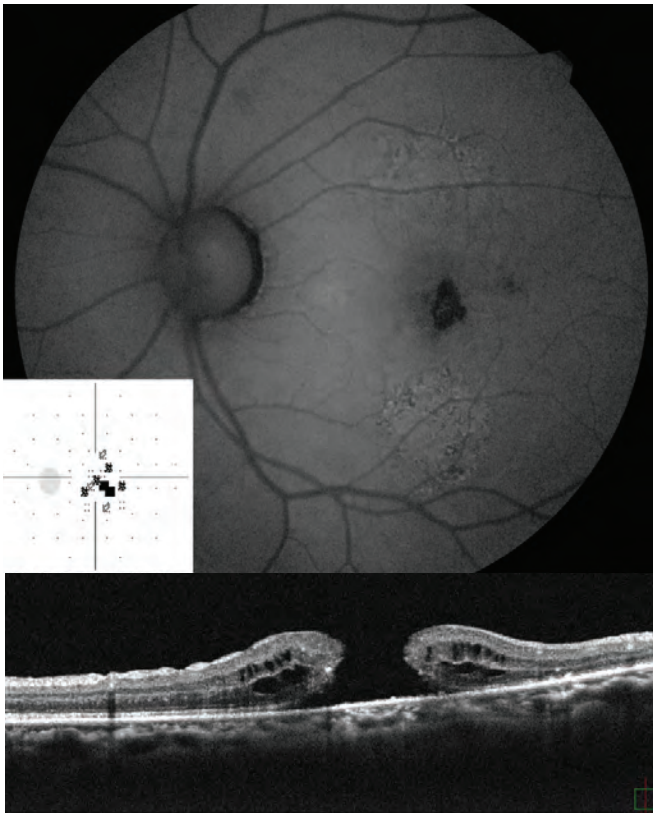
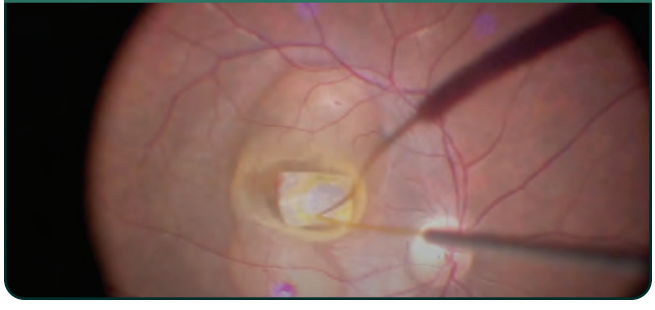


Figure 2. After the second surgery, during which the subretinal fluid application technique was used, the macular hole had yet to close.

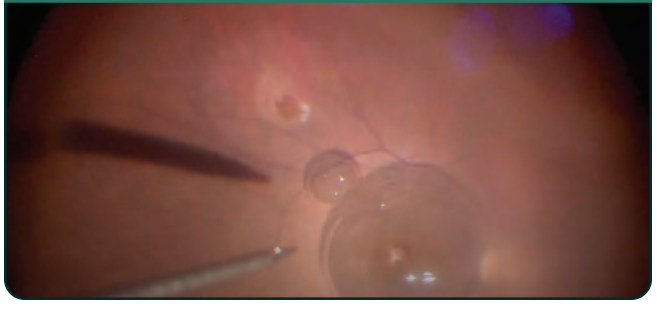
WATCH IT NOW

Video 1. Surgery to Remove Previous Human Amniotic Membrane and Repair Refractory Macular Hole



WATCH IT NOW

Video 2. Autologous Retinal Transplantation for Macular Hole Repair



WHEN CONVENTIONAL TECHNIQUES FAIL AND ILM IS UNAVAILABLE, ART REMAINS A VALUABLE SALVAGE PROCEDURE...

application would reproduce the principle of the subretinal fluid application technique for refractory macular holes described by Meyer et al.[2] Therefore, fluid-air exchange followed by long-acting gas tamponade was performed without additional tissue transplantation.

Despite our initial optimism, the macular hole remained open after gas absorption (Figure 2). Fundus autofluorescence demonstrated extensive retinal pigment epithelium (RPE) alteration surrounding the hole. We speculate that degeneration of the underlying RPE impaired retinal migration and prevented spontaneous hole closure despite successful hydrodissection.

CHANGING COURSE

Additional treatment options were subsequently considered. Because extensive ILM removal had already been performed during the primary surgery, both the inverted ILM flap technique and free ILM transplantation were not feasible. Furthermore, the hydrodissection effect achieved during the revision surgery was insufficient to close the hole.

Therefore, autologous retinal transplantation (ART), originally described in 2016 by Grewal et al, was performed.[3] The retinal graft successfully sealed the defect and achieved anatomic closure of the macular hole (Video 2; Figure 3). Her VA remained unchanged at 20/400, which was not unexpected given the chronic retinal damage, but she reported a marked reduction in the size of the central scotoma and was satisfied with the functional outcome.

LESSONS LEARNED

HAM transplantation has recently emerged as a potential option for refractory macular holes, serving as a scaffold for retinal tissue proliferation and migration.[4,5] In this case, however, the submacular embedded graft failed to achieve hole closure and appeared to interfere with normal retina-RPE interaction. Removal of the graft was technically feasible using controlled subretinal

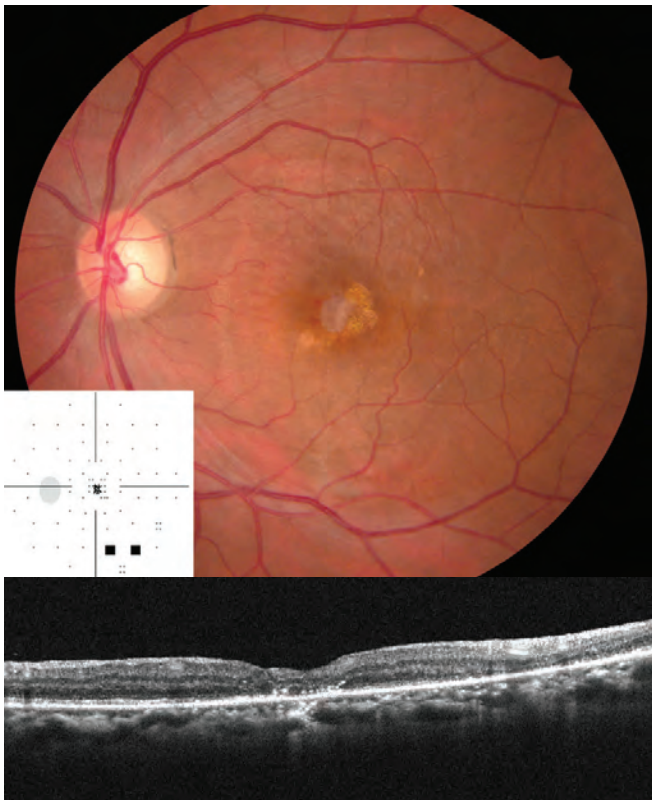


Figure 3. Finally, ART led to anatomic closure of the macular hole.

fluid application and hydraulic dissection. Nevertheless, hydrodissection alone was insufficient to achieve closure, likely because of irreversible RPE dysfunction surrounding the hole.

This case underscores the importance of appropriate graft sizing and selection of the HAM type in submacular amniotic membrane implantation. When conventional techniques fail and ILM is unavailable, ART remains a valuable salvage procedure capable of achieving anatomic closure and improving subjective visual function. ■

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FELLOWS'FOCUS

WHAT THE HIRING CONTRACT WON'T TELL YOU



It is important to understand whether a practice offers a clear path to autonomy, ownership, and a fair share of the value you will help create.

BY STEPHANIE B. ENGELHARD, MD

Choosing a first job in retina can be one of the most exciting yet unsettling transitions in your career. Until now, most major decisions have been shaped by the structure of medical school, residency, and fellowship. The first job is different. For the first time, you have real control over your career and your life.

It is easy to reduce the job search to a few requirements: salary, geography, call, and the contract itself. These factors are important, of course, but there are also a number of other critically important questions that have a larger influence on how your career will take shape, such as who makes decisions for the practice, how much control you will have over your own schedule, and how compensation and ownership structure affect your long-term economic outlook. This article gives an overview of factors to consider when evaluating contracts for partnership-track positions.

THINK BEYOND SALARY

Young retina specialists should not evaluate offers based on salary alone. A high guaranteed salary does not necessarily mean an associate is being fairly compensated for the value they bring to the practice. A lower starting salary may still be a good deal if the practice is transparent, the overhead is efficient, and the path to ownership is real. The point is not just what you make in year 1, but who controls your long-term earning potential. In a serious partnership-track position, transparency means understanding the business. You should clarify a wide range of economic factors before you commit to a job, paying particular attention to practice revenue, overhead allocation, total partner compensation, and what the buy-in purchases (Figure).

The core economic questions are simple: what value are you producing, what portion of that value are you keeping, and where is the rest going? An associate's worth to a practice is not an abstract number. It is tied directly to the revenue, clinical labor, surgical volume, call coverage, drug margins, and the overall economic value you produce. In a physician-owned practice, the closest benchmark is often partner-level economics, adjusted for volume and ramp-up period. If an associate is producing a meaningful share of partner-level work, the compensation structure should reflect that value.

ASK WHAT YOU ARE PAYING FOR

In a multi-partner group, profit retained from an associate's work may add relatively little to each partner's income while representing a substantial loss to the associate. That does not automatically make the arrangement unfair, but the associate should ask whether the tradeoff makes sense. If the practice is keeping a substantial portion of the associate's profits, that retained value should be explained. It may be reasonable, for example, if the practice provides infrastructure, staff, referral relationships, equipment, management, mentorship, and a path to partnership.

BE WARY OF LONG ASSOCIATE TRACKS

A long associate track deserves real skepticism. There may be legitimate reasons to have one, such as time to assess judgment, work ethic, clinical quality, and long-term fit, but "we are still evaluating you" should not be confused with "we are still keeping a large share of what you produce for no clear reason." If a practice truly needs a long time to assess fit, it can still design compensation such that the associate moves closer to production-based pay as their production grows.

This issue extends far beyond compensation. You should consider whether the practice behaves as a team, or whether new associates are expected to absorb disproportionate call, after-hours work, satellite coverage, and other practice burdens without meaningful support or fair compensation.

BE CAREFUL WITH JUNIOR PARTNERSHIP

Junior partnership can be reasonable, but in some cases, it is merely a label that makes limited economics sound more generous than they are. If a contract offers junior partnership, ask yourself:

Category	Questions to Ask	Score / 5
Economics and transparency	Have they explained the business clearly enough for me to understand how the practice makes money? Do I understand collections, overhead, partner compensation, and what the buy-in purchases? Do I understand what portion of the value I create I will keep?	
Profit distribution	If the practice is retaining a meaningful portion of my collections or profit, is that justified? Am I paying for real infrastructure, staff, mentorship, and a credible path to ownership, or mainly partner income?	
Associate track	How long is the associate period, and does that seem appropriate? Do the economics improve as production grows? Is the associate track about fit and development, or keeping associates in a subordinate economic position?	
Junior partnership and ownership rights	If there is junior partnership, what does it include? Do I get equity, voting rights, a meaningful share of profits, and access to ancillary revenue streams? Is there a defined path to full parity?	
Practice needs	Does this group need another future partner or another associate? Is there enough patient volume to support another physician at partner-level economics?	
Team structure and schedule	Does the practice function like a team? Is the distribution of call, after-hours work, satellite coverage, and general burden fair? What does the week look like in terms of clinic distribution, OR access, after-hours case coverage, and control over my schedule?	
Culture, people, and candor	Do the physicians and staff seem engaged, respectful, and comfortable with one another? Do different people in the practice tell the same story? When I ask hard questions, do I get clear answers, or polished but vague ones?	
Patterns, promises, and downside risk	Are books, buy-in, overhead, patient flow, parity, and timeline described clearly? Do I see a pattern of substance, or a pattern of warm language with little behind it? Could noncompetes or other restrictions trap me in a bad arrangement?	
Total Score		/40

Figure. When a job sounds good on paper, it helps to score it the same way. Look past the headline salary and ask whether the economics, autonomy, and ownership path are fair. Use the following metrics to complete this scorecard: 1 = major concern, 3 = acceptable but with reservations, and 5 = clear strength.

- Do I have real equity?
- Do I have voting rights?
- Will I get a meaningful share of profits?
- Will I have access to ancillary revenue streams?
- Is there a defined path to full parity?

Ask whether the partnership being offered includes the same financial and voting rights the senior partners hold. For example, an earlier partner may have accepted several years of reduced associate earnings in exchange for full participation in practice profits and decisions. However, these initial sacrifices made in the associate period represent a substantially different proposition if a new physician receives only a limited profit share, little voting authority, or no access to ancillary ownership opportunities available to senior partners. Before accepting the same tradeoff, ask whether you will receive the same benefits.

FIND OUT IF THERE IS ROOM FOR A NEW PARTNER

A practice that truly needs a future partner will have a plan for helping the new physician build volume. It will direct patients, share opportunities, and explain how the new associate reaches parity, and it should be able to explain how the market supports taking on a new partner.

The truth is some practices do not need another partner. They need another associate to help with call, satellite coverage, overflow clinics, and other burdens, but they may not have enough work to support another physician at partner-level economics. In those settings, the associate may find themselves competing with established partners for new patients, all while being told partnership will come "eventually." Reaching parity in these circumstances may take many years, if it happens at all. Thus, as a potential new associate, you should understand clinic distribution, satellite burden, OR access, after-hours coverage, and how much control you will have over the structure of your days. These details are easy to wave away during the interview process but hard to ignore once you are living with them.

PAY ATTENTION TO CULTURE

You are choosing your new colleagues as much as you are choosing a contract. How do the physicians and staff feel about working there? Do people seem engaged, respectful, and comfortable with one another? You will spend a lot of time in the practice environment, and the tone of it will significantly shape your day-to-day life.

With that being said, warm language about partnership, fairness, and future opportunity means very little if the details are vague. If basic questions about books, buy-in, overhead, patient flow, parity, or timeline are difficult to answer clearly, that's a sign to dig deeper.

THE CENTRAL QUESTION

Every conversation should circle back to the same question: Is this practice looking for its next partner or its next associate? Not every position needs to end in equal partnership. However, if a job is sold as a partnership-track opportunity while being structured to preserve existing partner economics, offload work, split call, and capture associate production, it is best to know before you sign.

An associate period should not mean being indefinitely subordinate, chronically overburdened, and excluded from the value you help create. In the right practice, it can be a transition to shared responsibility, real ownership, and long-term opportunity. ■

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TELEMEDICINE FOR GLOBAL ROP SCREENING



An initiative to remotely treat ROP is reaching more infants in Ghana and Ethiopia and revealing pathological distinctions.

BY AKWASI AHMED, MD, MBA; IMORO Z. BRAIMAH, MD; SADIK T. SHERIEF, MD; SARTHAK V. SHAH, MD; ARTHUR R. BRANT, MD; CINDY S. ZHAO, MD; AND DARIUS M. MOSHFEGHI, MD

Retinopathy of prematurity (ROP) is a preventable condition that remains the leading cause of childhood blindness.[1,2] In the 21st century, the third ROP epidemic has disproportionately affected low- and middle-income countries (LMICs), including many in sub-Saharan Africa. Many LMICs have expanded neonatal intensive care unit (NICU) capabilities and improved preterm infant survival rates, but health care infrastructure and resources to screen premature infants at risk of blindness from ROP have lagged.[3] Particularly in NICUs in rural areas, premature infants are still exposed to unfractionated oxygen at high rates due to limited numbers of oxygen blenders and continuous positive airway pressure machines. Access to ophthalmologists who can screen and treat ROP is also limited; in Ghana and Ethiopia, ophthalmologists are already in short supply, much less specialists in pediatric ophthalmology or retina.[4,5]

TELEMEDICINE PROGRAM TO ENHANCE ROP SCREENING

To bridge gaps in ROP screening, telemedicine-based ROP (teleROP) screening has been adopted and validated throughout LMICs and high-income settings alike, providing improved access within a country due to the concentration of specialists in major urban areas.[6] In the United States, the Stanford University Network for Diagnosis of Retinopathy of Prematurity (SUNDROP) initiative began in 2005 and has been validated to have high sensitivity and specificity for treatment-warranted ROP (TW-ROP).[7] Since 2007, the Karnataka Internet Assisted Diagnosis for Retinopathy of Prematurity model has successfully been screening infants throughout rural and semi-urban India with nonphysician imagers/graders who travel an average of 7,000 km each month.[8]

A pilot teleROP screening program was launched in 2024 as a partnership between quaternary teleROP experts at Stanford University and the Komfo Anokye Teaching Hospital. The model was then refined and scaled to three other metropolitan areas: Accra and Tamale in Ghana and Addis Ababa in Ethiopia. In the first 22 months of the program, more than 3,000 infants have been screened over nearly 13,000 visits, generating more than 185,000 images and treating 92 infants.

Such a program has been accomplished through the diligence of a team that includes eight full-time, in-country ROP coordinators and imagers, two country-wide managers, a network of local physicians (neonatologists, vitreoretinal surgeons, and pediatric ophthalmologists), and a quaternary teleROP expert at Stanford University.

After referral of infants meeting local ROP screening criteria (birth weight ≤ 2,000 g or gestational age ≤ 32 weeks in Ghana; birth weight ≤ 2,500 g or gestational age ≤ 34 weeks in Ethiopia; or medical course deemed high-risk by a local neonatologist), widefield fundus images are captured with a 120° or 130° camera. The images are graded by a local ophthalmologist within 24 hours and concurrently by a quaternary teleROP expert at Stanford University to determine appropriate follow-up. Infants deemed to have TW-ROP undergo treatment managed by the local ROP coordinators, typically initially with intravitreal bevacizumab (Avastin, Genentech/Roche), until laser to the peripheral avascular retina can be completed at an older age.

DISTINCT PATHOLOGIES ACROSS REGIONS

The pathology of ROP at the sites in Ghana and Ethiopia varied slightly from that which has been noted at Stanford University and in high-income countries generally, likely due to variations in neonatal practices in sub-Saharan African NICUs, although an underlying genetic predisposition to different phenotypes of ROP cannot be excluded.

Case Example

An infant was born at 26 5/7 weeks estimated gestational age with a birth weight of 1,000 g at an outside private NICU where inpatient ROP screening was not routinely performed because of the cost and logistical burden of transporting the screening team and widefield retinal camera. Although the infant ideally would have been screened at 30 weeks' postmenstrual age based on Ghana screening criteria, she presented through the outpatient referral network at 37 4/7 weeks' postmenstrual age with TW-ROP, including zone I plus disease in each eye (Figure A). She was treated with bilateral intravitreal bevacizumab at 37 5/7 weeks' postmenstrual age, with regression at 38 4/7 weeks (Figure B) and further regression at 40 4/7 weeks (Figure C). She later developed reactivation at 43 4/7 weeks' postmenstrual age (Figure D), underwent bilateral laser photocoagulation at 44 5/7 weeks, and was quiescent at 57 4/7 weeks (Figure E).

This case demonstrates that even delayed outpatient referral-based screening can identify and treat severe ROP in settings where universal inpatient and outpatient screening is not yet feasible.

The Need for Region-Specific Recommendations

Of note, this patient would not have met US ROP screening criteria by either her gestational age (≤ 30 weeks) or birth weight (≤ 1,500 g). These differences in ROP patterns across different international settings highlight the need for investigation of region-specific epidemiology and adoption of recommendations determined by local ROP experts.

As a corollary, a significant difference this program has noticed between the infant eyes treated in Ghana versus those treated in SUNDROP (ie, in the United States) is the absence of plus disease as a driver of TW-ROP. While only 7.5% of neonates in SUNDROP had TW-ROP driven by zone I stage 3 without plus disease, 40% of treated eyes in Ghana had treatment indications based on zone-driven disease.[9] As has also been noticed in other LMICs,[10,11] treated infants in Ghana have also been significantly older

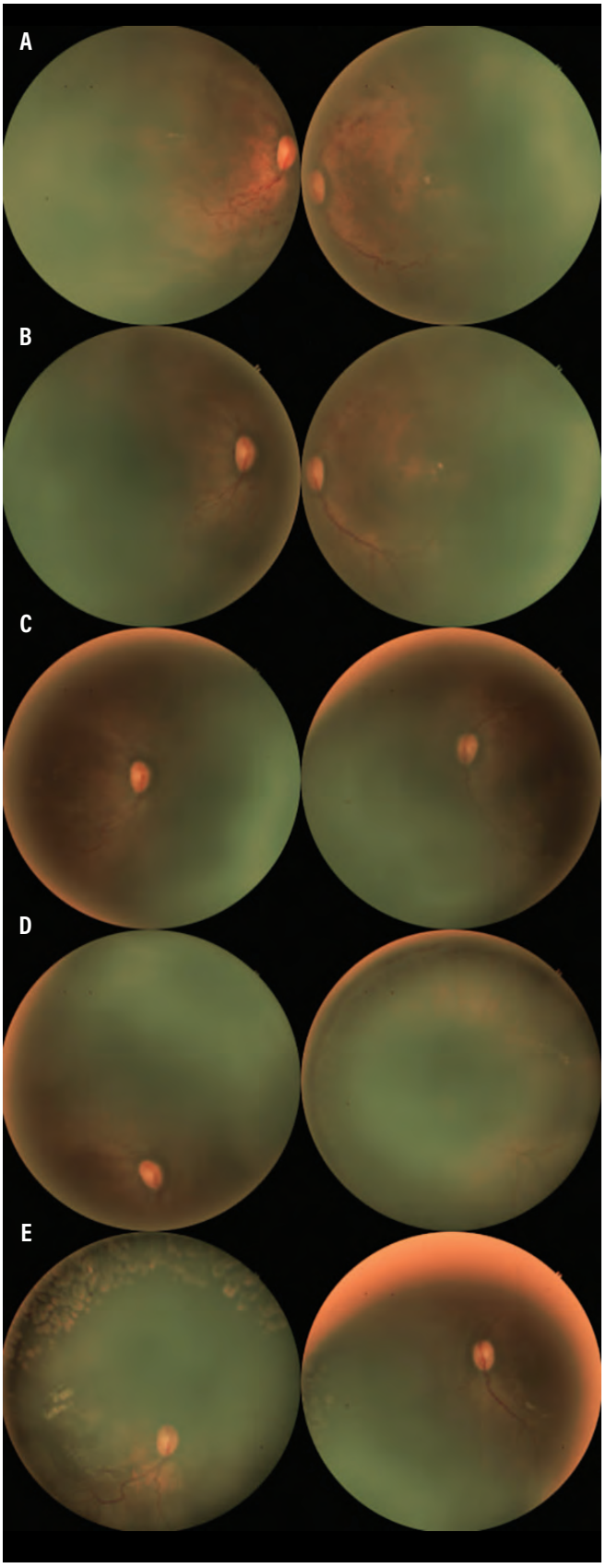


Figure. An infant presented at 37 4/7 weeks' postmenstrual age with zone I plus disease in each eye (A). Bilateral intravitreal bevacizumab led to regression at 38 4/7 weeks (B) and 40 4/7 weeks (C). Reactivation was noted at 43 4/7 weeks (Figure D), prompting bilateral laser photocoagulation. The eyes were quiescent at 57 4/7 weeks (Figure E).

and heavier at birth.[9] Aggressive ROP (AROP), which classically presents with plus disease, rapid neovascular proliferation, and lack of typical stage progression, has been observed in different phenotypes, which we have termed *typical minus plus-AROP* and *placoid minus plus-AROP*.

Another key difference is the outpatient setting in which much of neonatal care takes place. Unlike in many high-income countries, Ghana and Ethiopia have a care delivery model that relies heavily on follow-up by families from the outpatient setting. Due to resource capacity, many infants are discharged from the NICU shortly after they are weaned off oxygen, often at 34 to 35 weeks, the period during which they are at highest risk for active ROP. Hence, caregiver education, robust referral systems, and careful tracking for compliance by ROP coordinators is crucial.

ROP Grading Models

To simultaneously build local capacity for ROP screening and treatment, this program employs a dual-layer telemedicine grading model. Local ophthalmologists do the initial grading, and a teleROP expert at Stanford University contemporaneously validates the results within 24 hours. This model allows both the timely clinical decision making and parental counseling needed for patient safety and care, as well as increased autonomy of local graders over time.

AI models show promise to eventually improve screening and triaging efficiency,[12] but thorough validation will be required, especially given the regional variations in pathology.

As the program continues to reach infants at risk of blindness from ROP, its success hinges on partnerships with local physicians and an emphasis on the need for continued follow-up with parents. Treatments are readily available and often used in the same settings for adult diseases by retina specialists throughout the world. Different models may be required to adapt to unique settings; currently, our program in Ghana has a hub-and-spoke referral network, while the one in Ethiopia employs a mobile screening team.

From the perspective of cost, identifying and addressing TW-ROP at a total program cost of $450 per treated infant (~$50 for bilateral intravitreal bevacizumab) is negligible compared with the societal burden of childhood blindness.

PREVENT ROP WORLDWIDE

Through sufficient screening, improved awareness of pediatricians and neonatologists in sub-Saharan Africa, and increasing the capacity of local ophthalmologists, ROP, a preventable disease, does not need to be the leading cause of infant blindness. ■

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THE BUBBLE TECHNIQUE: VITREOUS BASE SHAVING IN PHAKIC EYES




A novel approach to circumvent the challenges of retinal detachment repair in this patient population.

BY NIVEDITA MURALI, DNB, FICO, FVRS, FAICO, AND NARESH BABU KANNAN, MS, FNB, MBA, FASRS

Vitreous base shaving is essential for a successful surgical outcome in retinal detachment (RD) repair.[1] However, this maneuver can be challenging in phakic eyes. Primary hurdles include difficulty assessing the instrument depth relative to the crystalline lens, limited visibility of the extreme periphery, and navigating complex visualization under air. To address these specific issues, we propose a maneuver we have termed the *bubble technique.*

THE IMPORTANCE OF VITREOUS BASE SHAVING

Residual vitreous base can act as a scaffold for proliferative vitreoretinopathy (PVR) formation after RD repair, and subsequent contraction of the remnant vitreous can lead to formation of new breaks.[1,2] Therefore, thorough base shaving is essential. The goal is to remove as much vitreous as possible without causing iatrogenic breaks.

To achieve this, surgeons can employ scleral indentation by the surgical assistant or use chandelier illumination to allow indentation by the surgeon. A wide-angle viewing system enables visualization of peripheral retina without the need for indentation. In addition, employing a high cut rate and low vacuum facilitates controlled removal of vitreous base. The advantages of vitrectomy under air are well known.[3]

THE BUBBLE TECHNIQUE: STEP-BY-STEP

To shave the vitreous base in phakic eyes while maintaining good visualization, surgeons can proceed with the following steps:

1. Perform standard pars plana vitrectomy and induce a posterior vitreous detachment, if not already present.
2. Complete a fluid-air exchange with subretinal fluid drainage with or without the assistance of perfluorocarbon liquid.

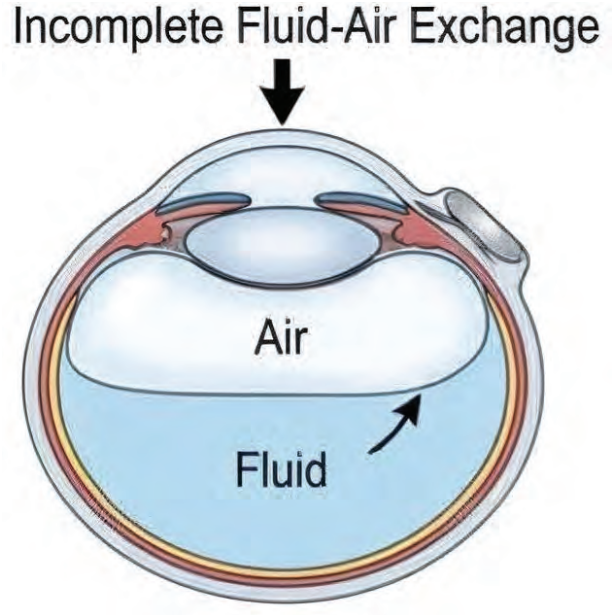


Figure. Illustration of the bubble technique: An incomplete fluid-air exchange maintains a buoyant anterior air bubble above the fluid, enabling peripheral visualization, while the distinct fluid-air meniscus provides crucial depth perception to prevent lens touch.
Note: The author used ibispaintx to create the image and Gemini 3.1 Pro (Google) to refine it.

3. Restart the fluid infusion to achieve an intentional, incomplete removal of air. The residual air bubble should be single and large enough to allow clear visualization of the periphery (Figure).
4. Upon scleral indentation, the air bubble dynamically occupies the area between the indented retina and the posterior lens capsule. This configuration places the air bubble above the fluid, which facilitates excellent peripheral visualization while maintaining critical depth perception for safe use of instruments.

EMPLOYING THE BUBBLE TECHNIQUE FACILITATES VITREOUS BASE SHAVING WHILE EFFECTIVELY AVOIDING COMPLICATIONS, SUCH AS LENS TOUCH, AND AFFORDING THE SURGEON THE DISTINCT ADVANTAGE OF EXCELLENT PERIPHERAL VISUALIZATION UNDER AIR. HOWEVER, THE SURGEON MUST BE AWARE OF THE LIMITATIONS ASSOCIATED WITH THIS TECHNIQUE

Note: This adjunctive step is intended for final base shaving only after initial peripheral debulking has been completed under fluid. Although the air tamponade compresses the residual vitreous closer to the retina, the resulting optical interface clearly demarcates the tissue boundaries, facilitating safe and precise removal. Importantly, this technique does not alter the physical constraints of the phakic lens and does not safely permit "crossing" the eye with instruments. To address this, a skilled assistant must indent the ora serrata with a posterior "rolling" motion, rather than direct inward pressure; this method safely displaces the vitreous base posteriorly and inward toward the central cavity, making it safe to approach. Finally, because the vitrectomy cutter inevitably aspirates air despite low vacuum settings, the surgeon must actively monitor and occasionally supplement the bubble volume to maintain optimal visualization.

5. Apply endolaser in difficult peripheral areas concurrently during the base shaving process in the presence of the air bubble. Upon successful completion of vitreous base shaving, proceed with routine endolaser and final endotamponade.

UNDERSTANDING THE OPTICS

The success of this technique relies heavily on fluid dynamics and optical physics. Because the specific gravity of air is less than that of balanced salt solution, air exhibits high buoyancy. In a supine position, this buoyancy causes the air to float in the anterior vitreous cavity in the presence of fluid. Dynamic scleral indentation displaces the peripheral retina inward bringing the target area into the accessible surgical field within the air medium. As the light rays reflect off the retina and exits the eye, they travel from the air medium (refractive index = 1.00) into the crystalline lens (refractive index = 1.40). Because of this large difference in refractive index at the convex posterior lens capsule, the posterior capsule acts as a strong converging optical surface, causing the extreme peripheral light rays to bend inward and allowing them to pass through the pupillary aperture. Thus, the bubble technique can overcome standard visual hindrances, such as the iris. Furthermore, the fluid-air interface acts as an optical reference plane, providing visual cues to gauge the exact location of the cutter or laser probe relative to the lens.

USE PHYSICS TO YOUR ADVANTAGE

Employing the bubble technique facilitates vitreous base shaving while effectively avoiding complications, such as lens touch, and affording the surgeon the distinct advantage of excellent peripheral visualization under air. However, the surgeon must be aware of the limitations associated with this technique, such as the dynamic fluidics altering the bubble volume and the proximity of the vitreous to the retina under air. ■

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HOW TO IDENTIFY AND STOP REVENUE LEAKS



Take a close look at your current processes to find ways to improve profitability.

BY JESSICA SCHROEDER, MPH, CPC, OCS, OCSR

As the year winds down, many retina specialists are anticipating another round of reimbursement cuts from payers. Practices face the continual challenge of having to do more with less while trying to remain profitable. There will always be a push to find new revenue streams, but it may behoove you to also ensure that your current revenue streams are performing their best. Taking a close look for both human and process errors could improve your bottom line.

Start with a broad look at your revenue cycle process. Remember, everyone in the practice is involved, not just your billing and coding staff. From patient intake to back-end claims, there are many areas to investigate for process improvement opportunities (Figure).

REVIEW INTERNAL PROCESSES

To confirm that your internal processes are functioning as intended, it is important to review written procedures and determine whether they are being followed. These may include patient intake, insurance card collection, technician screening, or billing and coding. In addition, even if they are being followed as written, it is possible that the procedures in place are no longer serving their original intent and, thus, causing process issues.

A good starting point would be to a review your historical write-offs and claim denials. Recurring patterns in these areas often reveal where a process is quietly failing—a step that is being skipped, a change in a payer's rule that is not reflected, or a particular workflow that no longer aligns

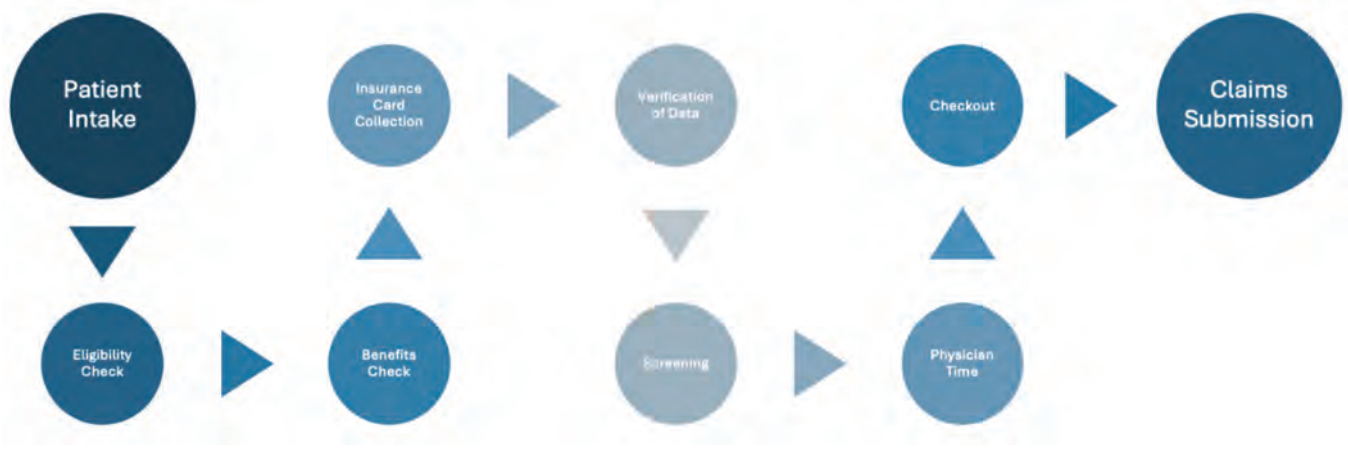


Figure. Explore your full revenue cycle process to ensure continuity and look for areas that need improvement.

TABLE. WHERE REVENUE LEAKS
Five Weak Points to Watch

1	Eligibility not verified in time
2	Missing or late authorizations
3	Documentation gaps
4	Coding errors
5	Slow accounts receivable/denial follow-up

with how the practice operates. Following these trends back to their sources will often point you toward the processes most in need of attention.

If there is an internal process to write off bundled denials without a coding review, you may be leaving reimbursement on the table. For example, at one point payers were inappropriately denying examination services when billed with diagnostic testing. Any claim that included a retina OCT, CPT 92134, was receiving a denial for the examination, stating it was bundled with the special ophthalmic services. Identifying a payer issue such as this one early would enable prompt action, consistent internal tracking, and faster reimbursement once resolved.

IDENTIFY WEAK POINTS

Once you understand how your processes flow, look closely at the points where revenue tends to leak (Table). A common example of a weak point is eligibility checks that are not run in a timely manner, which leave claims exposed to preventable denials due to change or termination of insurance. Authorizations obtained too late or missed entirely for the services that require them could leave a practice responsible for high drug costs if not reimbursed.

Other examples include documentation gaps for screenings or physician time that prevents billing a higher-level Evaluation and Management or Eye code the encounter would otherwise support. For example, if a physician is deciding whether to bill CPT 99213 or CPT 92014, but confrontational visual field testing or motility was not performed as required for a comprehensive examination, the only option left may be the one that reimburses less.

Confirm your team is using the most updated resources. Coding errors stemming from outdated references, missed modifiers, or misapplied guidelines could cause denials or audit failures. A common retina claim error is a claim denial for unit of measure. Billing for intravitreal anti-VEGF drugs, for example, often requires an "ML" unit of measure in box 24a of the claim, reported as a liquid medication measuring the volume in mL. Often, something as simple as a default system setting that incorrectly populates "ME" for milligram can cause a denial for N816 ("Missing/Incomplete/Invalid NDC Unit of Measure"). This small systems error can lead to significant recoupments or future denials.

Lastly, denial work that is queued too slowly, allowing claims to age past timely filing and appeal deadlines, may lead to lost revenue that cannot be recovered.

MAKE IT A HABIT

Process improvement should not be a one-time project. Invite the end users to participate in improvement activities, as those doing the work every day often spot the breakdowns first and come up with the most practical fixes. Foster a culture that always looks to do better and consider taking advantage of new tools such as AI automation to assist in flagging eligibility gaps, coding patterns, and prioritizing denials for follow-up.

FINAL TIPS FOR SUCCESS

A revenue cycle audit is only as valuable as the changes it drives. Keep these principles in mind as you turn your findings into results:

- Clarify priorities—address the denials and write-offs costing you the most in lost revenue before chasing smaller issues.
- Assign clear ownership for each fix, with a deadline and quantitative measure of success.
- Document your updated processes and train each team member in the practice, not just the billing and coding staff.
- Track key metrics, such as clean claim rate, denial rate, and days in accounts receivable on a regular basis, not just at year-end.
- Make the review a recurring habit so small problems get caught before they compound.

A healthy revenue cycle is not the result of a single fix, but rather the payoff of steady attention. ■

AI disclosure: Claude Sonnet 5 (Anthropic) was used to review grammar and check for spelling. Content was otherwise created, reviewed, and approved by the author.

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FURTHER READING

Using E/M and Eye Visit Codes When Surgical Reimbursement Declines

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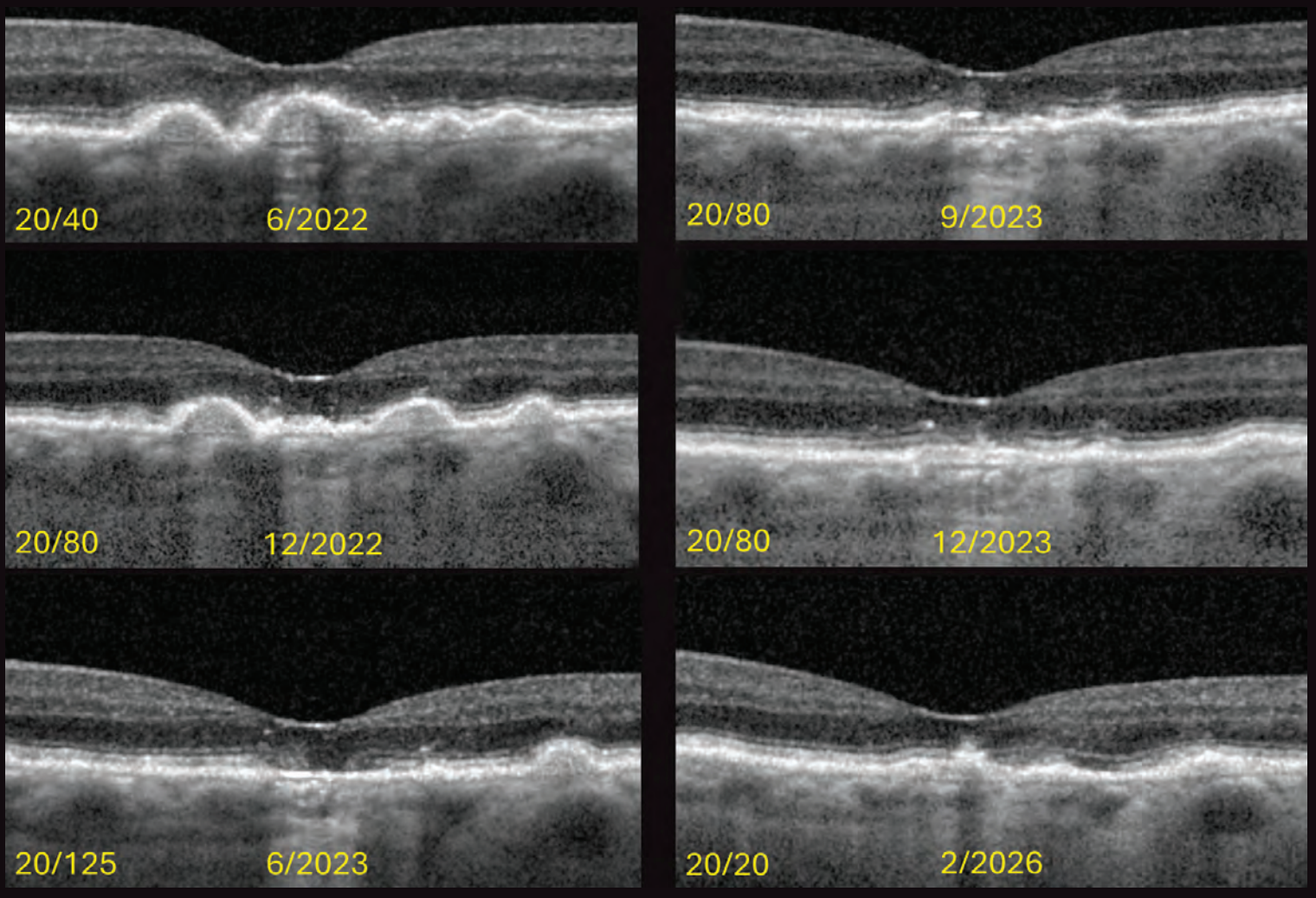


FIGURE 1

A SURPRISE REVERSAL OF AMD PROGRESSION



The outer retinal layer may be key to the development of atrophy in AMD.

BY TALISA E. DE CARLO FOREST, MD

A 73-year-old woman with intermediate AMD presented with a subfoveal drusenoid pigment epithelial detachment (PED) with a hypertransmission defect on OCT and a VA of 20/40 OS (Figure 1). At a 6-month follow-up appointment, the drusenoid PED was collapsing, and her VA had worsened to 20/80 OS.

Six months later, retinal pigment epithelium (RPE) and ellipsoid zone (EZ) atrophy of > 250 µm was noted with intact overlying outer retina, and a VA of 20/125 OS. However, 6 months later, the RPE had reformed, the EZ was recovering, the hypertransmission defect had resolved, and VA improved to 20/80 OS. Fundus imaging demonstrated early atrophy that seemed to resolve over time (Figure 2).

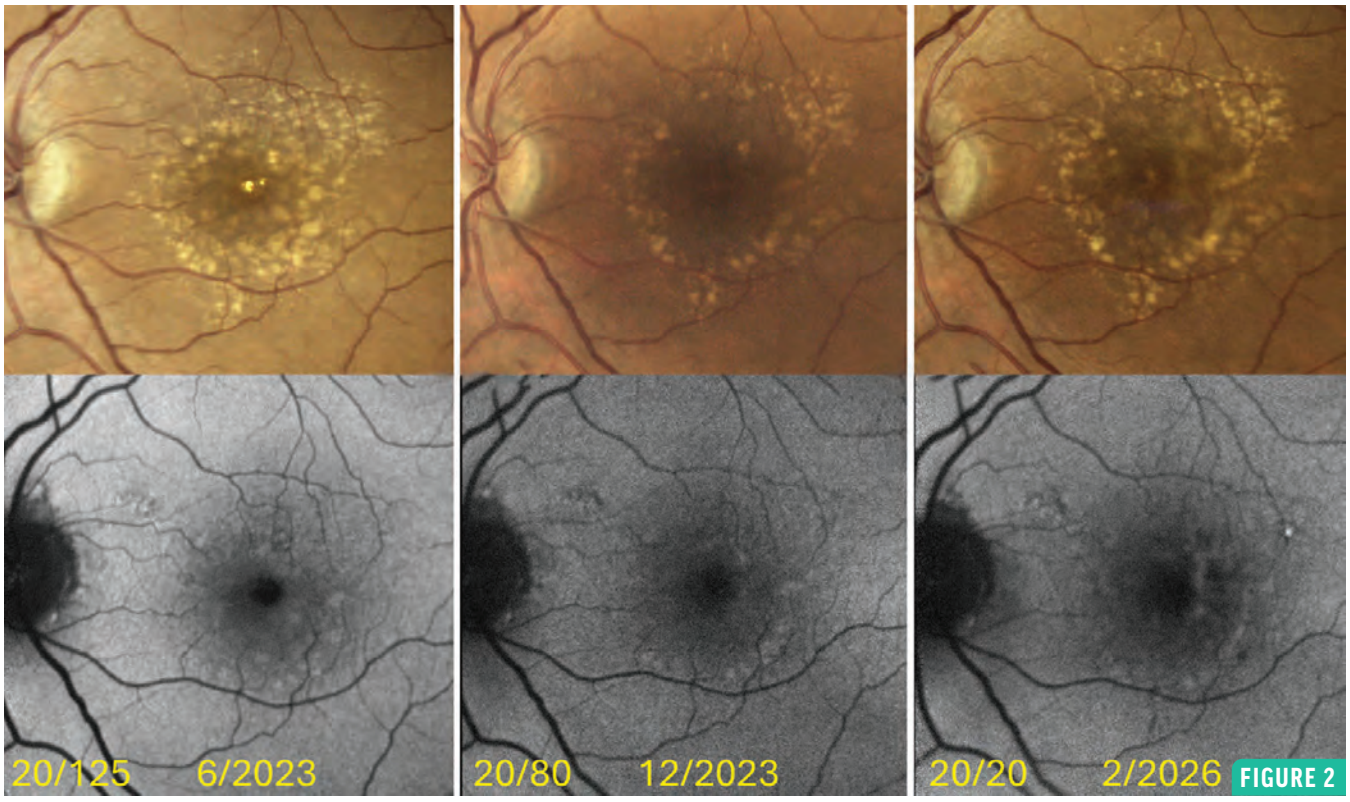


FIGURE 2

THE MAINTENANCE OF THE OUTER RETINAL LAYER IMPLIES THAT THE PHOTORECEPTOR CELLS WERE POSSIBLY STILL VIABLE. WHILE FURTHER STUDY IS NECESSARY, THIS CASE SUGGESTS THAT OUTER RETINAL LAYER THINNING MAY BE KEY FOR DEVELOPING ATROPHY.

Her VA gradually improved to 20/20 OS 3 years later with overall improvement in OCT layers and no choroidal neovascularization on OCT angiography. Of note, the patient did not receive AMD treatment, nor did she experience any change in her medical history. It's worth noting that although anticomplement therapy may have been reasonable, the patient did not yet met the criteria for geographic atrophy.

THE ROLE OF THE OUTER RETINAL LAYER

The classification of atrophy meetings (CAM) criteria describe precursor stages for inevitable geographic atrophy development.[1,2] The present case, in which the outer retinal layer appeared unaffected while the RPE and EZ were disrupted, did not fit into the CAM classification.

The maintenance of the outer retinal layer implies that the photoreceptor cells were possibly still viable. While further study is necessary, this case suggests that outer retinal layer thinning may be key for developing atrophy. ■

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WINNING THE BATTLE FOR LIFE, EYE, AND VISION



The field has evolved substantially to offer treatments for uveal melanoma beyond enucleation, but we still have far to go in preserving vision.

BY ANTONIO BECHARA GHOBRIL, MD, FEBOOPHTH, FMH; SALAAM BOTROS, MBBS; AND CAROL L. SHIELDS, MD

The management of posterior uveal melanoma has undergone a remarkable journey. The first battle was directed toward saving the patient's life with detection of uveal melanoma when the tumor is smaller and genetic information demonstrates fewer high-risk mutations.[1,2]

In the past, enucleation was the only treatment option. Today, plaque radiotherapy and proton beam radiotherapy are widely used, while gamma knife and CyberKnife (Accuray) radiotherapy are available in select centers. These globe-conserving therapies allow preservation of 85% of eyes with uveal melanoma and achieve excellent local tumor control, with recurrence rates of only 2% to 5%.[3] Despite these achievements, preserving the eye does not necessarily mean preserving vision.

Even with successful local tumor control, radiation maculopathy, radiation papillopathy, and other radiation-related complications remain principal causes of long-term visual impairment. Months or even years after treatment, radiation can progressively damage the macula and optic nerve, leading to irreversible vision loss (Figure). The current battle is therefore not simply to control the tumor, prevent metastasis, and retain the globe, but also to preserve functional vision whenever possible.

VISION DECLINE AFTER PLAQUE RADIOTHERAPY

We performed an analysis of 4,000 patients with plaque-irradiated uveal melanoma who experienced a loss of at least 15 letters of vision, roughly 3 lines on the visual acuity chart.[4] All patients were managed in the pre-anti-VEGF era, so there were no injections or treatments for vision decline. We found that vision loss often began early: 30% of eyes lost at least 15 letters within 1 year, 48% by 2 years, and 60% by 3 years. This increased to 73% at 5 years and 82% at 10 years. Overall, vision loss occurred at a mean of approximately 25 months, suggesting the first few of years after treatment are a particularly important period for close monitoring.[4]

Tumor size also mattered. Larger tumors were associated with earlier and more frequent vision loss of at least

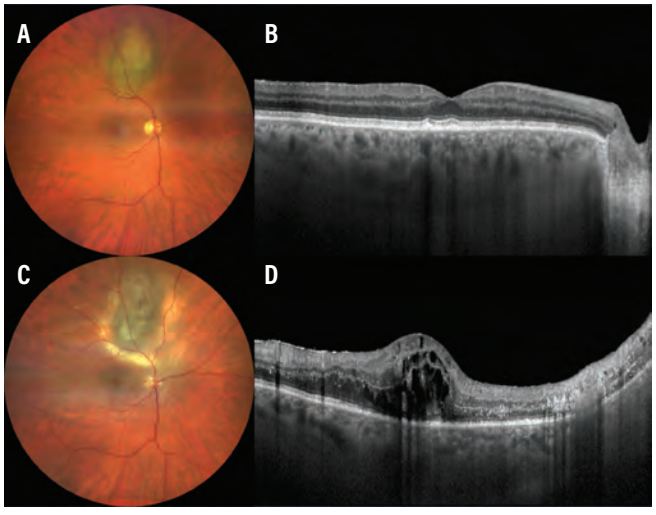


Figure. Multimodal imaging of a superotemporal choroidal melanoma in the right eye of a patient before and after plaque radiotherapy. Baseline color fundus photography demonstrates a superotemporal choroidal melanoma in the right eye (A). Corresponding OCT at baseline shows a preserved foveal contour without cystoid macular edema or subretinal fluid (B). Color fundus photography obtained 2 years after plaque radiotherapy shows the regressed superior paramacular tumor with surrounding retinal exudation and retinal pigment epithelium atrophy, additional cotton-wool spots at the optic disc, optic disc hemorrhage, and edema, consistent with radiation papillopathy. Also note the presence of numerous scattered dot hemorrhages, predominantly involving the superotemporal retina, consistent with radiation retinopathy (C). Corresponding OCT obtained at the same follow-up visit demonstrates severe cystoid macular edema and loss of the normal foveal contour, consistent with radiation maculopathy (D).

OUR GROUP IS NOW STUDYING PROPHYLACTIC INTRAVITREAL ANTI-VEGF INJECTIONS AFTER PLAQUE RADIOTHERAPY TO DETERMINE WHETHER SCHEDULED TREATMENT CAN REDUCE RADIATION-RELATED RETINAL DAMAGE AND VISION LOSS...

15 letters, occurring in 56% of small tumors (0 to 3 mm in thickness), 62% of medium tumors (3.1 mm to 8 mm), and 70% of large tumors (> 8 mm) over a mean follow-up period of 69 months. For small tumors, vision loss occurred at a mean of 33 months, for medium tumors at a mean of 25 months, and for large tumors at a mean of 13 months. Put simply, visual decline after plaque radiotherapy is common, accumulates over time, and occurs more rapidly in eyes with larger tumors.[4]

PATIENTS AT RISK FOR VISION DECLINE

Our second analysis of this cohort asked a practical question: Can we predict which patients are most likely to experience meaningful vision loss? On multivariate analysis, the most important risk factors for vision loss were greater tumor thickness and closer proximity to the foveola.[4] Each additional millimeter of tumor thickness increased the risk of vision loss by approximately 14%, and each millimeter farther from the foveola reduced the risk by approximately 7%.[4] Having diabetes also carried an independent increased risk for vision loss. In addition, treatment-related factors were significant, particularly greater radiation dose to the foveola and lens.

These findings divide risk into three categories: presence of comorbidities, including diabetes; characteristics of the tumor, particularly thickness and location; and the specific treatment, ie, radiation exposure to visually important structures. Tumor thickness remained particularly important for medium and large tumors, whereas foveolar proximity was most relevant for small and medium tumors. This gives clinicians a straightforward way to counsel patients: Thicker tumors, tumors close to central vision, diabetes, and greater radiation exposure all lead to a greater risk of post-treatment visual decline.[4]

Of note, many of these determinants are established well before treatment begins, including tumor thickness, location of the tumor relative to the foveola and optic disc, and patient characteristics. Although these factors cannot be changed, radiation exposure remains at least partially within our control.

RADIATION DOSE MATTERS

The third analysis we performed for this cohort focused on radiation dose to the optic disc and foveola.[5] There was no absolute dose at which vision was suddenly lost; rather, the study demonstrated a clear dose response relationship. When the optic disc received no more than 4,000 cGy, increasing the foveolar dose from ≤ 2,000 cGy to 2,001 cGy to 4,000 cGy was associated with a 71% higher risk of losing at least 15 letters. Increasing the foveolar dose further to 4,001 cGy to 6,000 cGy produced an additional increase in risk. When the optic disc dose exceeded 4,000 cGy, visual outcomes were generally poor, regardless of the foveolar dose. Thus, keeping the optic disc dose at or below 4,000 cGy and the foveolar dose below 2,000 cGy appears to offer the best chance of visual preservation. Careful treatment planning, including precise plaque and seed positioning, may help reduce radiation exposure to critical structures whenever tumor location allows.[5]

A novel strategy being explored is to reduce tumor size before plaque radiotherapy. Neoadjuvant therapy could permit lower radiation exposure to the foveola and optic disc.[6,7] Darovasertib, an oral protein kinase C inhibitor, has shown early evidence for tumor reduction before definitive treatment of primary uveal melanoma.[7] Tebentafusp improves overall survival in HLA-A*02:01 positive metastatic uveal melanoma, but it has yet to show efficacy as a neoadjuvant tumor-shrinking therapy.[8]

Although still investigational, neoadjuvant therapy to reduce tumor size prior to radiation may represent a new paradigm that could expand opportunities not only for globe preservation, but also for vision preservation.

WHAT COMES NEXT?

Our three studies sought to define how often vision is lost, which patients are most vulnerable, and how radiation dose affects risk.[4,5] They also provide a large, historical pre-anti-VEGF cohort for comparison with newer strategies. Our group is now studying prophylactic intravitreal anti-VEGF injections after plaque radiotherapy

to determine whether scheduled treatment can reduce radiation-related retinal damage and vision loss.

We have learned how to save the patient's life with early detection of tumor,[1,2] and we have learned how to save their eyes using plaque radiotherapy.[3] Now, we must learn how to save their sight. ■

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

INDICATIONS AND USAGE

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

CONTRAINDICATIONS

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

WARNINGS AND PRECAUTIONS

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

ADVERSE REACTIONS

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

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

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

PM: SYFOVRE monthly; PEOM: SYFOVRE every other month

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

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

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

USE IN SPECIFIC POPULATIONS

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

PATIENT COUNSELING INFORMATION

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

Manufactured for:
Apellis Pharmaceuticals, Inc.
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Waltham, MA 02451

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Treat Today
For Tomorrow, Tomorrow, and Tomorrow

SYFOVRE®
(pegcetacoplan injection)
15 mg / 0.1 mL



Only SYFOVRE has 5 years of clinical trial data—longer than any other FDA-approved treatment for GA.[1-4]

Patients treated with SYFOVRE achieved a reduced rate of GA lesion growth vs sham pooled in clinical trials at Year 2,* with long-term data out to 5 years. Help your patients look forward to what's next, instead of what's left behind.[1,2]

*At Year 2, SYFOVRE reduced GA lesion growth by **18% and 22%** with monthly dosing and **17% and 18%** with every-other-month dosing vs sham pooled.[1]

Start protecting your patients' tomorrows at **TreatGAtoday.com**

Study design: SYFOVRE safety and efficacy were assessed in OAKS (N=637) and DERBY (N=621), multicenter, 2-year, Phase 3, randomized, double-masked trials. Patients with GA (atrophic nonexudative age-related macular degeneration), with or without subfoveal involvement, secondary to AMD were randomly assigned (2:2:1:1) to receive 15 mg/0.1 mL intravitreal SYFOVRE monthly, SYFOVRE every other month, sham monthly, or sham every other month for 2 years. Change from baseline in the total area of GA lesions in the study eye (mm^2) was measured by FAF. SYFOVRE was also assessed in GALE, a 3-year, open-label extension study evaluating the incidence and severity of ocular and systemic AEs, and change from baseline in total area of GA lesion(s) in the study eye (mm^2).[1,3,5]

AE=adverse event; AMD=age-related macular degeneration; FAF=fundus autofluorescence; GA=geographic atrophy.

INDICATION

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

IMPORTANT SAFETY INFORMATION

CONTRAINDICATIONS

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WARNINGS AND PRECAUTIONS

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ADVERSE REACTIONS

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

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

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