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NEW VISUAL FIELD SOFTWARE
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Xiidra blocks LFA-1 on T cells from binding with ICAM-1 that may be overexpressed on the ocular surface in dry eye disease and may prevent formation of an immunologic synapse which, based on in vitro studies, may inhibit T-cell activation, migration of activated T cells to the ocular surface, and reduce cytokine release. The exact mechanism of action of Xiidra in DED is not known.1,2,5

†

The safety and efficacy of Xiidra were assessed in four 12-week, randomized, multicenter, double-masked, vehicle controlled studies (N=2133). Patients were dosed twice daily. The mean age was 59 years (range, 19-97 years). The majority of patients were female (76%). Use of artificial tears was not allowed during the studies. The study endpoints included assessment of signs (based on Inferior fluorescein Corneal Staining Score [ICSS] on a scale of 0 to 4) and symptoms (based on patient-reported EDS on a visual analogue scale of 0 to 100). Effects on symptoms of dry eye disease: a larger reduction in EDS favoring Xiidra was observed in all studies at day 42 and day 84. Xiidra reduced symptoms of eye dryness at 2 weeks (based on EDS) compared to vehicle in 2 out of 4 clinical trials. Effects on signs of dry eye disease: at day 84, a larger reduction in ICSS favoring Xiidra was observed in 3 out of the 4 studies.1

**Indication**

Xiidra® (lifitegrast ophthalmic solution) 5% is indicated for the treatment of signs and symptoms of dry eye disease (DED).

**Important Safety Information**

- Xiidra is contraindicated in patients with known hypersensitivity to lifitegrast or to any of the other ingredients.

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* When patients rely on artificial tears alone, inflammation may persist. Xiidra can disrupt the chronic inflammatory cycle in dry eye disease. It can provide lasting symptom relief in as little as 2 weeks.1-5†
**Important Safety Information (cont)**

- In clinical trials, the most common adverse reactions reported in 5-25% of patients were instillation site irritation, dysgeusia and reduced visual acuity. Other adverse reactions reported in 1% to 5% of the patients were blurred vision, conjunctival hyperemia, eye irritation, headache, increased lacrimation, eye discharge, eye discomfort, eye pruritus and sinusitis.
- To avoid the potential for eye injury or contamination of the solution, patients should not touch the tip of the single-use container to their eye or to any surface.
- Contact lenses should be removed prior to the administration of Xiidra and may be reinserted 15 minutes following administration.
- Safety and efficacy in pediatric patients below the age of 17 years have not been established.

For additional safety information about XIIDRA®, please refer to the brief summary of Full Prescribing Information on adjacent page.

**References:**
XIIDRA® (lifitegrast ophthalmic solution), for topical ophthalmic use
Initial U.S. Approval: 2016

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

1 INDICATIONS AND USAGE
Xiidra® (lifitegrast ophthalmic solution) 5% is indicated for the treatment of the signs and symptoms of dry eye disease (DED).

4 CONTRAINDICATIONS
Xiidra is contraindicated in patients with known hypersensitivity to lifitegrast or to any of the other ingredients in the formulation [see Adverse Reactions (6.2)].

6 ADVERSE REACTIONS
The following serious adverse reactions are described elsewhere in the labeling:
- Hypersensitivity [see Contraindications (4)]

6.1 Clinical Trials Experience
Because clinical trials are conducted under widely varying conditions, adverse reaction rates observed in 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.

In five clinical trials of DED conducted with lifitegrast ophthalmic solution, 1401 patients received at least one dose of lifitegrast (1287 of which received lifitegrast 5%). The majority of patients (84%) had less than or equal to 3 months of treatment exposure. One hundred-seventy patients were exposed to lifitegrast for approximately 12 months. The majority of the treated patients were female (77%). The most common adverse reactions reported in 5%-25% of patients were instillation-site irritation, dysgeusia, and reduced visual acuity.

Other adverse reactions reported in 1%-5% of the patients were blurred vision, conjunctival hyperemia, eye irritation, headache, increased lacrimation, eye discharge, eye discomfort, eye pruritus, and sinusitis.

6.2 Postmarketing Experience
The following adverse reactions have been identified during post-approval use of Xiidra. 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.

Rare serious cases of hypersensitivity, including anaphylactic reaction, bronchospasm, respiratory distress, pharyngeal edema, swollen tongue, urticaria, allergic conjunctivitis, dyspnea, angioedema, and allergic dermatitis have been reported. Eye swelling and rash have also been reported [see Contraindications (4)].

8 USE IN SPECIFIC POPULATIONS
8.1 Pregnancy
Risk Summary
There are no available data on Xiidra use in pregnant women to inform any drug-associated risks. Intravenous (IV) administration of lifitegrast to pregnant rats, from premating through gestation day 17, did not produce teratogenicity at clinically relevant systemic exposures. Intravenous administration of lifitegrast to pregnant rabbits during organogenesis produced an increased incidence of omphalocele at the lowest dose tested, 3 mg/kg/day (400-fold the human plasma exposure at the recommended human ophthalmic dose [RHOD], based on the area under the curve [AUC] level). Since human systemic exposure to lifitegrast following ocular administration of Xiidra at the RHOD is low, the applicability of animal findings to the risk of Xiidra use in humans during pregnancy is unclear [see Clinical Pharmacology (12.3) in the full prescribing information].

Data
Animal Data
Lifitegrast administered daily by IV injection to rats, from premating through gestation day 17, caused an increase in mean pre-implantation loss and an increased incidence of several minor skeletal anomalies at 30 mg/kg/day, representing 5,400-fold the human plasma exposure at the RHOD of Xiidra, based on AUC. No teratogenicity was observed in the rat at 10 mg/kg/day (460-fold the human plasma exposure at the RHOD, based on AUC). In the rabbit, an increased incidence of omphalocele was observed at the lowest dose tested, 3 mg/kg/day (400-fold the human plasma exposure at the RHOD, based on AUC), when administered by IV injection daily from gestation days 7 through 19. A fetal no observed adverse effect level (NOAEL) was not identified in the rabbit.

8.2 Lactation
Risk Summary
There are no data on the presence of lifitegrast in human milk, the effects on the breastfed infant, or the effects on milk production. However, systemic exposure to lifitegrast from ocular administration is low [see Clinical Pharmacology (12.3) in the full prescribing information]. The developmental and health benefits of breastfeeding should be considered, along with the mother’s clinical need for Xiidra and any potential adverse effects on the breastfed child from Xiidra.

8.4 Pediatric Use
Safety and efficacy in pediatric patients below the age of 17 years have not been established.

8.5 Geriatric Use
No overall differences in safety or effectiveness have been observed between elderly and younger adult patients.

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T2020-87
In what felt like an almost complete return to normalcy, in the first week of May, the Association for Research in Vision and Ophthalmology held its first live meeting in three years. Though virtual meetings were serviceable, there’s nothing like being present in the poster hall and circulating amid the presenters, or catching a podium presentation live and in-person. If you weren’t able to make it to this year’s meeting in Denver, here’s a look at some interesting presentations from the gathering.

• **Online AREDS vitamins.** Researchers say it’s “buyer beware” when your patients shop online for AREDS-formula ocular supplements. Researchers searched “AREDS” and “AREDS2” on Amazon and Google Shopping. They checked each product in the top 30 results (besides promoted ones) for compliance with the AREDS2 formula, allowing for both low (25 mg) and high (80 mg) zinc formulations. They also found the price per daily serving for each product and compared the prices of “compliant” vs. “non-compliant” formulas.

They found that 30.8 percent (37/120) of the products didn’t adhere to the AREDS2 formula, and 5.8 percent (7/120) followed the AREDS1 formula, which the researchers note is no longer recommended since it results in an increased risk of lung cancer for smokers. Products that deviated in any way from the AREDS2 formulation were 26 percent more expensive than those that didn’t. Also, products that were missing at least one of the ingredients in the AREDS2 formula were 26.9 percent more expensive than those that had the ingredients. The researchers say that “clinicians may wish to be specific in their recommendation of AREDS2 formulations to avoid inaccurate dosing.” *(Yu J. ARVO Abstract F0189, 2022)*

• **Novel visual acuity measurement.** A group of investigators say it may be possible to measure a patient’s visual acuity without actual VA testing. They found that a person’s answers to a series of yes/no questions about their vision can be used to estimate their VA, which might have implications for tele-ophthalmology exams in the future.

In the study, 333 patients with a mean age of 57 from four different testing sites responded to a set of 100 yes/no questions designed to assess acuity in recognizing familiar objects, such as silverware on a table, at typical viewing distances with normal to ultra-low vision. Measured VA values were available from all participants and converted to logMAR units, and it turned out that the percentage of “yes” responses answered by each participant was significantly correlated with his or her VA. A strong relationship, was also found between participants visual ability estimate from the two-parameter model and their VA. The average prediction error, calculated by the absolute difference between the predicted VA and the actual VA, was 0.23 logMAR.

The researchers say that the results show that a questionnaire can be useful in estimating VA worse than 20/40. *(Wu Y-H. ARVO Abstract [Paper] Estimating visual acuity without a visual acuity chart, 2022)*

• **New approach to complex IOL calculations.** Researchers from the University of Ghent say cataract surgeons might be able to accurately predict IOL powers in post-LASIK patients using an experimental ray-tracing technology.

The study looked at 75 patients with previous myopic or hyperopic LASIK who underwent cataract surgery. The surgeons entered the patients’ anterior and posterior corneal Zernike coefficients, corneal thickness, postoperative effective lens position and vitreous chamber depth, and IOL geometry into an optical design software program called Zemax (Radiant Zemax; Focus software), which is usually used for imaging and illumination systems. Using this software, the researchers built patient-specific eye models and calculated the resulting optical quality.

**A Sampling of Studies from the 2022 ARVO Meeting**
The surgeons found agreement between the predicted refraction of the proposed optimized methodology for IOL power calculation and the postoperative subjective refraction. Average spherical equivalent was -0.36 ±0.80 D (subjective) and -0.35 ±0.73 D (predicted). The percentage of eyes within ±0.5 D was 82.6 percent (M), 84.1 percent (J0) and 82.6 percent (J45), while the agreement within ±1 D was 93.3 (M), 98.6 (J0) and 97.3 percent (J45). (Perez-Merino P. ARVO Abstract F0417, 2022)

Long-term Luxturna. The revolutionary ophthalmic gene therapy Luxturna (voretigene neparvovec; Spark) has been available for several years now for patients with RP65-mediated inherited retinal dystrophy, and a group of researchers in the PERCEIVE study are starting to report its long-term effects.

In the study, 103 treated patients were followed for five years. At the most recent follow-up, 35 patients (34 percent) reported ≥1 ocular AEs including 17 with ocular “adverse events of special interest” (16.5 percent). Chorioretinal atrophic change events (at the injection site and/or elsewhere [13]) were most common. Ocular AESIs included foveal degeneration (4), vitritis (4), inflammation (3), retinal tear (2) and increased intraocular pressure (5).

Two patients had serious ocular AEs (one patient with inflammation, and one with increased IOP). Non-ocular AEs occurred in 80 patients, with the most frequent being headache (4). One patient, with no previous history, reported three psychiatric events. Visual function improved in terms of full-field light sensitivity threshold, and best-corrected visual acuity improved at Year 2, with a mean change from baseline of -13.67 ±22.62 decibels.

The researchers say chorioretinal atrophy has been identified as a new

(Continued on p. 69)
EXPLORE A DIFFERENT PATH TO TREATING DRY EYE DISEASE.2
Tyrvaya®, the first and only nasal spray approved to treat the signs and symptoms of dry eye, is believed to activate the trigeminal parasympathetic pathway via the nose, resulting in increased tear film production.2 The exact mechanism of action is unknown at this time.

Watch Tyrvaya in action at Tyrvaya-pro.com.

INDICATION
Tyrvaya® (varenicline solution) nasal spray is indicated for the treatment of the signs and symptoms of dry eye disease.

IMPORTANT SAFETY INFORMATION
The most common adverse reaction reported in 82% of patients was sneezing. Events that were reported in 5–16% of patients were cough, throat irritation, and instillation-site (nose) irritation.

Please see Brief Summary of Prescribing Information on the adjacent page and the full Prescribing Information at Tyrvaya-pro.com.


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REVIEW OF OPHTHALMOLOGY
Clinical advice you can trust

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REVIEWS

JUNE 2022

1 Review of Ophthalmology | June 2022
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**iStent inject®** W IMPORTANT SAFETY INFORMATION

INDICATION FOR USE. The iStent inject® W Trabecular Micro-Bypass System Model G2 W is indicated for use in conjunction with cataract surgery for the reduction of intraocular pressure (IOP) in adult patients with mild to moderate primary open-angle glaucoma. CONTRAINDICATIONS. The iStent inject W is contraindicated in eyes with angle-closure glaucoma, traumatic, malignant, uveitic, or neovascular glaucoma, discernible congenital anomalies of the anterior chamber (AC) angle, retrobulbar tumor, thyroid eye disease, or Sturge-Weber Syndrome or any other type of condition that may cause elevated episcleral venous pressure. WARNINGS. Gonioscopy should be performed prior to surgery to exclude congenital anomalies of the angle, PAS, rubeosis, or conditions that would prohibit adequate visualization of the angle that could lead to improper placement of the stent and pose a hazard. MRI INFORMATION. The iStent inject W is MRI-Conditional, i.e., the device is safe for use in a specified MR environment under specified conditions; please see Directions for Use (DFU) label for details. PRECAUTIONS. The surgeon should monitor the patient postoperatively for proper maintenance of IOP. The safety and effectiveness of the iStent inject W have not been established as an alternative to the primary treatment of glaucoma with medications, in children, in eyes with significant prior trauma, abnormal anterior segment, chronic inflammation, prior glaucoma surgery (except SLT performed > 90 days preoperative), glaucoma associated with vascular disorders, pseudoexfoliative, pigmented or other secondary open-angle glaucomas, pseudophakic eyes, phakic eyes without concomitant cataract surgery or with complicated cataract surgery, eyes with medicated IOP > 24 mmHg or unmedicated IOP < 21 mmHg or > 36 mmHg, or for implantation of more or less than two stents. ADVERSE EVENTS. Common postoperative adverse events reported in the iStent inject randomized pivotal trial included stent obstruction (6.2%), intraocular inflammation (5.7% for iStent inject vs. 4.2% for cataract surgery only), secondary surgical intervention (5.4% vs. 5.0%) and BCVA loss ≥ 2 lines ≥ 3 months (2.6% vs. 4.2%). CAUTION: Federal law restricts this device to sale by, or on the order of, a physician. Please see DFU for a complete list of contraindications, warnings, and adverse events.

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PM-US-0782
INDICATIONS
The XEN® Glaucoma Treatment System (XEN® 45 Gel Stent preloaded into a XEN® Injector) is indicated for the management of refractory glaucomas, including cases where previous surgical treatment has failed, cases of primary open-angle glaucoma, and pseudoexfoliative or pigmentary glaucoma with open angles that are unresponsive to maximum tolerated medical therapy.

IMPORTANT SAFETY INFORMATION
CONTRAINDICATIONS
XEN® Gel Stent is contraindicated in angle-closure glaucoma where angle has not been surgically opened, previous glaucoma shunt/valve or conjunctival scarring/pathologies in the target quadrant, active inflammation, active iris neovascularization, anterior chamber intraocular lens, intraocular silicone oil, and vitreous in the anterior chamber.

WARNINGS
XEN® Gel Stent complications may include choroidal effusion, hyphema, hypotony, implant migration, implant exposure, wound leak, need for secondary surgical intervention, and intraocular surgery complications. Safety and effectiveness in neonuclear, congenital, and infantile glaucoma has not been established. Avoid digital pressure following implantation of the XEN® Gel Stent to avoid the potential for implant damage.

PRECAUTIONS
Examine the XEN® Gel Stent and XEN® Injector in the operating room prior to use. Monitor intraocular pressure (IOP) postoperatively and if not adequately maintained, manage appropriately. Stop the procedure immediately if increased resistance is observed during implantation and use a new XEN® system. Safety and effectiveness of more than a single implanted XEN® Gel Stent has not been studied.

ADVERSE EVENTS
The most common postoperative adverse events included best-corrected visual acuity loss of ≥ 2 lines (≤ 30 days 15.4%; > 30 days 10.8%; 12 months 6.2%), hypotony IOP < 6 mm Hg at any time (24.6%; no clinically significant consequences were associated, no cases of persistent hypotony, and no surgical intervention was required), IOP increase ≥ 10 mm Hg from baseline (21.5%), and needling procedure (32.3%).

Caution: Federal law restricts this device to sale by or on the order of a licensed physician. For the full Directions for Use, please visit www.allergan.com/xen/usa.htm or call 1-800-678-1605.

IOP = intraocular pressure. MIGS = minimally invasive glaucoma surgery.

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Caring for your patients. Thriving as a business. That’s what matters. And to make that happen, you need a single integrated technology platform—not disparate solutions. Better workflows. Revenue capture. Claims and insurance processing. Interoperability. Plus... a superior way to engage with patients. All from one trusted source, who will be there for the life of your practice.

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Like the classic cartoon image of a small snowball rolling down a mountain, picking up more snow along the way, and eventually becoming a monstrous juggernaut by the time it reaches the bottom, small errors by Medicare Advantage Organization claim evaluators can add up to thousands of patients being denied necessary care and millions of dollars in lost reimbursement for providers. These mistakes came to light recently in a report by the U.S. Department of Health and Human Services Office of Inspector General, which found both patients and providers were getting bowled over by the system.

On the patient side, the report found that, “Of 12,273 denials of requests for services (prior authorization denials) issued by 15 selected MAOs during the first week of June 2019, an estimated 13 percent [actually] met Medicare coverage rules.” Annually, this would extrapolate out to almost 85,000 unjust denials in a single year. The OIG found that many of these denials were based on small errors. For instance in one case, the MAO declared that a beneficiary would need to wait at least a year for a follow-up MRI for an adrenal lesion, “because the size of the lesion (less than 2 cm) was too small to warrant follow-up.” However, there is no such Medicare rule, and the decision was eventually reversed after an appeal.

In another case, the OIG says an MAO denied a request for a walker for a patient in his 70s with post-polio syndrome because he had “already received a cane within the past five years.” The problem, the report states, is that this ruling was just plain wrong: There is no such Medicare ambulatory assistance device limit.

For physicians, these errors hurt their economic well-being more than their physical health. “Of the 160,378 payment denials issued by the 15 selected MAOs,” the OIG states, “an estimated 18 percent met Medicare coverage rules and MAO billing rules and should have been approved by the MAOs ... For an annual context, if these MAOs denied the same number of payment requests (28,949) in each of the other 51 weeks of 2019, they would have denied 1.5 million [valid] requests.”

As with the patients, the little things added up: “MAOs denied payments to providers because of human error during manual reviews ...” the report found. “However, these manual reviews are susceptible to human error, such as a reviewer’s overlooking a document in the case file or inaccurately interpreting CMS or MAO coverage rules.” Fortunately, it looks like there’s light at the end of the tunnel: In mid-May, the “Improving Seniors’ Timely Access to Care Act” achieved bi-partisan support in Congress, and is on its way to becoming law. The bill stipulates, among other things, that prior-authorization requests will be evaluated by qualified medical personnel. It looks to be a win for both doctors and their patients.

— Walter Bethke
Editor in Chief

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ABOUT RICK
Rick Bay served as the publisher of The Review Group for more than 20 years.
To those who worked for him, he was a leader whose essence was based in a fierce and boundless loyalty. To those in the industry and the professions he served, he will be remembered for his unique array of skills and for his dedication to exceeding the expectations of his customers, making many of them fast friends.
A First Look
At the EVO ICL

The EVO/EVO+ ICL’s unique design could pave the way for more patients to benefit from ICL technology.

LIZ HUNTER
SENIOR EDITOR

When phakic IOLs first hit the market, there was an undeniable level of enthusiasm about the promise of improving vision for those with high refractive errors but who weren’t candidates for LASIK or PRK. Yet, years later, many surgeons—especially in the United States—haven’t embraced them for reasons ranging from patient cost to associated risks and the success of LASIK.

Perhaps contributing to the slow adoption of phakic IOLs was the fact that there have been only two FDA-approved options available: the Staar Visian ICL and the Ophtec Verisyse/Artisan. A toric version of the ICL was also approved in 2018. However, both of these options required the creation of a peripheral iridotomy, an extra step that discouraged surgeons from using phakic IOLs.

That hesitation may change now that the FDA has approved the Staar EVO/EVO+ Visian ICL and EVO/EVO+ Visian Toric ICL, each of which come with a hole in its center called the KS-AquaPort. According to Staar, the hole is designed to improve aqueous humor circulation in the eye, thereby eliminating the need for an iridotomy.

Benefits of the Central Port
Although considered safe, laser peripheral iridotomy complications have been known to occur, including transient blurred vision, intraocular pressure rise, dysphotopsia, hyphema, closure of the iridotomy and damage to other tissues.

Neda Shamie, MD, based in Los Angeles, says the EVO is exciting for many reasons. “We’ve had experience with the implantable contact lens for many, many years, and the EVO is the same type we’ve had access to, but now it has a small opening in the center that essentially removes the need for us to perform a peripheral iridotomy,” she says. “So much of the challenge in placing the implantable contact lens was that surgeons didn’t want to do that peripheral iridotomy because it had its own inherent risks.”

Dr. Shamie says phakic IOLs appeal to patients because no tissue is being taken out and the lenses can be removed. “Patients see implantable contact lenses as an additive procedure,” she says. “You’re adding a contact lens, not removing tissue, and it’s essentially reversible. Performing an iridotomy really canceled out one of the main benefits of the ICL, which is that it can be taken out, while an iridotomy is a permanent defect in the peripheral iris that could potentially have complications associated with it.”

This reasoning could also be applied to position the ICL as an alternative to LASIK, says John Vukich, MD, who’s based in Wisconsin. “LASIK contours the cornea to create a new refraction, but it does so by removing tissue, and there’s a functional and practi-
EVO procedures have already been performed worldwide. U.S. surgeons have been hearing about the EVO’s success from their international peers for years, says Dr. Vukich. “The EVO model has been available for several years in virtually every country except the U.S. It’s a very popular device, especially in Asia, where the average number of individuals with myopia is higher than in Western countries,” he says.

A clinical study followed 327 patients with either the EVO/EVO+ Visian ICL or the EVO/EVO+ Visian Toric ICL. A total of 75.9 percent of patients reported 20/20 vision or better in the implanted eye, and 98.9 percent had 20/32 vision in the implanted eye after six months.2

The FDA advises not to use the EVO/EVO+ on anyone who is pregnant or nursing, younger than 21, has moderate to severe glaucoma, has shallow space in the anterior chamber or a small anterior chamber angle, or whose endothelial cell density falls outside of a specified range based on their age and the size of ICL being implanted.

Dr. Vukich has implanted the EVO in individuals who are unable to wear contact lenses. “One patient couldn’t wear them and the other developed an allergic reaction and had to give up wearing them,” he says. “They were extremely motivated, but corneal refractive surgery wasn’t for them, so these patients waited several months for the EVO to come in. They are just thrilled to be able to have that.”

**Surgical Tips and Adverse Effects**

Staar Surgical says the EVO implantation takes less than 30 minutes to perform.

Dr. Vukich says the surgery isn’t overly complicated. “It’s absolutely approachable and within the skill set of any anterior segment surgeon,” he says. “If a surgeon is already familiar with the precursor, the standard ICL, there’s no learning curve. It’s identical to how the lens sits and handles; this is simply a better version. For surgeons who are new to the ICL, it’s straightforward and can be done through a 2.6- or 2.8-mm clear corneal incision. For a surgeon who’s comfortable with intraocular surgery and comfortable...
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doing a cataract operation, the ICL is significantly less involved and requires fewer steps than a cataract operation."

One thing Dr. Shamie has learned is to ensure that all the viscoelastic is removed and to keep the pupil dilated. “If there’s any viscoelastic trapped behind the ICL you want to give it time to circulate out from behind it so that the central hole will be patent and allow for aqueous flow,” she says.

The EVO/EVO+ ICL study did require an IOP check at one to six hours postoperatively, which hadn’t been done with the previous ICL models. The study found a significant rate of IOP spikes, approximately 19.9 percent, which appear to have been related to incomplete removal of the dispersive OVD at the end of the procedure. These day-zero IOP increases were resolved with medication and/or paracentesis/AC tap.

Dr. Shamie uses multiple modes to measure the white-to-white and calculate the best ICL size. “Our approach is to measure the white-to-white using our biometer, slit lamp and UBM,” she says. “We compare the lens size calculated by each modality and decide accordingly. I have the greatest confidence in our UBM measurements, but I do look at the average. If the sizing for the ICL lands the patient between two sizes, I err on the smaller size with the EVO ICL because the small opening in the optic of the EVO lessens the risk of cataract formation, so there’s less concern about going too small.”

During conversations with patients, Dr. Vukich makes sure they know that there’s still an inherent risk of retinal detachment and a higher risk of cataracts at a younger age. “That’s not because they did or didn’t have the ICLs, it’s just part of being myopic,” he says. “I also tell them that, rarely, there could be a little bit of glare at night, especially for the very high nearsighted individuals. It’s unusual and not everyone has it, and when they do it’s really minimal.”

Both Drs. Vukich and Shamie believe the EVO will help make phakic IOLs a more popular choice in an ophthalmologist’s arsenal.

“ICLs have evolved and continue to gain traction around the world, and now we can offer them to patients with this added safety profile,” says Dr. Vukich.


DISCLOSURES

Drs. Vukich and Shamie are consultants for Staar.
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The Teachings Of Tobey
Musings on life, medicine and ophthalmology.

Mark H. Blecher
Chief Medical Editor

Life is a challenge. And if you approach it correctly, you should be looking for ways to meet those challenges. You should be looking for ways to be a better person and have a better life.

There are endless opportunities to learn from others and the world around us. But often those opportunities are a bit opaque or clouded by inconsistency. No role model is perfect, no lesson from the universe is clear. With one exception: dogs.

A movie came out not that long ago called, ‘The Purpose of a Dog.’ It was a two-tissue, tug-on-your-heartstrings story about the lessons a dog can teach us at all stages of life, theirs and ours. But, you might think, why dogs, why not cats? I’ll admit that while I love all animals, I’m totally on team canine.

The fact that dogs can have a positive effect on humans is one of evolution’s greatest successes. In 2019, researchers sought to find the secret to this success, and their work was published in an article in the Proceedings of the National Academy of Sciences titled, “Evolution of Facial Muscle Anatomy in Dogs.” In that paper, the investigators posited that the acquired ability of dogs to raise their inner eyebrow, specifically the levator anguli oculi medialis, in a more human (pae-domorphic) manner generated a positive hormonal response in humans, leading to canine domestication. I’ve seen this facial expression in action, and I call it the ‘worried Lab look.’

Tobey, my 6-year-old Labrador retriever, is my worried Lab. He’s my fourth in a series over the past 25 years—and perhaps the best. Those of you who are dog people know what I’m saying. Those who don’t, let me explain. Tobey, like most dogs, has a lot to teach us, if only we would pay attention. Usually, we’re spending our time trying to teach them how to control themselves so they don’t soil the house or jump on visitors, to restrain their energies and many of their natural instincts. This training enables them to live within our constrained and controlled world, and I certainly support a well-trained pup.

But, while we’re busy training them, are we missing the lessons they can teach us?

There is no end to the internet memes that list the advice our dogs could give; we all see them and chuckle. But really, we need to take these dog aphorisms more seriously: “Don’t hold grudges”; “love unconditionally”; “loyalty is a virtue”; and “delight in the simple,” just to name a few. But most importantly, “have a happy attitude.” Tobey is always happy. Happy to see me, and happy to see you if you visit. Happy to get fed, or to curl up next to me to take a nap. He’s just happy, with no perseverating on the past. No harboring of resentment, insults or injury. It’s a much less stressful way to live.

And when I come home, I feel the simplicity of his life. It cuts through the layers of crazy I’ve fought through all day, and it undoubtedly lowers my blood pressure, probably as much as my medications do. (But maybe not as much as a martini.) However, while I do like my martini, it can’t compare to the loyalty and quiet companionship of Tobey.

Tobey’s constant state of good humor is even more inspiring when you learn that he’s deaf. He was likely born deaf, though we didn’t realize that until he was 2. At that time, we had an older Lab, Cassie, who was very well trained and well behaved. Tobey did everything she did. He watched her, and us, very carefully. Since he couldn’t hear he had to see, to watch our every move. This has made for a bond between us like no other, especially since Cassie is no longer here. Tobey carries on, however, teaching me to trust my instincts, accept who I am and enjoy the journey. Oh, and to drink more water. Definitely drink more water.
For patients with Graves’ disease (GD), Thyroid Eye Disease (TED) may be hiding in plain sight.¹²

Up to 50% of patients with GD may develop TED, a separate and distinct disease which can progress if left untreated. Look out for the early signs and symptoms:²⁻⁷:

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- Sensitivity to light¹²
- Diplopia³
- Grittiness⁸⁻¹¹
- Dry eyes⁶⁻¹¹
- Pain or pressure behind the eyes¹³

If you identify new or changing signs or symptoms, consult with an eye doctor who specializes in TED right away.¹⁴

Visit TEDimpact.com to find a TED specialist or contact a Horizon Representative at 1-855-950-2076.

How to Develop Your Own Instruments

From concept to patent to finding a manufacturer—here’s how to get started in the world of custom instruments.

The Idea

The custom instrument journey depends in large part on your own goals, experts say. Some doctor entrepreneurs are interested in creating and managing a company (i.e., an instrument start-up), while others simply want to bring a new instrument to market or use it themselves.

Regardless, Matthew Chapin, senior vice president of the Asset Development & Partnering Group at Ora, an ophthalmic product development company based in Andover, Massachusetts, says that when developing your instrument, one of your first steps should be thinking about the endgame.

“Whenever you set out to develop a new product, it’s important to map out the ultimate goal,” he says. “Begin with the end in mind. When a new idea from a doctor comes across my desk, I ask the following:

— How will the instrument or device be used?
— What unmet need is it going to fill?
— Is it solving an actual problem?
— Is it a groundbreaking new tool?

“It’s one thing for a doctor to come up with a new tool that helps them in practice. The question is, is this tool something that all of their colleagues would also use?” Mr. Chapin says. “When developing your instrument, you need to ask yourself, ‘What kind of impact will the instrument have? How will using it affect the length of the procedure? How will that in turn affect patient flow?’

“These things need to be balanced,” he continues. “An instrument that’s clinically useful but leads to the procedure taking a long time will ultimately reduce the doctor’s case capacity. On the other hand, an instrument that can increase capacity, efficiency and quality of care has high value.”

Those performing surgery are often the first to identify a need for something new or different. “I thought it would be useful to be able to measure my capsulorhexis as I’m making it,” says Uday Devgan, MD, FACS, FRCS, chief of ophthalmology at Olive View UCLA Medical Center, a clinical professor at the UCLA School of Medicine, and in private practice at Devgan Eye Surgery in Los Angeles. Many of his instruments include measurement marks. “My capsulorhexis forceps have marks at 2.5 and 5 mm from the tip to measure the radius and diameter of the capsulorhexis. I like my instruments to have more than one use.”

Patents

“If you have a really great idea, ask yourself: Do I want to patent this idea? Do I want royalties?” Dr. Devgan says. “I don’t receive royalties for my instruments. The good thing about that is that companies may promote your instruments more when they don’t have to pay you royalties. Do you want to get your instrument out there with your name on it just to help people or do you also want to make some money? If you want to make money, be sure to patent the instrument and negotiate royalties.”

Mr. Chapin says you should start talking to a patent attorney early on, once you have an idea. Historically, the person who created an invention first had patent priority, but since 2013 when the first-to-file rule was instituted in the America Invents Act, it’s important to act quickly to secure your invention's status.

Many instrument-making companies have engineers who can help you develop your instrument, says Uday Devgan, MD.
Act, the applicant who files their patent application first receives priority.

“There are two elements to intellectual property patents,” Mr. Chapin explains. “The first is freedom to operate. Is there someone else out there who’s blocking you—i.e., are you going to be able to develop and commercialize this product without having to license someone else’s product? The second part is: Is your invention patentable? Does it pass the novelty hurdle? Are there a lot of prior inventions already out there that would get in the way of being granted a patent at the patent office?

“These are all discussions that should happen as early as possible in the process,” he says. “You certainly don’t want to be talking to any companies or investors until you have a patent filed.”

Manufacturers

Once you have a patent, Mr. Chapin says you can begin speaking with companies to see if anyone wants to pick up your product. “It’s always incredibly valuable to talk to companies early on and see what they’re interested in,” he says. “You can learn a lot. There may be certain aspects of your instrument that they comment on that can be modified early in the process.

“Any value coming to a doctor will likely be some type of royalty, rather than a huge buyout upfront, unless it’s a real game-changer,” he adds. “If you’re not interested in larger commercialization, it’ll come down to the type of instrument and whether the company can produce it on a scale small enough for you and your practice.”

If you go to an instrument maker directly with your drafts and ideas, Dr. Devgan points out that many of these companies have engineers you can work with to develop your instrument. “They’re incredibly bright people and come up with some great ideas for you,” he says. “If the company has a similar instrument, you can start with that and modify it. You’ll go through various iterations and your instrument will evolve. The manufacturer will make it for you to test. These companies want to partner up and make great instruments.

“Materials choice is important,” he adds. “My instruments are made of titanium. The advantage of titanium is that it lasts longer than steel, and surgeons only have to buy the instrument once, which is also better for the environment. If you’re looking for royalties, you may choose to go with disposable instruments so surgeons will buy them over and over again.”

Building Value

To build more value into your invention before pitching it to companies, Mr. Chapin says that doctors can personally invest or fundraise to design and engineer prototypes or run some clinical trials to make the instrument more attractive to companies. “Then, the doctor can sell the instrument for a much higher amount to a consulting company for a license or an acquisition,” he says. “If the instrument or device is worth more, this obviously entails more cost and risk.”

Feedback from Peers

Getting feedback from your colleagues is also important. “You can conduct a small market survey among your colleagues,” Mr. Chapin says. “With online surveys, doctors should be able to get a couple dozen survey responses pretty quickly. This will provide valuable data on how other doctors view it or how they’d use it. That’s all useful information for the entrepreneur to take to a company or to investors, if they’re raising money.

“Ophthalmology also has many great conferences for networking,” he adds. “Networking is a great place to start when you’re developing a new product. Events such as Eyecelerator at the ASCRS and AAO meetings and the Ophthalmology Innovation Source summits are where industry comes together. You have doctors, pharmaceutical and device companies and investors all together in one room. There are unique opportunities there.”

MORE QUESTIONS TO ASK YOURSELF

Here are some other key questions to think about as you develop your custom instrument:

• What’s the instrument’s purpose?
• What’s the specific user sub-population you’re targeting?
• What are the instrument’s characteristics and features?
• What makes it unique or competitive?
• What are the efficacy and safety endpoints you’re aiming at?
• How’s it going to be supplied? (e.g., is it disposable or can it be sterilized and reused?)
• What’s your business model?
Visual field testing remains an essential part of detecting and monitoring the progression of glaucoma, so it should be no surprise that new product options for performing this type of testing continue to proliferate, while existing options continue to be refined. Currently, more than 14 companies offer an in-office perimeter, using different algorithms to detect glaucomatous defects and analyze the data. In addition, with the advent of head-mounted virtual perimetry and tablet-based perimetry, a long list of additional companies and testing approaches have entered the picture.

All of this technology is helping to make the doctor’s job easier and potentially make results more accurate. “Today’s machines incorporate a lot of technology that not only helps us collect the data but also helps us assess whether the disease is getting worse and whether the test was reliable,” notes Steven L. Mansberger, MD, MPH, Chenoweth Chair of Ophthalmology and director of the Glaucoma Services at the Legacy Devers Eye Institute in Portland, Oregon. “That’s significant, because we’re all very busy.”

Here, to help make sense of the increasing number of options, multiple surgeons and researchers share their experiences with these technologies. In particular, given the popularity of the Zeiss Humphrey perimeter in the United States, they focus on the different SITA algorithms and when it makes sense to use each of them.

Is Faster Better?
One of the questions facing clinicians who use the Humphrey perimeter is, which version of SITA (Swedish Interactive Threshold Algorithm) testing should they use: SITA Standard, SITA Fast or SITA Faster? There are also questions centering around the recently available SITA 24-2C test, which checks additional points in the visual field.

“SITA Standard has been well-proven to be very reliable, because it double-checks the sensitivity at each spot,” Dr. Mansberger explains. “In contrast, SITA Fast and Faster do not. As a result, we can do visual fields in less time with SITA Fast and SITA Faster, but we have to test patients more often to ensure reliable results.”

Stuart K. Gardiner, PhD, a senior scientist at Devers Eye Institute in Portland, Oregon, who has contributed to the development of visual field software, says the differences between the two faster options—SITA Fast and SITA Faster—are relatively small. “They made a few tweaks to get from SITA Fast to SITA Faster that are fairly inconsequential for patient care,” he notes. “It uses a slightly different way to assess variability; it’s quicker because it’s not based as much on catch trials. I don’t see a big reason not to switch from SITA Fast to SITA Faster, for clinical purposes.”

Of course, the length of time spent taking a visual field test is partly determined by the patient. In addition to the level of patient cooperation, Jonathan S. Myers, MD, chief of the Glaucoma Service at Wills Eye Hospital and a professor of ophthalmology at Thomas Jefferson University’s Sidney Kim-
Dr. Myers notes relevant data from two studies. One study done at five centers tested one eye each of 126 patients either diagnosed with glaucoma or considered glaucoma suspects. The patients were tested with SITA Standard, SITA Fast and SITA Faster at each of two visits. The data showed that SITA Faster gave results very similar to those of SITA Fast, but with slight differences compared to SITA Standard.1

The authors of this study point out two key technical differences between SITA and SITA Faster:

• A key part of the test is conducting a threshold evaluation to determine an appropriate stimulus intensity for the patient, which takes time. The early SITA programs started testing at 25 dB, a value inherited from the Humphrey full threshold test, which was created before researchers had any knowledge of normal age-corrected sensitivity values. The newer versions of the test save time by starting at or near the age-corrected normal threshold value.

• The early tests assessed the patient’s fixation by projecting stimuli into the blind spot to see if the patient responded. (Those machines had no way to perform optical or video surveillance of the patient’s gaze.) Using this approach has several flaws: 1) It adds time to the length of the test; 2) it can only check fixation periodically; 3) the blind spot may be inaccurately located, causing the machine to report poor fixation when fixation was actually good; and 4) the patient’s visual field status is known to have a big impact on the accuracy of this approach. With gaze tracking technology now available, the developers of SITA Fast and Faster felt that this was a good substitute for the blind spot fixation assessment method—especially when combined with observations by the technician running the test.

The other study noted by Dr. Myers was conducted at the Wilmer Eye Institute.2 This study tested 421 patients twice with SITA Standard and once with SITA Faster (in that order), with a mean time between tests of 13.9 months. They looked at the differences between the first two tests (both done with SITA Standard) and the differences between the last two (SITA Standard vs. SITA Faster). They compared the results in three groups: patients with mild, moderate and advanced disease severity. The study found that converting from SITA Standard to SITA Faster led to similar visual field performance in patients with mild glaucoma, but resulted in higher mean deviation values in patients with moderate or advanced glaucoma.

Making the Switch
“Many of these technological differences are smart choices,” notes Dr. Myers. “However, some clinicians may not be happy about another one of them: The new tests don’t do false-negative trials. In these trials, the machine shows a stimulus the patient should see; if the patient doesn’t see it, it’s a sign that the patient may be distracted or tired. Not doing these trials saves time, but many of us look for a high false-negative score to warn us that a test result may not be representative of the patient’s best visual result.”

Dr. Myers says he has limited experience with SITA Faster because his practice primarily uses SITA Fast when using the Humphrey machine; in addition, some patients at his other offices are tested on Haag-Streit’s Octopus perimeter. Nevertheless, he says that the switch to SITA Faster reminds him of the switch from full threshold to SITA several years ago. “A lot of patients with moderate to advanced disease looked better when tested with the SITA algorithm,” he recalls. “At the time, we debated whether this was because it was a faster test, so patients didn’t get as fatigued, or because the thresholding algorithm was substantially different.

“The change from SITA to SITA Fast or Faster seems similar,” he says. “The new test is quicker, and many patients look better on the new test. Nevertheless, if a patient is stable, I think you can switch and re-establish a baseline. But you have to be careful if you think a patient is progressing and you’re considering advancing therapy if the change is confirmed. That’s not the time to switch testing algorithms.”

Some clinicians say they’ve already adopted the SITA Faster algorithm as their primary testing algorithm in the clinic, including David Fleischman, MD, MS, FACS, an associate professor in the Department of Ophthalmology at the Icahn School of Medicine at Mount Sinai in New York City. "The change from full threshold to SITA was more of a fringe change in my practice. The change from SITA to SITA Faster appears to be a more significant one, and it’s likely that we’ll see more widespread adoption.”
Cover Story  VISUAL FIELDS

GLAUCOMA HEMIFIELD TEST RESULTS OBTAINED WITH THE THREE SITA STRATEGIES

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<th>Glaucoma Hemifield Test Classification</th>
<th>SITA Standard Tests</th>
<th>SITA Fast Tests</th>
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A 2019 study compared the three SITA speeds, analyzing results from 125 patients (51 percent female, mean age 67 years). Mean test times were 369.5 seconds for SITA Standard, 247 seconds for SITA Fast and 171.9 seconds for SITA Faster (p<0.001).

of Ophthalmology at the University of North Carolina at Chapel Hill, and perioperative medical director at UNC Hillsborough. “The number of complaints about visual fields that I used to hear from my patients when I started with SITA Standard was reduced considerably when I adopted SITA Fast. Since switching to SITA Faster those complaints have become rare.

“I acknowledge that SITA Standard is considered the gold standard,” he continues. “However, I was tired of having to inform my patients that they didn’t perform their test reliably and that they’d need to repeat it. Repeating these tests takes up considerable staff time and effort in clinic, and the patient feels like a failure. I can eat the increase in variability that comes with SITA Faster in exchange for the patient feeling better about the testing, and I have no qualms repeating this test frequently over the course of a year. That helps me gauge the status of a field—and just as important, the speed of progression.”

The Patient Factor

As already noted, a big reason for switching to a faster testing strategy is that patients find most visual field tests difficult to tolerate—and the longer the test, the less they like it.

Dr. Myers confirms that the faster test is definitely appreciated by patients, making it feasible to test more often. “That’s part of the reason we switched to the Octopus perimeter in some of our offices,” he notes. “We found that the TOP (tendency oriented perimeter) algorithm used in the Octopus was substantially faster than SITA Standard or SITA Fast. Our patients really appreciate that, and they’re more willing to take the test. We thought it was worth losing a little bit of accuracy to gain the option of doing the test more often.”

Dr. Gardiner points out, however, that the time savings from using the faster test aren’t actually as dramatic as they may seem at first. “SITA Faster brings the test time down from five or six minutes to two or three minutes, but the time it takes to set up, get the patient’s information into the instrument and so forth, doesn’t change,” he says. “For that reason, switching to SITA Faster might only shorten the entire process from 25 minutes to 20 minutes for both eyes. So in terms of workflow in the clinic, it’s not as dramatic an improvement as it might sound. It’s certainly not cutting the overall testing time in half.”

So, how should a clinician decide which test to use for a new patient? “When choosing a test for a new patient, I’d consider a couple of factors,” says Dr. Gardiner. “For one thing, some patients can tolerate and give good results with a longer test. However, if someone has trouble concentrating for five minutes but can manage two minutes, then it’s worth doing a shorter test.

“Another factor is that, if someone already has vision loss, or you think there’s a good chance that they’re getting worse rapidly, then you need to have the most accurate information possible,” he continues. “It’s worth taking the time to do the longer test to get more accurate information on those patients. That may be fine with the patient, because if a patient has obvious vision loss or is getting worse fairly quickly, it’s much easier to persuade them that it’s worth doing a six-minute test instead of a two-minute test. Conversely, if a patient is normal or has very early loss, and your clinical opinion is that it’s less urgent, the shorter test might be acceptable.”

“I’d say that for early glaucoma patients and suspects, using a test that’s faster is probably OK,” Dr. Mansberger says. “If you have someone who’s older and has more severe glaucoma—someone who has more variability to begin with in terms of visual field testing—then it might be better to use a standard visual field algorithm like SITA Standard. You don’t want to give an older patient a shorter test that might produce an abnormal result, because you might end up thinking they’re getting worse when they just had a bad day.”

The 24-2C Test

The SITA 24-2C test expands the testing range of the SITA Faster test to include some central visual field locations, normally not tested except by a separate test such as the 10-2 test. Dr. Gardiner says that he was one of a number of people who worked on developing the 24-2C test. “The grid that’s used in the standard 24-2 test isn’t designed to pick up localized defects in the center of the visual field,” he explains. “The usual way to compensate for that is by giving the 10-2 test; it has good coverage of the center of the field, but no coverage in the periphery. The 24-2C was designed to be a compromise that checks all the same locations as the 24-2, plus a few extra central ones from the 10-2 test. The idea was to get more complete coverage without having to spend
Apellis is exploring the role of complement in Geographic Atrophy\(^1\)

C3 is the linchpin of complement overactivation in GA.\(^2\)\(^-\)\(^7\)

All three complement pathways converge at C3 and it drives multiple downstream effects — inflammation, opsonization, and formation of the membrane attack complex — all of which can ultimately lead to retinal cell death. Increased levels of complement activity have been found not just in the lesion itself, but also in the area just outside the lesion, known as the pre-lesion.\(^2\)\(^-\)\(^9\)

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Cover Story  VISUAL FIELDS

COMPARING ALGORITHMS

A number of different algorithms beside SITA are available for use in visual field testing. Stuart K. Gardiner, PhD, a senior scientist at Devers Eye Institute in Portland, Oregon—who has worked with many of them—says that the GATE (German Adaptive Threshold Estimation) algorithm, available on the Octopus perimeter, is similar to SITA. "It's designed for clinical care," he notes. "One notable difference is that the Octopus perimeter has included more central locations in its test grid for many years.

"All of these programs initially try to come up with a sensitivity estimate at each location," he explains. "Once that’s done, both SITA Standard and GATE apply a spatial filter that incorporates information from neighboring locations to reduce the data noise a bit. That’s good for clinical care but less ideal for research purposes, because we need to know what the original estimates were for each location.

"That’s where an algorithm like ZEST (zippy estimation by sequential testing) comes in," he continues. "ZEST is open-source, so there are no proprietary secrets; we know exactly how it works. Unlike the commercial algorithms, ZEST doesn’t do any post-processing of the measured data. That makes it more predictable. The tradeoff is that it doesn’t reduce the variability of the results as much as the more widely used commercial algorithms do.

"I believe ZEST is mostly being used for research, and I don’t think it would offer any clinical advantage over SITA or GATE," he says. "In fact, I believe that adding extra central testing locations, as the SITA Faster 24-2C or Octopus GATE algorithms do, will have much more of an impact on clinical care than the differences between the testing algorithms."

Another algorithm is TOP (tendency oriented perimetry), available on the Octopus instrument. "TOP takes spatial filtering to an extreme, trying to shorten test time as much as possible by using information from neighboring locations," Dr. Gardiner explains. "It makes it a much faster test, but you lose a lot of localized information. The idea is similar to SITA Faster, although the algorithms aren’t identical." ~CK

the time it takes to do two tests. “A group of experts helped the company decide which central locations to add to the grid,” he continues. “The locations we chose weren’t random—they were the ones most likely to pick up glaucomatous defects that were being missed with the 24-2 test. Of course, if we added every central location from the 10-2, the test would take a lot longer, and if a test takes too long, then the patients get tired and the results become less reliable.

“At the moment, only the SITA Faster algorithm on the Humphrey can run the 24-2C test grid,” he adds. "Of course, adding the extra central points makes the test take a little bit longer than the original SITA Faster test—but only a little. It still takes less time than doing the SITA Standard test. In any case, I think it’s really important to test the extra locations in the central part of the field, because they affect activities of daily living.”

Dr. Myers says he’s read a number of studies evaluating the potential pros and cons of adding some central points to the 24-2 test. “The literature makes it clear that while the 24-2C may pick up some paracentral defects that you might otherwise miss, there are still a lot of paracentral defects that it won’t pick up,” he explains. “For example, most clinicians won’t change treatment because we see one isolated abnormal point in a field. We assume it’s a mild depression and we don’t make much out of it, because patients don’t test perfectly. Most of us require two or three contiguous abnormal points on the field to feel that something significant may be happening.

“Two studies show a challenge with the 24-2C [relating to this],” he continues. “Because it doesn’t have as many paracentral points, it often won’t show two or three abnormal points next to each other—where the 10-2 would. It’s not likely to retest everyone who has one abnormal paracentral point on the 24-2C, and as a result, we could miss a lot of people who have paracentral defects—people we wouldn’t miss if we tested with the 10-2. Of course, this doesn’t mean that the 24-2C test doesn’t add value; it just means that the value is limited. So if you’re really concerned about central defects, the 10-2 is a more definitive test.”

So which test should you use for the majority of your patients? “From a practical standpoint, you want to choose a test with an algorithm that your technicians can follow through on easily and quickly,” Dr. Mansberger says. “The 24-2C, which is only available on the HFA3, uses the same algorithm as SITA Faster but also checks the central visual field. I suspect that most doctors who have the HFA3 would choose the 24-2C for most patients, because it tests more locations.

“However, if a patient is progressing, you might move that patient from the 24-2C to a SITA Standard 24-2, just to get lower variability and be able to follow them more carefully,” he adds. “If a patient only has central visual field left, you’d move them to a 10-2 visual field. For patients with lots of variability and lots of loss, but more than just a central island of vision left, you might switch to a size 5 stimulus. This will allow you to get some information from areas with a sensitivity worse than 19 dB.”

Dr. Mansberger says he does like to get a 10-2 field on every glaucoma patient. “This gives us a sense of their central visual field sensitivity,” he explains. “Then, we repeat it every one or two years to see if there’s a change in that area. Of course, the patients who should be tested regularly with a 10-2 test are those with visual field loss close to fixation. In that case, you may want to do 10-2
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testing exclusively. If the patient only has vision left in the center, why spend time testing parts of the visual field that are already gone?”

**Portable Perimetry**

There are two new approaches to perimetry that are portable: virtual reality headsets and perimetry done on computer tablets.

“In contrast to the massive, expensive instruments used in the clinic, tablet perimeters are designed for use at home, especially for frequent testing,” notes Dr. Gardiner. “However, they’re not as repeatable, because the test-taking conditions aren’t as controlled. You have to do more frequent testing to make up for that, but patients can do more frequent testing quite easily.

“…There are two primary problems with tablet perimetry,” he continues. “The biggest problem I see is that the room lighting can make a big difference in your results. If you do the test in a brightly lit room, you won’t get the same result as if you do it in a dimly lit room. The second problem is that you have to keep the tablet at a constant distance from your eyes. That’s certainly possible, but how well it’s done in the real world is an open question.

“For those two reasons, the results of perimetry done using a tablet will be quite a lot more variable,” he concludes. “However, if you have a patient that you trust to do it once a week with the setup the way you want it to be, you can get fantastic data from them. That would more than make up for the variability.”

**Head-mounted Virtual Reality**

A number of head-mounted perimeters are now available, including Vivid Vision, the HERU perimeter, the VisuAll (Olleyes), the VirtualEye Perimeter (BioFormatix), the Palm-Scan VF2000 (MicroMedical), the eCloud Perimeter (Elisar), the IMO perimeter (Crewt Medical Systems), and the Toronto Portable Perimeter (VEM Medical Technologies).

“A number of glaucoma clinics are already using these,” notes Dr. Mansberger. “The technology is generally not too expensive; it’s around $10,000 for a device, compared to a visual field machine which might cost $30,000.”

Dr. Gardiner points out that the virtual reality headset perimeters provide more repeatable data than tablets because they block out almost all of the outside light. “Also, the viewing distance is kept constant,” he notes.

“…To get reliable results with any of these [portable] perimeters, your eyes have to adapt to the background light level before taking the test.

—Stuart K. Gardiner, PhD

“…The virtual reality headsets cost more than a tablet, but they’re still a lot less expensive than a standard perimeter,” Dr. Gardiner continues. “So, if you use these options you save money and gain convenience, but you’ll have higher variability in your data.”

“We do a fair amount of head-mounted perimetry in our offices,” notes Dr. Myers. “From our perspective in the clinic, it makes life easier, because instead of moving patients to the room with the machine, the head-mounted perimeter goes to wherever the patient is. That saves a lot of technician time. And, we have multiple headsets, so we don’t get as backed up on the machine.

“We’ve also done some limited home testing,” he continues. “Mathematical modeling of visual field variability has provided evidence that testing every week or every month will detect visual field progression six months to two years earlier than conventional yearly perimetry.” We’ve already done a pilot trial with patients testing themselves every week at home using the Olleyes device, but that only involved about a half-dozen patients. We’re currently doing a larger trial with about 50 patients.”

Dr. Myers notes that his office has worked with Olleyes on their VisuAll perimeter. “Last year,” he says, “we published a study comparing it to Humphrey. We found that there’s a fair amount of agreement, but also a fair amount of difference.”

Although Dr. Myers admits that so far he has no comparative experience with other head-mounted perimeters, he’s impressed with the multiple tasks the Olleyes device is capable of performing. “In addition to visual field testing, the VisuAll can do visual acuity testing, contrast testing and color vision testing,” he says. “One reason this is helpful is that the instrument has a virtual assistant that talks to the patient, much the way a technician instructs the patient through a test. If the patient starts to perform less well on the visual field test, the assistant says things to encourage the patient to get back in the game, or encourages them by saying they’re doing a great job. That means that these tests can be run without a technician present. In the current era in which we have a shortage of technicians, this raises the possibility of helping with our workflow in the clinic.”

How do the patients feel about this option? Apparently, some elderly patients are bothered by wearing a device on their head. “For some older people it can be uncomfortable,” says Dr. Gardiner. “These devices aren’t super heavy, but they’re not light. Of course, this complaint won’t be universal, but an older person with neck issues will hate wearing a device on their head.”

However, Dr. Myers says his office has found that virtual perimetry is more ergonomically comfortable for many elderly patients. “They don’t have to lean into the visual field machine,” he points out. “So most—though not all—of our elderly...
patients appreciate the ergonomics.”

Dr. Gardiner points out a problem that potentially applies to both tablets and head-mounted perimeters—and sometimes is a problem in the clinic as well. “To get reliable results with any of these perimeters your eyes have to adapt to the background light level before taking the test,” he explains. “That can take several minutes.

“As you can imagine, this is a problem with patients conducting visual field tests on their own, whether they’re using a tablet or a head-mounted perimeter,” he continues. “If you’ve been out in the sun, you can’t just take the test right away and expect to get good results. So, if you have your patients use one of these options, they need to understand about allowing time for their eyes to adapt to the lighting level. In research studies, we make sure that this is managed. Ironically, even in the clinic, I suspect this may sometimes be overlooked.”

**Looking Ahead**

Dr. Mansberger looks forward to future improvements in visual-field-testing technology. “Of course, head-mounted perimetry could become very useful in the future,” he says. “In the meantime, we’re already seeing algorithms that incorporate factors such as whether the patient needs to be tested with a size 5 stimulus. Maybe in the future we’ll have a visual field machine that we won’t even need to program. We’ll just start it and it will figure out the best algorithm relative to the patient’s sensitivity; then it will determine whether the patient is progressing, and also look at the central visual field. We know that a lot of patients have central visual field loss, but we don’t routinely test for that today.”

“As time goes by, we’re getting more information about the costs and benefits of these different perimetry options,” Dr. Gardiner notes. “I don’t think there will ever be a consensus that one test is universally better; it will always be about balancing the costs and benefits for different individuals in different situations. That definitely includes the amount of visual damage already present. The closer someone is to losing most of their vision, the more it’s worth spending the time and effort to get the most accurate results.

“I honestly wouldn’t want to bet on which of these options will end up being the standard of care in the future,” he adds.

“It’s an exciting time for these new vision testing devices,” Dr. Myers concludes. “They’re not yet proven, but at least we’re starting down that road. I’m excited about the new ideas and new technologies these companies are developing for our patients.”

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Optical coherence tomography enables clinicians to detect structural damage in their glaucoma patients. It’s become a standard tool for diagnosing and monitoring the disease—but it’s not infallible. In this article, glaucoma specialists share their tips for detecting progression on OCT and avoiding being fooled by artifacts for optimal interpretability.

**OCT Overview**

OCT is most useful in glaucoma suspects and in cases of mild to moderate disease. In early stages, the peripapillary nerve fiber layer is the most sensitive parameter, explains David Huang, MD, PhD, associate director and director of research at the Casey Eye Institute, Peterson Professor of Ophthalmology and a professor of biomedical engineering at the Oregon Health & Science University in Portland.

He notes that the macular ganglion cell complex is another key parameter. A 2020 study reported that, compared to other macular thickness measurements such as full macular, GCIPL, GCL and outer retinal layer thickness, GCC measurements were most likely to detect structural worsening along the glaucoma severity spectrum.1 “Macular changes start slightly later and last longer,” Dr. Huang says. “They’re a complement to the NFL because changes in mild to moderate perimetric glaucoma will be more detectable.”

Dr. Huang says he generally looks at the global average thickness in those structures. “You can also look at the sectors, but of course, that’s a little noisier,” he says. “Sector change may be more useful in patients with a more focal type of glaucoma where damage is concentrated in one sector or one hemisphere of the macula.”

OCT is less useful in later stages of the disease when the device runs into the “floor effect,” when RNFL loss is no longer detectable at about 40 to 45 µm. At this point, clinicians may feel a false sense of security upon seeing very little structural change. “Due to the presence of blood vessels and glial tissue, the RNFL thickness should never be zero—if it is, then there’s a segmentation error,” notes Denise John, MD, FRCSC, a clinical assistant professor of ophthalmology and visual sciences at the Kellogg Eye Center and chief of ophthalmology at the VA Ann Arbor Healthcare Systems in Michigan.

When Dr. John assesses the average RNFL thickness in her patients, she looks for a change greater than 5 µm in average RNFL and/or 10 µm in the sectors, especially in the inferior and superior sectors which are commonly affected by glaucoma. She confirms any concerns about progression with a repeat scan.

The American Academy of Ophthalmology’s Preferred Practice Patterns recommends acquiring an OCT at least once a year. “I typically get an OCT annually for glaucoma suspects and those with stable, mild disease, and I may get an OCT as often as twice per year in those with moderate disease, depending on the stability of the glaucoma,” Dr. John says.

“Therefore, one of the drawbacks of OCT is that it doesn’t image...”
any hemorrhages on the nerve,” says David A. Lee, MD, MBA, a clinical professor at the Cizik Eye Clinic in the Ruiz Department of Ophthalmology and Visual Science at McGovern Medical School in Houston. “One of the other indicators of progression is bleeding on the optic nerve tissue. That’s why looking at the optic nerve directly under the microscope or ophthalmoscope or by taking color photographs (stereoscopic optic disc photographs) is still useful, because we can see and document hemorrhages with photography where they wouldn’t otherwise show up on OCT.”

**Angiographic OCT**

OCT-angiography is a non-invasive newcomer to glaucoma imaging that provides both a qualitative and quantitative assessment of the retinal and optic nerve head vasculature. It’s a good complement to visual field tests and OCT, experts say.

Dr. Huang is currently managing a longitudinal, NEI-funded study on both structural OCT and OCTA, with the goal of improving the diagnostic sensitivity of both modalities—especially for early glaucoma—as well as improving the ability to monitor progression over time. He says that though OCTA isn’t widely used in the clinic now, down the road, a combination of structural OCT and angiographic OCT may aid clinicians in detection of disease and progression, and adjustment of therapy.

“Structural OCT and OCTA are important at different stages of the disease,” he explains. “Structural OCT is sensitive to change in the early stages, such as pre-perimetric or early-perimetric glaucoma, but it runs into the floor effect between moderate and advanced glaucoma. Even in moderate glaucoma, the NFL reaches a low point where it doesn’t really change in terms of micrometers of thickness, so OCT is then no longer sensitive to progression. That’s where OCTA could take over. Superficial vessel density loss in the peripapillary and macular areas changes gradually, and OCTA still has enough dynamic range in moderate and severe disease to detect change.”

**Speed of Progression**

Dr. Huang says you have to be aware of the stage of the disease to meaningfully interpret the speed of progression. “If you follow a patient for a long time, you’ll notice their progression speeds up on visual field and seems to slow down on OCT,” says Dr. Huang. “That’s really a measurement artifact. You have to be aware of that when you interpret the data. The NFL changes very quickly early on, at about 1 to 3 µm per year, but very slowly in severe glaucoma—a fraction of a micron—for the same level of visual change in decibels per year.

“Interpreting whether this speed of progression is fast or slow can be tricky because the progression speed on these two modalities doesn’t correlate well. It can be difficult to clinically judge progression speed based on structural OCT measurements. Additionally, OCT uses a linear scale (µm) and visual field maps use a logarithmic scale (dB).

“You need to see how fast the disease is progressing to decide whether to intervene or change your treatment, so you need some sort of consistent metric for that in decibels per year,” he explains. “That’s not currently available when we look at structure in microns or perfusion in capillary density. Those numbers are hard to interpret because they depend so much on disease stage.”

Dr. Huang and his colleagues recently developed a way to convert NFL thickness or NFL plexus capillary density into a decibel scale that’s equivalent to visual field mean deviation. He says this partially harmonizes the assessment of the speed of progression.

The new OCT parameter his team devised, NFL mean deviation (NFL MD), has better correlation with VF MD, greater diagnostic sensitivity than average NFL thickness and better reproducibility than VF MD, he says. He and his colleagues calculated the NFL MD parameter in the decibel scale from the peripapillary NFL thickness profile nonlinear transformation and visual field area-weighted averaging. However, though NFL MD agrees well with VF MD in early glaucoma, it still underesti-
mates damage in moderate to advanced stages. They tested NFL_MD in Advanced Imaging for Glaucoma study participants (245 normal, 420 pre-perimetric glaucoma and 289 perimetric glaucoma eyes) and found that it had a significantly higher correlation with VF_MD than the overall NFL thickness ($p<0.001$) and also had significantly higher sensitivity for detecting PPG and PG at the 99-percent specificity level. The NFL_MD was also more reproducible than VF_MD ($p<0.001$). Differences between the two parameters were -0.34 ±1.71 dB; -0.01 ±0.08 dB; 3.54 ±3.18 dB; and 7.17 ±2.68 dB for pre-perimetric and early, moderate, and severe perimetric glaucoma subgroups, respectively. He and his colleagues plan to continue studying the use of NFL_MD in monitoring glaucoma progression using the same dataset. (The article notes that Dr. Huang and another author, Ou Tan, PhD, have significant financial interest in Optovue, which “may have a commercial interest in the results of this research and technology.”)

**Assistive Software**

Identifying progression in glaucoma is challenging. Fortunately, OCT machines such as the Cirrus HD-OCT (Carl Zeiss Meditec), Spectralis (Heidelberg Engineering), Optovue Avanti (Visionix, formerly Optovue) and Maestro2 (Topcon) all contain software to aid clinicians in detecting disease progression. Experts note that although progression analysis software is helpful, it’s still important to review all of the original scans to ensure nothing was missed.

Most OCTs display a black-and-white image of the optic nerve and another image in a horizontal-linear format showing the pattern of the RNFL thickness, delineated with red and green lines along the inner and external borders of the NFL. “The computer measures the distance between those two lines and compares it with the normal standard for the scanned population so you can see how your individual patient compares with the normal standard,” says Dr. Lee. “This is usually shown in colors of red (abnormal), yellow (borderline) or green (normal). Looking at the nerve texture itself, you can see where the abnormality was detected.”

The Cirrus HD-OCT’s Guided Progression Analysis report performs event- and trend-based RNFL thickness analysis. In its event-based analysis, the GPA assesses changes from baseline compared to expected variability and flags the change as progression if it falls outside of this expected range. Its trend-based analysis examines the rate of change over time using linear regression. The GPA software requires a minimum of three tests to determine whether there’s “possible” progression and a minimum of four tests to determine whether there’s “likely” progression. But what about progression between two visits? According to a 2021 study by Donald C. Hood, PhD, and colleagues, comparing topographical changes in different OCT maps and comparing visual fields to OCT probability maps can help.

The Spectralis uses the Glaucoma Module Premium Edition software. “The Spectralis progression software is based primarily on the values from the RNFL calculation circle and BMO-MRW,” says Dr. John. “For RNFL, there’s both an event- and trend-based analysis, while the BMO-MRW, as part of the GMPE software, provides a trend-based analysis so you can see the rate of change. This can be calculated based on the global BMO-MRW or per sector.”

The Optovue Avanti wide-field OCT includes the Avanti trend analysis software, which tracks RNFL and GCC thickness changes and estimates future progression. Dr. Huang says he conducted his research using this system with Angiovue OCTA software (Visionix) and currently uses the Optovue Solix system from the same company. (Solix isn’t FDA approved.)

Topcon’s fully automated Maestro2 OCT includes the Hood report, an alternative to conventional RNFL thickness graphs in the TSNIT sequence that offers a shifted circumpapillary RNFL and simulated threshold map. (The Spectralis’ Hood report differs slightly in terms of the scanned area of the retina and threshold overlay.) Topcon says its...
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Important Safety Information
CONTRAINDICATIONS: Most viral disease of the cornea and conjunctiva including epithelial herpes simplex keratitis (dendritic keratitis), vaccinia, and varicella, and also in mycobacterial infection of the eye and fungal disease of ocular structures. Hypersensitivity to any components of the medication.

WARNINGS & PRECAUTIONS:
• IOP increase – Prolonged use may result in glaucoma with damage to the optic nerve, defects in visual acuity and fields of vision. IOP should be monitored.
• Aminoglycoside sensitivity – Sensitivity to topicaly applied aminoglycosides may occur.
• Cataracts – Posterior subcapsular cataract formation may occur.
• Delayed healing – May delay healing and increase the incidence of bleb formation. Perforations of the cornea or sclera have occurred. Slit lamp biomicroscopy, and fluorescein staining should be conducted.
• Bacterial infections – May suppress host response and increase secondary ocular infections. In acute purulent conditions, steroids may mask infection or enhance existing infection. If signs and symptoms fail to improve after 2 days, the patient should be re-evaluated.
• Viral infections – Use with history of herpes simplex requires great caution. The course and severity of many viral infections of the eye (including herpes simplex) may be exacerbated.
• Fungal infections – Fungal infections of the cornea may occur and should be considered in any persistent corneal ulceration.
• Use with systemic aminoglycosides – Total serum concentration of tobramycin should be monitored.

ADVERSE REACTIONS:
The most frequent adverse reactions (<4%) to topical ocular tobramycin are hypersensitivity and localized ocular toxicity, including eye pain, eyelid pruritus, eyelid edema, and conjunctival hyperemia. The reactions due to the steroid component are increased intraocular pressure with possible development of glaucoma, and infrequent optic nerve disorder, subcap-sular cataract, and impaired healing.

The development of secondary infection has occurred. Fungal infections of the cornea may occur. Secondary bacterial ocular infection following suppression of host responses also occurs. Non-ocular adverse events (0.5% to 1%) included headache and increased blood pressure.

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

REFERENCES:

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Brief Summary

This Brief Summary does not include all the information needed to use TOBRADEX ST safely and effectively. Please see Full Prescribing Information for TOBRADEX ST at MyTobraDexST.com.

INDICATIONS AND USAGE

TOBRADEX ST is a topical antibiotic and corticosteroid combination for steroid-responsive inflammatory ocular conditions for which a corticosteroid is indicated and where superficial bacterial ocular infection or a risk of bacterial ocular infection exists.

Ocular steroids are indicated in inflammatory conditions of the palpebral and bulbar conjunctiva, cornea and anterior segment of the globe where the inherent risk of steroid use in certain infective conjunctivitides is accepted to obtain a diminution in edema and inflammation. They are also indicated in chronic anterior uveitis and corneal injury from chemical, radiation or thermal burns, or penetration of foreign bodies.

The use of a combination drug with an anti-infective component is indicated where the risk of superficial ocular infection is high or where there is an expectation that potentially dangerous numbers of bacteria will be present in the eye.

DOSAGE AND ADMINISTRATION

Recommended Dosing: Instill one drop into the conjunctival sac(s) every four to six hours. During the initial 24 to 48 hours, dosage may be increased to one drop every 2 hours. Frequency should be decreased gradually as warranted by improvement in clinical signs. Care should be taken not to discontinue therapy prematurely.

CONTRAINDICATIONS

Nonbacterial Etiology: TOBRADEX ST is contraindicated in most viral diseases of the cornea and conjunctiva including epithelial herpes simplex keratitis (dendritic keratitis), vaccinia, and varicella, and also in mycobacterial infection of the eye and fungal diseases of ocular structures.

Hypersensitivity: Hypersensitivity to any component of the medication.

WARNINGS AND PRECAUTIONS

IOP increase: Prolonged use of corticosteroids may result in glaucoma with damage to the optic nerve, defects in visual acuity and fields of vision. IOP should be monitored.

Aminoglycoside sensitivity: Sensitivity to topically applied aminoglycosides may occur.

Cataracts: May result in posterior subcapsular cataract formation.

Delayed healing: May delay healing and increase the incidence of bleb formation after cataract surgery. In those diseases causing thinning of the cornea or sclera, perforations have been known to occur with the use of topical steroids.

Bacterial infections: May suppress the host response and thus increase the hazard of secondary ocular infections. In acute purulent conditions, steroids may mask infection or enhance existing infection. If signs and symptoms fail to improve after 2 days, the patient should be re-evaluated.

Viral infections: Treatment in patients with a history of herpes simplex requires great caution. Use of ocular steroids may prolong the course and may exacerbate the severity of many viral infections of the eye (including herpes simplex).

Fungal infections: Fungal infections of the cornea are particularly prone to develop with long-term use. Fungal invasion must be considered in any persistent corneal ulceration.

Use with systemic aminoglycosides: Use with systemic aminoglycoside antibiotics requires monitoring for total serum concentration of tobramycin.

ADVERSE REACTIONS

The most frequent adverse reactions to topical ocular tobramycin (TOBREX®) are hypersensitivity and localized ocular toxicity, including eye pain, eyelids pruritis, eyelid edema, and conjunctival hyperemia. These reactions occur in less than 4% of patients. Similar reactions may occur with the topical use of other aminoglycoside antibiotics.

Non-ocular adverse events occurring at an incidence of 0.5% to 1% included headache and increased blood pressure.

The reactions due to the steroid component are: increased intraocular pressure (IOP) with possible development of glaucoma, and infrequent optic nerve disorder, subcapsular cataract, and impaired healing.

Secondary Infection: The development of secondary infection has occurred. Fungal infections of the cornea are particularly prone to develop with long-term use. Fungal invasion must be considered in any persistent corneal ulceration. Secondary bacterial ocular infection following suppression of host responses also occurs.

USE IN SPECIFIC POPULATIONS

Pregnancy and Nursing Mothers

There are no adequate and well controlled studies in pregnant women. TOBRADEX® ST ophthalmic suspension should be used during pregnancy only if the potential benefit justifies the potential risk to the fetus. Caution should be exercised when TOBRADEX® ST is administered to a nursing woman.

Pediatric Use: Safety and effectiveness in pediatric patients below the age of 2 years have not been established.

Geriatric Use: No overall differences in safety or effectiveness have been observed between elderly and younger patients.

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Hood report helps clinicians see which areas of the visual field should be examined for agreement between structural and functional loss.

“Glucoma progression functions provide you with a global speed of change, whether it’s visual field in decibels per year or thickness in microns per year,” says Dr. Huang. “They’re useful because OCT data is much easier for the clinician to interpret when there’s a number to hang your hat on if you can’t compare against literature or compare between patients.”

One thing to note, Dr. Huang continues, is that progression displays don’t tell you where the damage is. “To find the damage, you also need to look at the visual field map, OCT sectors or the profile in terms of the nerve fiber layer or macula,” he adds. “You can actually look at the GCC map, which has even better localizing, to see where the damage is primarily focused. Of course, if it’s closer to fixation—i.e., closer to the fovea—it’s much more alarming. Both macular profile display and trend analysis are important, and you have to look at both.”

Artifacts
When false positives or false negatives occur, they’re referred to as “red disease” or “green disease,” respectively. This color-coding used by the OCT machine is helpful, but it shouldn’t be the final word in a diagnosis or determination of progression. Many factors—from scan quality to the patient’s relationship to the normal database—may produce erroneous results and lead to misinterpretation of OCT data.

“Red disease may result from low signal strength, high myopia, tilted discs, peripapillary atrophy, media opacities that may block the signal (e.g., PVD) and shifted RNFL peaks,” explains Dr. John. “Green disease may occur in the setting of retinal edema, vitreoretinal traction, myelinated nerve fibers or, if the thinning is focal, it may not be detected in the quadrant and sector scans since the device averages the values.”

“Papilledema may change the appearance of the ONH,” Dr. Lee notes. “Initially, if it’s short term, it may appear as a thicker nerve fiber, but over time the nerve fiber atrophies and grows thinner. You may also see thickening of the nerve due to papillitis. This is often seen in patients with very poorly controlled blood glucose, such as in diabetes. Buried drusen in the ONH may also cause elevation. Having the comparison of progression is very useful to see if drusen are growing over time and causing atrophy of the nerve fiber layers.” He adds that malignant hypertension often causes swelling of the optic nerve, and colobomas may affect how the nerve appears as well.

“Be sure to look at the quality factors of the scan before you interpret whether the OCT shows progression or stability,” Dr. Lee says. “The quality of the image can vary between different technicians. How well a technician focuses the instrument and whether or not the patient was cooperative and fairly stationary during the exam affect image quality.”

OCT machines have their own quantitative parameters to check image quality. Optovue (now Visionix) OCT Is have a “signal strength index” (where only scans with a signal strength ≥30 should be considered, per the company’s recommendation); Cirrus’ scan quality index is called “signal strength” (use only scans with a signal strength ≥6, per Zeiss’ recommendation); and the Spectralis has a Q-value. Dr. John notes that on the Spectralis, “The Q-value should be greater than 15. A low-quality value can make the RNFL seem thinner than it really is (red disease).”

Dr. John says other factors that may affect OCT scan accuracy include whether the scan is appropriately segmented and whether the patient falls within the normative database. Additionally, the presence of anatomical variations or artifacts could affect the interpretation of the results.

The magnification effect is another potential confounder since it affects the RNFL thickness measurement, says Dr. Huang. “That may affect diagnosis,” he points out. “Certain parameters may be over- or underestimated if this isn’t corrected for. For example, in a patient with highly myopic eyes, the true scan area could be much larger than the default 3-mm-diameter scan. Nerve fibers spread out and become thinner farther from the disc, so highly myopic eyes may seem to have glaucoma without the pathology because their nerve fibers
appear thinner on the scan. This is sometimes called red disease—these patients have red colors on the NFL OCT display, but they don’t really have glaucoma. However, progression analysis for these patients won’t be as affected because the eye’s length doesn’t change much in the typical glaucoma patient’s age range.

“For OCTA, the way we measure flow signal is affected by reflectance signal strength,” Dr. Huang continues. “If your patient has floaters, a small pupil or dry eye, or the focus isn’t adjusted correctly—any reason the signal is decreased could artificially lower vessel density measurements. That tends to be noise because the quality of the scan can change from visit to visit, depending on the operator and patient cooperation.

“You need very high-quality scans for OCTA,” he notes. “This one of OCTA’s limitations. As patients get older, they may develop a cataract or dry eye that reduces the signal. It’s important to compensate for signal strength when measuring vessel density. My group has researched an algorithm that’s unaffected by signal strength. We’ve also developed methods to compensate for it.”

**Pearls**

Here are some pearls to keep in mind when interpreting OCT data:

- **Use the same machine and consider the same parameters.** “If you want to compare a patient’s scans over time, be sure to have some stability in terms of the type of OCT machine you use and the parameters you’re looking at,” Dr. Huang says. “You can’t compare scans from different machines when you’re trying to assess change over time. Each machine has a different segmentation algorithm, and their NFL thickness measurements will be systematically biased—some will be slightly thicker and others thinner.”

  The same goes for OCTA. “These measurements are relatively new, and different companies have different definitions of vessel density,” Dr. Huang continues. “Some use percent area covered by vessels in certain layers, called slabs, and others use length of blood vessels. So, you have to be careful which quantity you’re looking at. OCTA machines could be significantly different in terms of the area they look at, resolution, quantity, type of area vs. length, threshold for deciding vessel vs. non-vessel, focus, pixel size, etc.”

  Additionally, experts say to check for any changes with software updates or machine upgrades from the OCT manufacturer. Though most manufacturers try not to change their measurements between models and perform substantially equivalent comparisons, there may still be small differences. “Technology improves over time, with both hardware and software,” Dr. Lee points out. “It’s good if your OCT manufacturer gives you upgrades. They should let you know how they compare across different time points.”

- **Ensure the patient falls within the normative database.** “One thing to keep in mind when using your device’s software for analyzing progression is that the normative database may not be representative of every patient you see,” Dr. John says. “Before you interpret the OCT data, be sure to check whether your patient falls within the normative database.”

  Additionally, she says the normative database doesn’t include all normal anatomical variations that can lead to misinterpretation of results. “There may be issues with segmentation errors and artifacts,” she notes. “Also be sure that the patient information is entered correctly. The normative database is based on age (and BMO area for the Spectralis’ progression analysis software).”

- **Take baseline measurements early.** Experts say taking baseline measurements as early as possible is important, especially for those with relatively healthy or normal retinal nerve fiber layers. “In patients with healthier RNFLs, there’s more potential for change than if they were close to end-stage disease, so you need your baseline measurements,” says Dr. Lee.

  High myopes aren’t included in the normative database, but Dr. John says there’s still utility in obtaining an OCT in these patients, assuming there are no issues with segmentation that preclude getting a good scan. “You wouldn’t be able to compare the patient to the normative database, but you can use that first scan as their baseline and compare future scans to that baseline,” she says.

- **Double check your image quality.**

  “Review all the images and scans provided, including the raw scans to see if there are any issues with segmentation, normal anatomical variations or artifacts that may affect the results,” says Dr. John.

- **Review TSNIT profiles for focal loss.** “Because the quadrant and sector profiles represent average values, small changes may not be detected if you only look at those scans,” Dr. John says.

- **Turn to macular scans in advanced glaucoma.** “In advanced
glaucoma or if RNFL pathology is present, the macular scans may be useful for monitoring and detecting glaucoma,” Dr. John says. “Once the RNFL reaches the floor effect, macular thickness or ganglion cell thickness measurements can be used to follow these patients.”

- **Consider the entire clinical picture.** While detecting structural changes over time is important, these findings must correlate with the whole clinical picture for the clinician to fully interpret the results. Dr. Lee says, “I always like to compare the OCT and the visual fields because, for example, if you have a defect in the RNFL that’s on the interior part of the optic nerve, that’ll often correlate with a visual field defect in the superior part of the visual field, such as a paracentral scotoma, an arcuate scotoma or even a nasal step, and vice versa if the RNFL defect is in the upper part of the nerve. Structural changes are usually predictive of functional changes. The Ocular Hypertension Treatment Study showed that changes in the RNFL on OCT often predate the appearance of a corresponding visual field defect. The defect could occur anywhere from one to five years later.

  “Additionally, sometimes you may see changes on the OCT early on, but when you check the pressure in the patient, they seem to be very well controlled,” he says. “It’s well known that compliance is sometimes an issue with glaucoma medications. Several studies have shown that patients tend to be a little more compliant right before their office visit when we check their pressure, and sometimes they’ll forget more often when they’ve been away from the doctor’s office for a longer period. Many doctors mistake this for low-tension glaucoma, where, in spite of low or normal pressures in the eye, the patient continues to experience RNFL loss and visual field defect progression.”

- **Use OCT to distinguish between glaucoma and non-glaucomatous optic neuropathy.** “There may be a discrepancy between the thinning noted on RNFL and macular scans and the optic disc/BMO-MRW scans,” Dr. John says.

- **Show the patient their OCT results.** Dr. Lee says he finds it helpful to display the OCT exam results on a large computer screen to show his patients. “Most patients find it very interesting to see since they’ve never seen a picture of their optic nerve before,” he says. “Showing an image helps me to explain why we’re doing what we’re doing, regarding pressure lowering, and how we measure it. I find it quite educational for patients.”

An Update on ‘Monofocal-Plus’ IOLs

How the latest non-diffractive lenses are fitting into the field, and what results to expect.

Vivity

The AcrySof IQ Vivity from Alcon was the first non-diffractive EDOF IOL available in the U.S. Using technology on the anterior surface of the IOL to achieve the extended-depth-of-field vision, this lens has a negative spherical aberration on the anterior surface, which compensates for the positive spherical aberration of the cornea. The Vivity is composed of a hydrophobic acrylate/methacrylate copolymer with a blue-light-filtering chromophore and standard UV-light filtration. It’s available in powers of +15 D to +25 D in 0.5-D increments, and also comes in a toric version.

Alcon says this lens delivers “monofocal-quality distance vision with excellent intermediate and functional near vision.”

“This really is a novel type of lens category for us,” says Brandon Baartman, MD, of Omaha, Nebraska, who was also part of the clinical trial as a surgical fellow. “We’ve had extended-depth lenses before, but not ones that were truly non-diffractive in the way they work.”

Instead of splitting light into multiple zones of vision as is done with traditional multifocal IOLs, the Vivity uses a central optical element to change the shape of the wavefront. “This lens was born...
out of the desire to achieve a more functional range of vision after cataract surgery, without some of the more glaring downsides of a light-splitting or diffractive-type multifocal lens,” Dr. Baartman continues. “The way patients are using this lens speaks to its strengths, which are distance and dashboard vision.”

The ideal candidate for Vivity is someone with a refractive mindset who desires more freedom from glasses, he says. “This is where the lens really shines. Compared to a monofocal lens, the defocus curve is such that it allows better acuities at intermediate ranges. Compared to a trifocal or bifocal, the Vivity will have the added benefit of fewer dysphotopsias—in particular fewer halos around lights at night, compared to true diffractive multifocals,” Dr. Baartman says.

It’s been a little more than a year since the FDA approved the Vivity. In the clinical study, only 1 percent of patients reported that they were bothered “very much” by halos, and there were no complaints of glare. The study also showed, at six months postop, 98 percent, 97 percent and 58 percent of patients reached 20/32 or better for binocular distance, intermediate and near vision, respectively.

Dr. Baartman believes there’s an opportunity to create a better blended monovision with a slight offset in the non-dominant eye. “That’s been an exciting newer use of this technology,” he says. “Whereas I would never offset one of the eyes for a near target with a true multifocal—there wouldn’t be a purpose—a lens like Vivity would help overcome some of the obstacles we face with monofocal monovision, namely an intermediate dead zone for patients who want good distance and near vision. Now you can get that with a little less of the reduction in intermediate vision.”

He says hitting the refractive target is important. “Early on, I thought that, perhaps with the extended focal depth, there might be a little bit more forgiveness with refractive error. But for those patients who are getting Vivity, keep in mind that these are refractive-minded patients who are expecting a lot. Excellent cataract surgery starts with excellent and meticulous biometry and care for the tear film and preparation of a patient’s eye for surgery,” Dr. Baartman says.

“Once you’re in surgery, I think the proper techniques for any refractive cataract surgery apply, including the use of the best available technology, whether it’s intraoperative aberrometry or femtosecond laser in that particular surgeon’s hands,” he continues. “And, treating any significant astigmatism with a toric lens or limbal relaxing incisions is beneficial at the time of surgery to help improve outcomes.”

In his experience, patients with significant corneal or retinal pathology wouldn’t be good candidates. “People with ectasia, corneal scars or even significant post-refractive keratotomy may not be the best candidates, as well as those with severe glaucoma,” Dr. Baartman says. “But I think with Vivity, patients with a mild ERM, or early macular degeneration that’s been stable are patients who might be reasonable candidates.”

Eyhance

The Tecnis Eyhance from Johnson & Johnson Vision is a one-piece monofocal designed to extend the depth of focus compared to other multifocals. Its shape is unique, with a 6-mm biconvex, aspheric anterior surface and a frosted 360-degree posterior square edge. J&J Vision says the Eyhance IOL delivers a 30-percent improvement in contrast in low-light conditions at 5 mm vs. a standard monofocal. Its powers range from +5 D to +34 D in 0.5-D increments, and it comes in a toric version. The lens is available on the preloaded Tecnis Simplicity delivery platform.

Douglas D. Koch, MD, a professor and Allen, Mosbacher and Law Chair in Ophthalmology at Baylor

**Figure 1. Tecnis Eyhance IOL (ICB00) vs. Tecnis monofocal 1-piece IOL (ZCB00): Intermediate and distance vision at six months post-surgery. The Eyhance achieved a statistically significant, 1.1-line improvement in monocular and binocular intermediate vision at six months vs. a monofocal. The monofocal had 0.4-line better distance vision than the Eyhance.**
College of Medicine in Houston, has been closely involved with the development of this lens and says it’s essentially the first “monofocal plus” IOL.

“The lens gives you that monofocal-type sharpness of vision, with about one more line of near vision than a standard monofocal, on average. It does so by having a very subtle increase in steepness over the central zone (2 mm) so it just blends in, compared with a discrete zone,” Dr. Koch says. “The benefit I find is that many patients can get great distance vision and yet still see their cell phone at arm’s length. I’ve also found that there are no dysphotopsias associated with the optical benefits of this lens.”

The one-line advantage at near has been demonstrated in both laboratory and clinical studies, but Dr. Koch says it’s important to point out that he—and likely many other surgeons—don’t indicate that to the patient preoperatively. “Eyhance doesn’t meet the FDA criteria for EDOF, and some patients may get increased near and some may not. For example, if the patient is plano, you may have some near, but if the patient is +0.25, the patient may not have any near benefit. They may have great distance vision if they end up a little hyperopic because of the flatter landing zone, but they may not have the near benefit, so I don’t talk to them about it in advance. If the patient gets the one line of near vision postoperatively, then that’s a wonderful side benefit. But because it’s such a subtle amount, it’s hard to convey that to the patient, and we hate to raise expectations.”

When it comes to nailing the distance side, Dr. Koch says he’d be wary of aiming too far on the minus side. “I might aim for plano, or even +0.1, so that I get really good distance vision for the dominant eye. For the non-dominant eye, you can aim for, say, -0.5 and that will give them 20/25 at distance, yet they might get quite a bit of near benefit from it,” he says. “That’s one way to do a micro-monovision. Or you can aim for plano in both eyes. You can often get a near benefit, but it’s kind of nice to do a little bit of a variation in one eye versus the other.”

The bigger and flatter landing zone is an advantage for post-LASIK eyes, says Dr. Koch. “It’s a little more tolerant to defocus and you’re more likely to get 20/25 or even 20/20 uncorrected in post-LASIK eyes because of the flatter landing zone,” he notes. Dr. Koch says Eyhance may not be ideal for patients who have a lot of irregular astigmatism or who have had hyperopic LASIK because of the lens’s amount of negative spherical aberration.

### Table 1. Visual Acuity One Month Postoperative for the RayOne EMV

<table>
<thead>
<tr>
<th>Value</th>
<th>Acuity (LogMAR)</th>
<th>Snellen Approximation</th>
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</thead>
<tbody>
<tr>
<td>Binocular UDVA (n=18)</td>
<td>-0.03 ±0.05</td>
<td>20/20</td>
</tr>
<tr>
<td>Dominant Eye UDVA (n=18)</td>
<td>-0.02 ±0.07</td>
<td>20/20</td>
</tr>
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<td>Binocular UDVA (n=17)</td>
<td>0.08 ±0.12</td>
<td>N8 @ 100 cm</td>
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<td></td>
<td></td>
<td>J1/2 @ 40 cm</td>
</tr>
<tr>
<td>Binocular UDVA (n=5)</td>
<td>N6 Range</td>
<td>20/32</td>
</tr>
</tbody>
</table>

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Europe has enjoyed a variety of lenses for years, and to be able to customize and personalize the lens choice for each patient is fantastic.”

- Lisa Nijm, MD

Eyhance is delivered via the one-step Tecnis Simplicity system. “This platform has superb optical quality in terms of a very high Abbe number with reduced chromatic aberration. The surface is pristine and doesn’t deteriorate over time,” Dr. Koch says. “The toric version comes on the new Toric II platform with roughened or textured outer edges on the haptics.

“I haven’t heard of any adverse events, other than the occasional patient with glare,” he adds. “I haven’t seen anything that indicates there are any complications associated with the design.”

### RayOne

The latest IOL to be approved is the RayOne EMV (“enhanced monovision”) from Rayner Global. This monofocal lens offers up to 2.25 D (with 1-D offset) of extended depth of focus. The single-piece design is 12.5 mm, made of Rayacryl hydrophilic acrylic, and available in powers of +10 to +30 D in 0.5-D increments. The lens is suitable for patients who aren’t candidates for diffractive trifocals and are looking for some spectacle independence and reduced dysphotopsia.

In the one-month postoperative period, patients in the clinical study reported high satisfaction with their refractive outcome, including 70 percent who said they had spectacle independence at distance, intermediate and near. One-hundred percent of patients in the study were dysphotopsia-free.

The company says that, like other IOLs in its catalog, the RayOne EMV has reduced sensitivity to decentration and tilt. “With the aspheric lens, there tends to be better centration so it’s less dependent on the pupil location and size,” says Lisa Nijm, MD, an assistant clinical professor of ophthalmology at the UIC Eye and
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I am happy to announce an exciting addition as we continue into our seventh year of Mackool Online CME. This year, with the generous support of several ophthalmic companies, my son Dr. RJ Mackool and I will share the honor of presenting our surgical cases to you. Together we will continue to demonstrate the technologies and techniques that we find to be most valuable to our patients, and that we hope are helpful to many of our colleagues.

I will continue to narrate all of the cases, even as we share the surgical duties and thereby expand the variety of the cases that we bring to you. As before, one new surgical video will be released monthly, allowing our colleagues the opportunity to earn CME credits or just observe the case. New viewers are able to obtain additional CME credit by reviewing previous videos that are located in our archives.

I thank the many surgeons who have told us that they have found our CME program to be valuable and instructive; I appreciate your comments, suggestions and questions. Thanks again for joining us on Mackool Online CME.

Richard J. Mackool, MD

Episode 78:
“Cataract-IOL in an Aniridic Eye: The Artificial Iris”
Surgical Video by: Richard J. Mackool, MD

Video Overview:
A patient with congenital aniridia undergoes phacoemulsification, IOL insertion, and insertion of an artificial iris device.

To view CME video go to: www.MackoolOnlineCME.com

Richard Mackool, MD, a world renowned anterior segment ophthalmic microsurgeon, has assembled a web-based video collection of surgical cases that encompass both routine and challenging cases, demonstrating both familiar and potentially unfamiliar surgical techniques using a variety of instrumentation and settings.

This educational activity aims to present a series of Dr. Mackool’s surgical videos, carefully selected to address the specific learning objectives of this activity, with the goal of making surgical training available as needed online for surgeons motivated to improve or expand their surgical repertoire.

Learning Objective
After completion of this educational activity, participants should be able to:
• demonstrate the technique and discuss the indication for implantation of an artificial iris at the time of cataract-implant surgery.

Satisfactory Completion - Learners must pass a post-test and complete an evaluation form to receive a certificate of completion. You must listen to/view the entire video as partial credit is not available. If you are seeking continuing education credit for a specialty not listed below, it is your responsibility to contact your licensing/certification board to determine course eligibility for your licensing/certification requirement.

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How to Manage the Complex Dry-Eye Patient

The first step is to determine whether the correct diagnosis has been made.

Most dry-eye patients respond to one of the first several medications initiated. However, there is a subset of patients who have long-standing dry eye that has resisted treatment. These cases are typically referred to a corneal specialist.

According to Brad Kligman, MD, who is in practice in Manhasset, New York, “The first step in caring for these patients is just having the patience to do so,” he says. “It can take a lot of time to get to the bottom of the problem, so just understanding that you need to talk to these patients at length and kind of hold their hand through the treatment is important.”

Establishing a Diagnosis

According to Dr. Kligman, when a patient is referred to his practice for dry eye that hasn’t responded to treatment, the first step is to take a very careful history. “It’s important to understand exactly what his or her symptoms are,” he notes. “Is it a burning or stinging? Is it blurry vision?”

Additionally, he recommends asking what time of day the patient experiences symptoms and whether he or she wears contact lenses. “Make sure to find out what types of lenses they’re wearing, how long they wear them, and whether they are sleeping in their lenses,” he says. “Those things don’t always get asked right away, and that can lead you to a delay in diagnosis. You want to ask about their sleeping habits and whether they have symptoms in both eyes or only one. If they only sleep on one side, that can point you to a different diagnosis. You want to get to the root of the problem and not just cover up symptoms.”

The next step is an exam that focuses on all parts of the eye. Start with the eyelids to determine how easily meibum is expressed. “When you talk about dry eye, patients assume it’s because the eye isn’t making enough tears,” Dr. Kligman says. “But the majority of dry eye is evaporative, where you’re not getting that good oil layer to hold the tears in place. So, I really focus on the lids and see if targeting lipid secretion will lead to resolution of symptoms. I also find it very important to flip the eyelids. That will let you know if there are allergies or signs of chronic infection. I often...
discover floppy-eyelid syndrome in these patients. When you’re manipulating the lids, see how easy it is to pull the lid away from the eye. That can point towards floppy-eyelid syndrome. If the lids are loose, pillows can physically push the eyes open during sleep and cause physical irritation. If you make patients aware of it, they can try to change their sleeping habits and add protective ointments or shields. That alone can lead to resolution of their symptoms.”

Christopher J. Rapuano, MD, in practice at Wills Eye Hospital in Philadelphia, adds that dryness resulting from floppy eyelids tends to be worse in the morning, while aqueous deficiency dry-eye symptoms tend to be worse at night. “Another diagnosis that you can make from flipping the eyelids and having the patient look down is superior limbic keratoconjunctivitis,” he says. “This condition is missed all the time and has symptoms very similar to dry eye.”

Dr. Kligman adds that the finding of floppy eyelids can also lead to a diagnosis of sleep apnea. “This is one way that we, as ophthalmologists, can help diagnose systemic disease,” he avers. “This not only helps their eyes feel better but can also potentially save lives down the road, because sleep apnea can lead to serious pulmonary and cardiac conditions. I’ve diagnosed dozens of people with sleep apnea just based on an exam for what they thought was dry-eye syndrome.”

Another component of a careful exam is to stain the cornea. “With contact lens wearers, you actually want to wait a little bit longer with the staining because that can bring out a very specific pattern that will tell you that it’s not really dry eye,” Dr. Kligman notes. “It can be corneal limbal stem cell deficiency, which is more common than people think, but you need to take the time and look for it. This also changes the treatment protocol, because patients really just need to completely stay out of their contact lenses. If you treat it with drops and medications but they still wear the contact lenses, it will never get better. It can actually become a vision-threatening condition. You’re looking for little comma-shaped areas of staining emanating from the limbus rather than the discrete dots that we typically associate with dry eye.”

It’s also important to examine the conjunctiva. Often, when patients complain of a foreign body sensation, it’s due to conjunctivochalasis, a laxity and redundancy of the conjunctiva. “When they’re blinking, they’re actually feeling the conjunctiva between their lids,” Dr. Kligman explains. “This is another instance where the traditional treatments for dry eye won’t necessarily make the symptoms better. In these cases, we might need to perform a procedure to shrink or excise the redundant conjunctiva.”

Dr. Rapuano agrees that conjunctivochalasis is a fairly common diagnosis that’s often missed, and these patients often get treated for dry eye without significant improvement. Another one is mucous membrane pemphigoid. “Have the patient look up and look at the inferior fornix to see if there’s inferior fornix shortening or scarring of the inferior conjunctiva,” he explains. “This tends to occur in older patients, more in women than in men, and it’s a potentially blinding disease. Obviously, when it’s severe, it’s much easier to make the diagnosis, but blinding disease starts off as a mild disease. If you make the diagnosis early, you can treat these patients a lot better.”

After all these evaluations, it may turn out to be a more typical aqueous deficient dry eye. “Those alone are kind of rare, so you have to dig a little bit deeper to find out why they’re not producing dry eye,” Dr. Rapuano advises. “If their Schirmer score is less than 5 mm and they have really bad staining across their corneas, that’s when you want to get into a more targeted medical history and find out if they have joint pain, muscle aches or a history of rheumatologic disease. Either you or a rheumatologist might want to run an inflammatory lab panel to find out if the patient has an autoimmune or rheumatologic disease that might be contributing to dry eye.”

Neurotrophic keratitis and exposure keratitis are other conditions to watch for. “Some people’s eyes just don’t close very well, they don’t blink very well, and they’re open at nighttime, causing the eyes to get dried out,” Dr. Rapuano says. “So, it’s not necessarily that they’re not making a lot of tears—they’re just getting dried out during the nighttime.”

If a patient has significant chalazia, especially in one eye, be sure to flip the eyelid and examine it for signs of sebaceous carcinoma. “This is skin cancer of the eyelid and the underside of the conjunctiva. It’s rare, but it’s potentially blinding—if not lethal,” Dr. Rapuano says. “That’s at the very extreme, of course, and that’s more blepharitis differential than dry-eye differential.”
Feature COMPLEX DRY EYE

Treatments
According to Dr. Kligman, when initiating treatment, make sure that patients understand that it’ll be a process and that you will be working with them long-term. “This is a chronic condition that needs to be managed, like blood pressure or cholesterol,” he says. “That helps put them in the mindset of really committing and following through with the recommendations. It’s important to set expectations with patients that it can be a long process, but you’re going to be there to see them through these different treatments and see what works.”

Fortunately, there are many treatments available for dry eye. For a while, the mainstays were cyclosporine and lifitegrast. “Tyrvaya (varnericline) nasal spray is a new option, and there are several products in the pipeline,” Dr. Kligman says. “The good thing is, in the past five years, we have had a big jump in available treatments. Eysuvis also recently became FDA-approved; that’s another formulation of loteprednol that’s approved for pulse treatment of dry-eye flares. We now have a steroid formulation in Eysuvis that has been studied in this specific population. We can more confidently prescribe to patients and not worry about pressure spikes quite as much.” Other recent additions include Klarity-C (cyclosporine ophthalmic emulsion 1%, ImprimisRx) and Cequla (cyclosporine ophthalmic emulsion 0.09%, Sun Ophthalmics).

For evaporative dry-eye disease patients who have blepharitis and meibomitis, there are several tools and procedures that can be performed to help open the glands. Patients can start with lid scrubs, lid sprays and at-home warm compresses. “If those aren’t fully successful,” Dr. Kligman says, “then you can move on to procedures that are done in the office, like BlephEx, which physically removes the build-up of surf at the lash bases, and you can use heating and expression devices, like iLux2, LipiFlow and TearCare, which help heat and express the glands all at once and help to reset these meibomian glands to get people back to producing healthy meibum that actually flows out of the lids.”

Dr. Rapuano adds that other treatment options include punctal plugs, steroid drops and serum tears. “You can then proceed to scleral lenses in bad dry eye patients,” he notes. “In the really bad ones, especially if the patients are older and are less concerned about cosmetics, you can do a small permanent lateral tarsorrhaphy. I’ve done that in several patients who have Sjogren’s syndrome, where they get ulcerations or scratches in the eye. You can just do a little lateral tarsorrhaphy, and that significantly decreases the palpebral fissure, so there’s much less evaporation.”

According to Stephen Pflugfelder, MD, who is in practice at Baylor College of Medicine in Houston, patients with Stevens-Johnson syndrome require aggressive therapy. “These patients can be in the acute phase or the chronic phase,” he says. “It’s usually during the chronic phase that most doctors end up seeing these patients. At that point, they can have a lot of conjunctival and lid margin scarring, irregular lid margins, lashes that grow in (trichiasis) and no tear production. And, in some cases, because the lids are so irregular, they can develop corneal epithelial defects and even corneal ulcers. If patients have lids that turn in, they’ll need surgery to rotate the lid margin out, away from the eye. They may need what’s called a mucous membrane graft to resurface the back of their eyelids. They usually need serum or plasma drops, and they usually need scleral contact lenses.”

Another condition is graft-versus-host disease, which can develop in patients who’ve had allogeneic bone marrow transplants. “By about 90 days out, 40 to 50 percent of patients will experience severe dry eye, and they can also experience eyelid scarring,” Dr. Pflugfelder says. “We first try conventional dry-eye treatments, but they don’t often work. These patients may also require serum or plasma drops and scleral lenses to feel better. Anti-inflammatory treatments, like cyclosporine or topical corticosteroids, can also be helpful.”

Neurotrophic keratitis can result in reduced corneal or ocular surface sensation due to nerve damage or degeneration. This can be a result of herpes, chemical injuries, neurosurgery, diabetes and some neurodegenerative diseases. “In addition to standard dry-eye treatment, these patients can be treated with cenermin (Oxervate, Dompe), which is recombinant nerve growth factor,” Dr. Pflugfelder says.

According to Dr. Kligman, these treatments can often be life-changing for patients who are struggling with dry eye. “For those physicians willing to take the time and get the history and do the really careful exam,” he says, “they can create a very loyal following of happy patients who have been suffering for a long time. You can potentially identify an underlying condition that was overlooked previously and really improve these patients’ quality of life.”
Courses are restricted to US-based 3rd-year residents enrolled in a US-based ophthalmology resident program and within their third year at the time of the course.

There is no registration fee for these activities. Air, partial ground transportation in Forth Worth, hotel accommodations and modest meals will be provided through an educational scholarship for qualified participants.

Satisfactory Completion – Learners must complete an evaluation form to receive a certificate of completion. Your chosen sessions must be attended in their entirety. Partial credit of individual sessions is not available. If you are seeking continuing education credit for a specialty not listed below, it is your responsibility to contact your licensing/certification board to determine course eligibility for your licensing/certification requirement.

Accreditation Statement – In support of improving patient care, this activity has been planned and implemented by Amedco LLC and Review Education Group. Amedco LLC is jointly accredited by the Accreditation Council for Continuing Medical Education (ACCME), the Accreditation Council for Pharmacy Education (ACPE), and the American Nurses Credentialing Center (ANCC), to provide continuing education for the healthcare team.

Physicians (ACCME) Credit Designation – This live activity has been approved for AMA PRA Category 1 Credit(s)™.

Dear CSE 3rd-Year Resident Program Director and Coordinator,

We would like to invite you to review the upcoming 3rd-Year CSE Ophthalmology Resident CME Programs and Wet Labs for 2022 in Fort Worth, Texas. The programs offer a unique educational opportunity for third-year residents by providing the chance to meet and exchange ideas with some of the most respected thought leaders in ophthalmology. The programs are designed to provide your residents with in-depth didactic program and state-of-the-art wet lab experience with one-on-one wet lab guidance from faculty. The courses also serve as an opportunity for your residents to network with residents from other programs.

After reviewing the material, it is our hope that you will select and encourage your residents to attend one of these educational activities, which are CME accredited to ensure fair balance.

Best regards,
Kendall Donaldson, MD, MS; Yousf Khalifa, MD and Mitchell P. Weikert, MD, MS

Registration open www.ReviewEdu.com/CSE3rdYr2022

Courses are restricted to US-based 3rd-year residents enrolled in a US-based ophthalmology resident program and within their third year at the time of the course. There is no registration fee for these activities. Air, partial ground transportation in Forth Worth, hotel accommodations and modest meals will be provided through an educational scholarship for qualified participants.

For more information visit the registration site above or call Denette Holmes at 866-627-0714 or email dholmes@postgradhealthed.com

Supported by an independent medical education grant from Alcon

Jointly provided by Amedco and Review Education Group
Diagnosing Pigmented Choroidal Lesions

Here’s how to tell all the various lesions apart to ensure you don’t miss anything serious.

A variety of pigmented choroidal lesions can be encountered in clinical practice, and differentiating between benign and malignant lesions is critically important for the ophthalmologist. Additionally, each individual lesion can have a heterogenous range of clinical presentations, often with overlap between different conditions that can lead to diagnostic uncertainty in select cases. Choroidal melanoma remains the most common concerning pigmented choroidal lesion. However, the following lesions can simulate melanoma:

- choroidal nevus;
- congenital hypertrophy of the retinal pigment epithelium;
- peripheral exudative hemorrhagic chorioretinopathy;
- choroidal melanocytosis;
- pigmented choroidal metastasis from cutaneous or choroidal melanoma;
- melanocytoma;
- bilateral diffuse uveal melanocytic proliferation;
- retinal pigment epithelium adenoma/adenocarcinoma; and
- suprachoroidal hemorrhage.

While a detailed clinical examination is the most important component in diagnosing these conditions, a thorough history and multimodal imaging can also be critical in correctly identifying the pigmented lesions listed above and choosing the appropriate management strategy.

Here, we’ll describe how we approach each of them.

**Choroidal Melanoma**

Choroidal melanoma is the most common primary intraocular malignancy in adults, occurring at an age-adjusted incidence of 4.3 per million in the United States. It usually presents in the sixth decade of life, most commonly as a pigmented lesion. In one large series, the mean largest basal dimension was 11.1 mm and average thickness was 5.5 mm. Clinical features supportive of a diagnosis of choroidal melanoma include the presence of subretinal fluid, presence of lipofuscin (orange pigment) associated with the lesion and rupture through Bruch’s membrane (Figure 1).

Enhanced depth imaging optical coherence tomography (EDI-OCT) is extremely valuable in the correct identification of choroidal melanoma. Serial widefield color fundus photography can be particularly helpful when following indeterminate lesions for subtle evidence of growth, as well as monitoring treated choroidal melanomas for signs of local recurrence. Fundus autofluorescence (FAF) is another useful adjunct capable of confirming the presence of lipofuscin pigment as well as active or resolved areas of subretinal fluid, which can be subtle clinically but appear brightly hyperautofluorescent (Figure 1, B and D).

**Dr. Regillo** is the director of the Retina Service of Wills Eye Hospital, a professor of ophthalmology at Thomas Jefferson University School of Medicine and the principle investigator for numerous major international clinical trials.

**Dr. Yonekawa** is an assistant professor of ophthalmology at Sidney Kimmel Medical College at Thomas Jefferson University. He serves on the Education Committee of the American Society of Retina Specialists and on the Executive Committee for the Vit Buckle Society, where he is also the vice president for academic programming.

This article has no commercial sponsorship.
thickness, spontaneous vascular pulsations, a sign of an intrinsic blood supply and the presence of extraocular extension.

Systemic screening is routinely performed for patients with choroidal melanoma to assess for distant metastasis, even though only 4 percent of patients are noted to have metastasis at the time of diagnosis. This workup is even more important in cases of diagnostic dilemmas in which a choroidal metastasis remains in the differential. When clinical examination and ancillary testing don’t clearly reveal the diagnosis, lesion biopsy, predominantly using fine-needle aspiration (FNAB) or a vitrector-assisted approach, can be performed. Biopsy is performed for cytopathology with or without immunohistochemistry, and more recently the DNA mutational profile can be ascertained to help establish the diagnosis using next-generation sequencing (NGS). On cytopathology, uveal melanoma demonstrates the presence of spindle and/or epithelioid cells often with the presence of cytoplasmic melanin. Immunohistochemical stains like SOX10, HMB-45 and Melan-A confirm the melanocytic origin of the lesion, but don’t differentiate between a benign nevus and a malignant melanoma. Mitotic activity can be assessed using the Ki-67 stain, which can help distinguish these lesions and is associated with an increased risk of metastasis in uveal melanoma.5,6

The most common mutations include GNAQ, GNA11, PLCB4 and CYSLTR2, but less frequent initiator mutations are likely still to be discovered.5,7,8 Secondary mutations like BAP1, SF3B1 and EIF1AX are required for a lesion to have malignant potential, and their presence is indicative of a melanoma.5,9,10 The absence of either initial or secondary mutations doesn’t definitively rule out a melanocytic origin, and the absence of a secondary mutation in the presence of an initial mutation doesn’t definitively rule out a malignant lesion. NGS has not yet been studied prospectively, so its ultimate role in identification of tumor origin remains to be determined.

Figure 1. Ultra-widefield fundus photograph showing a pigmented choroidal melanoma along the superotemporal arcade with a central nodule secondary to break through Bruch's membrane, overlying lipofuscin and surrounding subretinal fluid (A). Autofluorescence demonstrates hyperautofluorescence overlying the lesion corresponding to lipofuscin (orange pigment) and surrounding shallow subretinal fluid (B). Ultra-widefield fundus photograph showing a circumpapillary pigmented choroidal melanoma (C). Autofluorescence demonstrates extensive subretinal fluid from 2 to 12 o'clock, which appears hyperautofluorescent (D). Ultra-widefield fundus photograph demonstrating a large choroidal melanoma overhanging and obscuring the optic nerve (E). Corresponding B-scan ultrasonography shows a typical mushroom-shape lesion with overlying retinal detachment (F). Ultra-widefield fundus photograph showing a temporal dome-shaped choroidal melanoma with B-scan ultrasonography demonstrating low/medium internal reflectivity of the lesion and associated exudative retinal detachment (G-H).
WHAT COULD SHE SEE THIS YEAR?

EYLEA® (aflibercept) Injection
For Intravitreal Injection

Inspired by a real patient with Wet AMD.

IMPORTANT SAFETY INFORMATION

CONTRAINDICATIONS

• EYLEA is contraindicated in patients with ocular or periocular infections, active intraocular inflammation, or known hypersensitivity to aflibercept or to any of the excipients in EYLEA.

WARNINGS AND PRECAUTIONS

• Intravitreal injections, including those with EYLEA, have been associated with endophthalmitis and retinal detachments. Proper aseptic injection technique must always be used when administering EYLEA. Patients should be instructed to report any symptoms suggestive of endophthalmitis or retinal detachment without delay and should be managed appropriately. Intraocular inflammation has been reported with the use of EYLEA.

• Acute increases in intraocular pressure have been seen within 60 minutes of intravitreal injection, including with EYLEA. Sustained increases in intraocular pressure have also been reported after repeated intravitreal dosing with VEGF inhibitors. Intraocular pressure and the perfusion of the optic nerve head should be monitored and managed appropriately.

• There is a potential risk of arterial thromboembolic events (ATEs) following intravitreal use of VEGF inhibitors, including EYLEA. ATEs are defined as nonfatal stroke, nonfatal myocardial infarction, or vascular death (including deaths of unknown cause). The incidence of reported thromboembolic events in wet AMD studies during the first year was 1.8% (32 out of 1824) in the combined group of patients treated with EYLEA compared with 1.5% (9 out of 595) in patients treated with ranibizumab; through 96 weeks, the incidence was 3.3% (60 out of 1824) in the EYLEA group compared with 3.2% (19 out of 595) in the ranibizumab group. The incidence in the DME studies from baseline to week 52 was 3.3% (19 out of 578) in the combined group of patients treated with EYLEA compared with 2.8% (8 out of 287) in the control group; from baseline to week 100, the incidence was 6.4% (37 out of 578) in the combined group of patients treated with EYLEA compared with 4.2% (12 out of 287) in the control group. There were no reported thromboembolic events in the patients treated with EYLEA in the first six months of the RVO studies.

EYLEA is a registered trademark of Regeneron Pharmaceuticals, Inc.

REGENERON
PROVEN VISUAL OUTCOMES AT YEAR 1 IN THE VIEW STUDIES

Fewer injections with EYLEA Q8 vs ranibizumab Q4

Demonstrated in the largest phase 3 anti-VEGF trials completed to date in Wet AMD (N=2412)

Proportion of patients who maintained vision (<15 ETDRS letters lost of BCVA) at Year 1 from baseline

<table>
<thead>
<tr>
<th></th>
<th>Primary Endpoint (Year 1)</th>
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<tr>
<td>VIEW 1</td>
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<tr>
<td>EYLEA Q4</td>
<td>95% (12.6 injections)</td>
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<tr>
<td>EYLEA Q8</td>
<td>94% (7.7 injections)</td>
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<td>ranibizumab</td>
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<td>VIEW 2</td>
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<tr>
<td>EYLEA Q4</td>
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<td>EYLEA Q8</td>
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<td>ranibizumab</td>
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EYLEA was clinically equivalent to ranibizumab.

VIEW 1 and VIEW 2 study designs: Two multicenter, double-masked clinical studies in which patients with Wet AMD (N=2412; age range: 49-99 years, with a mean of 76 years) were randomized to receive: 1) EYLEA 2 mg Q8 following 3 initial monthly doses; 2) EYLEA 2 mg Q4; 3) EYLEA 0.5 mg Q4; or 4) ranibizumab 0.5 mg Q4. Protocol-specified visits occurred every 28 (±3) days.

ADVERSE REACTIONS

• Serious adverse reactions related to the injection procedure have occurred in <0.1% of intravitreal injections with EYLEA including endophthalmitis and retinal detachment.

• The most common adverse reactions (≥5%) reported in patients receiving EYLEA were conjunctival hemorrhage, eye pain, cataract, vitreous detachment, vitreous floaters, and intraocular pressure increased.

• Patients may experience temporary visual disturbances after an intravitreal injection with EYLEA and the associated eye examinations. Advise patients not to drive or use machinery until visual function has recovered sufficiently.

INDICATIONS

EYLEA (aflibercept) Injection 2 mg (0.05 mL) is indicated for the treatment of patients with Neovascular (Wet) Age-related Macular Degeneration (AMD), Macular Edema following Retinal Vein Occlusion (RVO), Diabetic Macular Edema (DME), and Diabetic Retinopathy (DR).


Please see Brief Summary of Prescribing Information on the following page.
**BRIEF SUMMARY—Please see the EYLEA full prescribing information available on HCPEYLEA.US for additional product information.**

**1 INDICATIONS AND USAGE**
EYLEA ( aflibercept ) injection is a vascular endothelial growth factor (VEGF) inhibitor indicated for the treatment of patients with:

- Neovascular (wet) Age-Related Macular Degeneration (AMD), Diabetic Macular Edema (DME), Diabetic Retinopathy (DR).

- Macular Edema Following Retinal Vein Occlusion (RVO), Diabetic Macular Edema (DME), Diabetic Retinopathy (DR).

- Macular Edema Following Retinal Vein Occlusion (RVO).

- Neovascular (wet) Age-Related Macular Degeneration (AMD).

**2 CLINICAL TRIALS**

In practice.

In the days following EYLEA administration, patients are at risk of developing endophthalmitis or retinal detachment. If the clinical signs and symptoms of endophthalmitis are present, proper aseptic injection technique must always be used when administering EYLEA. Patients should be instructed to report any symptoms suggestive of endophthalmitis or retinal detachment without delay and should be managed appropriately.

**3 ADVERSE REACTIONS**

EYLEA is a vascular endothelial growth factor (VEGF) inhibitor indicated for the treatment of patients with:

- Neovascular (wet) Age-Related Macular Degeneration (AMD), Diabetic Macular Edema (DME), Diabetic Retinopathy (DR).

- Macular Edema Following Retinal Vein Occlusion (RVO).

- Neovascular (wet) Age-Related Macular Degeneration (AMD).

- Macular Edema Following Retinal Vein Occlusion (RVO).

- Neovascular (wet) Age-Related Macular Degeneration (AMD).

**4.2 Active Intraocular Inflammation**

Intraocular pressure increased.

**4.3 Hypersensitivity**

Eyelid edema <1% 1% 1% 0%

**4.4 Active Control with EYLEA**

Intraocular inflammation 1% 1% 0% 0%

**4.5 Endophthalmitis and Retinal Detachment**

Injection site pain 3% 1% 1% 0%

**5.1 Vision Problems**

**5.2 Increase in Intraocular Pressure**

Injection site pain 2% <1% 2% <1%

**5.3 Thromboembolic Events**

**5.4 Clinical Trial Exclusions**

Injection site pain 2% 2% 2% 2%

**6 ADVERSE REACTIONS**

**5.5 Endophthalmitis and Retinal Detachment**

Injection site pain 3% 1% 1% 0%

**6.1 Immunogenicity**

Injection site pain 2% <1% 2% <1%

**6.2 Immunogenicity**

Injection site pain 2% <1% 2% <1%

**6.3 Thromboembolic Events**

Injection site pain 2% <1% 2% <1%

**6.4 Active Control with EYLEA**

Injection site pain 2% <1% 2% <1%

**6.5 Thromboembolic Events**

Injection site pain 2% 2% 2% 2%

**6.6 Hypersensitivity**

Injection site pain 2% <1% 2% <1%

**6.7 Active Control with EYLEA**

Injection site pain 2% 2% 2% 2%

**6.8 Active Control with EYLEA**

Injection site pain 2% <1% 2% <1%

**7 PATIENT COUNSELING INFORMATION**

Injection site pain 2% 2% 2% 2%

**8 USE IN SPECIFIC POPULATIONS**

Injection site pain 2% <1% 2% <1%

**8.1 Pregnancy**

Injection site pain 2% 2% 2% 2%

**8.2 Lactation**

Injection site pain 2% <1% 2% <1%

**8.3 Children**

Injection site pain 2% 2% 2% 2%

**8.4 Pediatric Use**

Injection site pain 2% <1% 2% <1%

**8.5 Maternal and Neonatal Effects**

Injection site pain 2% 2% 2% 2%

**8.6 Carcinogenesis, Mutagenesis, Impairment of Fertility**

Injection site pain 2% <1% 2% <1%

**8.7 Pregnancy Data**

Injection site pain 2% 2% 2% 2%

**8.8 Male Reproduction**

Injection site pain 2% <1% 2% <1%

**8.9 Female Reproduction**

Injection site pain 2% 2% 2% 2%

**9 DRUG INTERACTIONS**

Injection site pain 2% <1% 2% <1%

**10 CLINICAL PHARMACOLOGY**

Injection site pain 2% 2% 2% 2%

**11 NONCLINICAL TOXICOLOGY**

Injection site pain 2% <1% 2% <1%

**12 CLINICAL STUDIES**

Injection site pain 2% 2% 2% 2%

**13 ADVERSE REACTIONS**

Injection site pain 2% <1% 2% <1%

**14 PATIENTS REPORTED**

Injection site pain 2% 2% 2% 2%

**15 PRECAUTIONS**

Injection site pain 2% <1% 2% <1%

**16 DERMATOLOGY**

Injection site pain 2% 2% 2% 2%

**17 PATIENT COUNSELING INFORMATION**

Injection site pain 2% <1% 2% <1%

**18 WARNINGS AND PRECAUTIONS**

Injection site pain 2% 2% 2% 2%

**19 ADVERSE REACTIONS**

Injection site pain 2% <1% 2% <1%

**20 ADVERSE REACTIONS**

Injection site pain 2% 2% 2% 2%

**21 ADVERSE REACTIONS**

Injection site pain 2% <1% 2% <1%

**22 ADVERSE REACTIONS**

Injection site pain 2% 2% 2% 2%

**23 ADVERSE REACTIONS**

Injection site pain 2% <1% 2% <1%

**24 ADVERSE REACTIONS**

Injection site pain 2% 2% 2% 2%

**25 ADVERSE REACTIONS**

Injection site pain 2% <1% 2% <1%
Choroidal Nevus

Choroidal nevi are the most common intraocular tumors in adults. They are benign, acquired lesions that are typically discovered on routine dilated fundoscopic examination.

The reported prevalence of choroidal nevi in the United States is 4.7 percent, but this may be an underestimation as many may go undetected due to peripheral location and lack of symptoms. They most commonly present as pigmented, flat or minimally elevated choroidal lesions, but some nevi have mixed pigmentation or are predominantly amelanotic.

Although benign, choroidal nevi may cause symptoms if they are subfoveal, associated with subretinal fluid, or a choroidal neovascular membrane (CNVM) develops.

While small, flat choroidal nevi are relatively easy to recognize, nevi that are larger, elevated and/or associated with high-risk features may be difficult to distinguish from small choroidal melanoma given the overlapping range of average dimensions, thickness and other clinical features. As such, multimodal imaging may assist in the diagnosis and management. On clinical examination, choroidal nevi are more likely to display signs of chronicity including overlying drusen, RPE atrophy and fibrous metaplasia, and can rarely be associated with a CNVM (Figure 2).

The average nevus diameter was 1.25 mm in the Blue Mountains Eye Study and overlying drusen were present in 42 percent of lesions, but studies from tertiary referral centers have demonstrated larger average dimensions, likely because suspicious nevi are more likely to get referred to these practices. Multiple mnemonics have been developed to help clinicians risk-stratify melanocytic choroidal lesions, but no single feature can distinguish between a nevus and melanoma in isolation.

The most commonly used mnemonic, To Find Small Ocular Melanoma (TF-SOM), has been recently updated to To Find Small Ocular Melanoma Doing IMaging (TFSOM-DIM), incorporating multimodal imaging features. This stands for Thickness >2 mm (by ultrasound), Subretinal Fluid (on optical coherence tomography), Symptoms of vision loss (visual acuity <20/50 by Snellen acuity), Orange pigment (on fundus autofluorescence), Melanoma acoustic hollowness (on ultrasonography), and Diameter >5 mm (on fundus photography).

This highlights the value of widefield color fundus photography, FAF, EDI-OCT and B-scan ultrasonography to identify meaningful risk factors.

Even when diagnosed accurately, a choroidal nevus must be monitored given the risk of malignant transformation to melanoma. The Cole Eye Institute’s Arun D. Singh, MD, and co-workers estimated the annual risk of malignant transformation of choroidal nevi at 1 in 8,845, while Wills Eye’s Carol Shields, MD, and co-authors reported a malignant transformation rate of 2, 9 and 13 percent of eyes at 1, 5 and 10 years.
10 years in a cohort of 2,500 patients with many high-risk lesions. Lesions that have overlapping features of choroidal nevi and choroidal melanoma, sometimes referred to as “indeterminate melanocytic lesions” must be closely observed for signs of lesion growth. In select cases, FNAB can be performed for cytopathologic diagnosis, as well as genetic mutational risk analysis of the lesion using gene expression profile testing or other molecular analysis. Cytopathology of choroidal nevi demonstrates polygonal or spindle cells with small nuclei and lack of signs of cellular atypia.13

**Congenital Hypertrophy of the Retinal Pigment Epithelium**

Congenital hypertrophy of the retinal pigment epithelium (CHRPE) is a lesion of the RPE that most commonly presents as a flat, darkly pigmented lesion with or without lacunae (Figure 3, A).20 They tend to have geographic borders and are often located in the periphery. In a large series of 330 patients, 97 percent of patients presented without symptoms, and on B-scan ultrasonography the mean thickness of the lesions was 0.8 mm.20

The largest series of CHRPE demonstrated that these lesions can have benign growth with enlargement of basal dimensions over time.20 Rarely, CHRPE lesions can be associated with an RPE adenoma/adenocarcinoma, that appears as an elevated nodule in the context of CHRPE.20,22 Key clinical features distinguishing CHRPE from other pigmented choroidal lesions include lack of measurable thickness, dark pigmentation of the lesion and the presence of lacunae.20 FAF of CHRPE shows hypoautofluorescence of the lesion, with most lacunae demonstrating isoautofluorescence (Figure 3, B). OCT is helpful in confirming that the lesion is located in the RPE, demonstrated by thickening of the RPE, thinning/disorganization of the overlying neurosensory retina and an underlying choroid that is thin or normal in thickness.22,23 In areas of lacunae, OCT shows absence of RPE, allowing an increased transmission signal (Figure 3, D). Given the benign nature of CHRPE, these lesions are routinely observed.

**Peripheral Exudative Hemorrhagic Chorioretinopathy**

Peripheral exudative hemorrhagic chorioretinopathy (PEHCR) goes by a number of names, including extramacular disciform lesion and peripheral disciform pseudotumor. It’s characterized by hemorrhagic retinal degeneration, most commonly affecting the temporal, peripheral retina.24,26 While numerous descriptions of the disease process have been published in the literature, the term PEHCR was coined by Wills Eye’s William Annesley Jr., MD, in 1980.25 In a series of “pseudomelanomas,” PEHCR was the second most frequent lesion referred for choroidal melanoma, behind choroidal nevi.27 PEHCR can manifest in a myriad of ways, but the presentation that most mimics choroidal melanomas is a focal pigmented elevated peripheral lesion. Choroidal melanoma was the referring diagnosis in 99 and 41 percent of cases ultimately diagnosed as PEHCR at an ocular oncology tertiary referral center and a series of non-ocular oncology practices, respectively, reinforcing the diagnostic uncertainty.24,26

PEHCR most commonly presents in the seventh and eighth decades of life, occurs in Caucasians in the vast majority of cases, and has a female predominance.24,26,28 Clinically, PEHCR presents as a focal hemorrhagic...
lesion, or with more diffuse exudation and/or hemorrhage (Figure 4, A). Vitreous, subretinal and sub-RPE hemorrhage can occur with PEHCR, and active simultaneous, bilateral disease occurs in 21 to 43 percent of cases. This may be an underestimation of the actual prevalence of bilateral disease, as patients may have chorioretinal pigmentary changes in the “uninvolved” eye, indicative of previous active disease. Bilaterality is an important distinguishing feature of PEHCR, as bilateral choroidal melanoma is incredibly rare. When present, exudation near the lesion is another distinguishing feature of PEHCR, as choroidal melanoma isn’t typically associated with exudation prior to treatment. A medical history, review of systems and medication evaluation can be helpful in obtaining a diagnosis, as 9 to 44 percent of people with PEHCR are on anticoagulation. Close observation may be another helpful diagnostic tool as lesion regression or stability occurs without intervention in nearly 90 percent of cases.

On indocyanine green angiography, peripheral polypoidal dilations are common. On fluorescein angiography, hypofluorescence from blockage is often seen secondary to hemorrhage. Late irregular hyperfluorescence is also common while obvious CNVMs are less frequently visualized. Studies of OCT features in PEHCR demonstrate the presence of pigment epithelial detachments in many cases and have also shown increased choroidal thickness temporal to the fovea compared to control eyes. Peripheral OCT of the posterior border of the lesion can also be helpful if visualization is sufficient to localize the lesion to the subretinal or sub-RPE space (Figure 4D). On B-scan ultrasonography, the average thickness of PEHCR lesions is around 3 mm, and the lesions may demonstrate a multilobulated, dome, plateau or irregular shape.

Choroidal Melanocytosis
Choroidal melanocytosis is a congenital hyperpigmentation of the choroid that most commonly presents as a unilateral sectoral or diffuse hyperpigmentation. Demographics and clinical examination are helpful in distinguishing choroidal melanocytosis from other pigmented lesions. It’s thought to be a congenital lesion and is often diagnosed at an earlier age than most other pigmented choroidal lesions. External and anterior segment examination is critical to detect periciliar, scleral and/or iris hyperpigmentation. On fundoscopic examination, there’s no appreciable choroidal thickening of the lesion. Additionally, the absence of drusen and chronic RPE changes helps to distinguish the lesion from broad-based choroidal nevi, and the absence of lipofuscin and subretinal fluid can help distinguish the lesion from a diffuse choroidal melanoma. The risk of uveal melanoma development in Caucasian patients with ocular or oculodermal melanocytosis is 1/400. The risk of developing uveal melanoma in patients with isolated choroidal melanocytosis is not known, but appears to be increased. This increased risk of uveal melanoma var-
‘Must-Have’ OCT Technology for Today’s Cataract & Refractive Surgeon

By Dee Stephenson, MD

As a cataract and refractive surgeon performing a high volume of surgical procedures, including minimally invasive glaucoma surgery (MIGS), I need technology that can help me keep pace with my busy practice. I’ve found that one device in particular gives me a wealth and breadth of information that is essential from a workflow and surgical planning perspective. The robotic Maestro2 OCT and Color Fundus Camera (Topcon Healthcare; Tokyo, Japan) which generates a color fundus photo and OCT scan in a single acquisition, has streamlined my operations and offered important diagnostic insights.

When I am evaluating a patient post-MIGS, for example, the widefield OCT scan enables me to look at the optic nerve and macula simultaneously. This capability not only saves me time, but it offers a more complete picture of the patient’s post-op status. If the findings are normal, no other scan needs to be done at that time.

I also value the ability to take a follow-up scan, usually at about 6 weeks post-surgery, which I then compare to the initial post-op scan. This is especially useful after cataract surgery to look for any subclinical cystoid macular edema (CME) that can affect the patient’s visual acuity. Maestro2 enables me to see those kinds of subtle changes that help with my clinical decision making.

Maestro2 Key Features
- User-friendly, robotic OCT and fundus camera with single-touch automated capture
- 12 x 9mm 3D widefield scan encompassing the macula and optic disc, along with the option to use the Hood Report for glaucoma
- High-resolution imaging
- Clinical reports yielding comprehensive analysis of the macula, optic disc and anterior segment
- Compact footprint fits into many practice settings

Features Helping to Increase Surgical Success
I am amazed at the things that I cannot normally see with a 90D slit lamp lens, such as epiretinal membranes (ERM) with vitreomacular traction and psuedoholes. All of these are seen so well with the Maestro2 OCT and they can be shown to the patient in 3D. This helps make me a better diagnostician and is invaluable in patient care.

For example, the device has helped me detect the presence of ERM which can have a negative effect on a patient’s cataract or refractive surgery outcome. It’s so important to know this information in advance of surgery so I can counsel the patient or send them to a retina specialist to potentially have a vitrectomy procedure first increasing the chance for better results once the patient undergoes cataract or refractive surgery.

I also appreciate Maestro2’s multi functionality and its ability to take photos of the anterior segment in patients exhibiting any evidence of pterygia, as this can induce corneal astigmatism and impact the plans for cataract surgery. The device’s anterior angle analysis software aids me in evaluating the angle pre- and post-surgery.

In advance of MIGS surgery, the Hood Report offers a closer look at the patient’s nerve fiber layer for better tracking of glaucomatous damage. The disc trend analysis is another tool that is extremely informative as it compares the disc parameters and retinal nerve fiber layer (RNFL) over time, enabling me to see any progression of damage. All of these capabilities help me determine which MIGS procedure is most appropriate for a given patient.

Sponsored by Topcon Healthcare

Widefield OCT Scan. A 12 x 9mm widefield OCT scan encompassing the macula and disc can be taken with the Maestro2. Images: Topcon Healthcare
Maestro2 has proven to be invaluable to my cataract and refractive surgical practice because of its ease of use. Its single-touch, robotic-capture functionality makes it a user-friendly system to learn and operate. With just one touch, the software will align, focus, and optimize the image. On occasion I need to take an OCT myself, and even I can use this device with proficiency. It helps my busy office run so much more efficiently.— Dee Stephenson, MD

**Advanced Technology to Support the Busy Practice**

The Maestro2 automated OCT, true-color fundus photography leverages robotic technology to improve practice efficiency for optimal patient care. It automatically performs alignment, focus, optimization, and capture for routine cases, while a manual/semiautomatic capture option can aid with more challenging cases. The 360° rotating monitor provides operator distance and an optional anterior segment attachment.

Clinical information from a 12 x 9mm widefield OCT scan including the macula and optic disc is incorporated into a glaucoma report providing thickness and reference data for the retina, RNFL, ganglion cell layers and disc topography. Ideal for an annual eye exam, the Hood (glaucoma) Report correlates structural (GCL/RNFL) with functional vulnerability to aid decision making. Additional glaucoma related reports are available for further clinician insights. An anterior segment add-on provides anterior segment OCT scanning without the need for an additional attachment lens. The Maestro2 is also able to produce cornea and anterior chamber scans, corneal thickness measurements, contact lens clearance, and anterior segment angle analysis using integrated caliper tools.

Maestro2 Hood Report. Visually correlates OCT structural findings to functional vulnerability to help accelerate glaucoma diagnostic decision-making.

**Ease of Use**

Maestro2 has proven to be invaluable to my cataract and refractive surgical practice because of its ease of use. Its single-touch, robotic-capture functionality makes it a user-friendly system to learn and operate. With just one touch, the software will align, focus, and optimize the image. On occasion I need to take an OCT myself, and even I can use this device with proficiency. It helps my busy office run so much more efficiently.— Dee Stephenson, MD

The device's built-in automation is extremely helpful, but sometimes manual or semiautomatic capture mode is needed for challenging cases or hard-to-see areas. Fortunately, this option is also easy to learn and has allowed my technicians to image patients with more complex eyes. Maestro2 is such an unbelievable machine—all of its capabilities are right at your fingertips.

**An Essential Device for Patient Care**

I use a pre-op OCT of the macula on every cataract patient (billing only for those with a billable diagnosis) and I am always amazed when I look at the 3D Macula Report at how much I miss with exams alone. Comparing the reports over time also gives me important information to make better decisions for patient care.

I would encourage anyone considering adding another OCT to their practice to absolutely make the technology investment in the Maestro2. This compact, user-friendly machine can give you such great true-color photography and OCT with the touch of a button, is so efficient, and has such a plethora of valuable information for the clinician—from the anterior surface to the macula. Without question, this is a must-have OCT.

Dee Stephenson, MD, is a board-certified ophthalmic surgeon with extensive expertise in microincisional cataract surgery and implantation of premium intraocular lenses, as well as custom laser cataract techniques, and the founder of Stephenson Eye Associates in Venice, Florida.
Pigmented Choroidal Metastasis

While choroidal metastasis from carcinoma usually presents as an amelanotic lesion, metastasis from primary cutaneous or uveal melanoma may appear as a pigmented lesion. Additionally, rare cases of pigmented choroidal metastasis from a neuroendocrine tumor and lung adenocarcinoma have been published. EDI-OCT of choroidal melanocytosis shows slight choroidal thickening compared to the adjacent non-affected choroid while B-scan ultrasonography demonstrates no appreciable thickening. Significant thickening or subretinal fluid seen on EDI-OCT or ultrasonography should raise suspicion for choroidal melanoma or choroidal nevus.

Cases suspicious for choroidal metastasis warrant a detailed anterior and posterior segment exam to identify other metastatic lesions in either eye. Metastatic cutaneous melanoma also has a propensity for vitreous involvement, which has been previously reported to rarely occur simultaneously with a pigmented choroidal lesion. Pigmented choroidal metastatic lesions can also rarely occur from metastatic choroidal melanoma in the same or fellow eye. Tehran’s Babak Masoomian, MD, and his fellow investigators studied 13 patients with choroidal or ciliary body melanoma with metastasis to the contralateral ocular and periocular structures, out of 13,000 total uveal melanoma cases. In their study, four patients demonstrated choroidal metastasis in the fellow eye, with 3/4 demonstrating multifocal choroidal lesions. The rate of contralateral metastasis of choroidal/ciliary body melanoma was 13/13,000 (0.1 percent) and 11 of these patients (85 percent) demonstrated evidence of systemic metastasis. Metastatic choroidal melanoma has also been reported to metastasize to the ipsilateral and/or contralateral orbit or eyelid, and can present with new-onset diplopia, in addition to choroidal involvement.

On clinical examination, choroidal metastases from cutaneous or choroidal melanoma typically present as dome- or plaque-shaped pigmented choroidal lesions. These lesions may be multifocal and can be bilateral, but can also present as unifocal. The presence of multifocal lesions should raise concern of metastasis (Figure 6, A and B). Extensive subretinal fluid and the presence of lipofuscin can accompany these tumors, thus making these lesions especially difficult to distinguish from primary choroidal melanoma.

In addition to widefield color fundus photographs demonstrating pigmented unifocal or multifocal lesions, FAF can be used to confirm lipofuscin when present. EDI-OCT can be very helpful in identifying metastatic lesions, as they often present with an undulating appearance and more subretinal fluid than a choroidal melanoma of similar size. Some primary choroidal melanomas can also present with an undulating appearance, so this configuration isn’t pathognomonic. B-scan ultrasonography typically demonstrates an acoustically dense lesion with high internal reflectivity compared to primary choroidal melanoma, which more commonly has medium to low internal reflectivity. Given the clinical and imaging overlap between metastatic melanoma and primary choroidal melanoma, a known history of previous choroidal melanoma or skin melanoma is especially important to elicit.

Melanocytoma

Melanocytoma is a darkly pigmented, benign variant of a melanocytic nevus with a low risk of malignant transformation. These lesions may be located anywhere in the posterior...
segment but are most commonly located at the optic nerve. Prior to the landmark paper by Lorenz Zimmerman in 1962, melanocytomas were commonly thought to be malignant lesions requiring enucleation. Following that histopathological investigation demonstrating the benign nature of these lesions, conservative management was adopted. Demographically, melanocytomas are more likely to occur in African-American patients than choroidal nevi or choroidal melanomas. Wills Eye’s Jerry Shields, MD, and co-workers reported 29 percent of melanocytoma cases occurring in African Americans, as compared to less than 1 percent of patients with uveal melanoma.

Key clinical findings of melanocytomas include a unilateral, darkly pigmented lesion, most commonly overlying the optic disc, with or without extension to the adjacent retina or choroid (Figure 7, A). While often an incidental finding, melanocytoma, especially when located at the optic disc, can cause blurred vision; visual field defects; afferent pupillary defects; disc edema; and intraretinal and subretinal edema. Less commonly, melanocytoma of the optic disc can present with tumor necrosis or central retinal vein occlusions. Clinically, melanocytomas tend to be more darkly pigmented than choroidal melanomas. They also may overlie the optic disc, while melanomas can abut or surround the disc and don’t typically primarily overlie the disc unless they are larger in size than most melanocytomas.

While clinical examination is often sufficient for making the diagnosis of melanocytoma, multimodal imaging can help in cases of diagnostic ambiguity. FAF demonstrates hypoautofluorescence of the lesion. OCT of melanocytomas most typically demonstrates an elevated lesion with a hyperreflective anterior surface, posterior shadowing and a disorganized overlying retina, although other OCT patterns have been described (Figure 7, B). B-scan ultrasonography and color fundus photography can be performed to document the lesion size and clinical appearance for future comparison, but often don’t help differentiate melanocytomas from other pigmented posterior segment lesions.

**Bilateral Diffuse Uveal Melanocytic Proliferation**

Bilateral diffuse uveal melanocytic proliferation (BDUMP) is a rare ocular paraneoplastic syndrome most commonly associated with urogenital cancer in women and lung carcinomas in men, although a variety of associated malignancies have been reported, typically occurring in the sixth to eighth decades of life. BDUMP was first described by Robert Machemer, MD, in 1966, and J. Donald M. Gass, MD, described its five cardinal features, including focal areas of red pigmentation at the level of the RPE, multifocal hyperfluorescence of these focal red patches, multiple focal pigmented and nonpigmented uveal lesions with slight elevation, exudative retinal detachment and rapidly progressing cataracts. Patients typically present with bilateral progressive vision loss associated with exudative retinal detachment, outer retina disruption and cataracts. This is the first indication of systemic malignancy in greater than 40 percent of patients.

The multiple, minimally elevated, pigmented lesions of BDUMP are unlikely to be confused with choroidal melanoma given their multifocality, size and minimal elevation, but could simulate multifocal choroidal nevi, choroidal metastases from skin or uveal melanoma, or the multifocal pigmented lesions seen in Gardner syndrome.

FAF highlights the typical pattern of both hypo- and hyperautofluorescent areas, corresponding to RPE atrophy and hyperplasia. EDI-OCT and B-scan ultrasonography are also helpful ancillary tests in patients with suspected BDUMP as they can document and measure the uveal thickening. Additionally, UBM can be performed to identify iris pigment epithelium and/or ciliary body cysts, which have been described in some cases of BDUMP. A detailed history should address any previously known systemic malignancy and include a thorough review of systems to identify signs of an undetected malignancy. Systemic imaging should be performed in the absence of known systemic cancer or if the patient is presumed to be in remission but hasn’t had a recent evaluation.

**Retinal Pigment Epithelium Adenoma/Adenocarcinoma**

Retinal pigment epithelium adenoma/adenocarcinoma is a very rare tumor of the RPE that classically presents as a darkly pigmented, abruptly elevated, unilateral, nodular lesion. Given the clinical similarities, these lesions are commonly misdiagnosed as choroidal melanoma. Because RPE adenomas/adenocarcinomas are retinal lesions, they may have feeding arteries (extremely rare in choroidal melanoma) and draining veins (not previously reported in melanoma). Vitreous seeding may also be seen with RPE adenomas/adenocarcinomas, but is rare for choroidal melanomas unless they’ve broken through Bruch’s membrane and invaded the retina. Another differentiating factor is surrounding or distant lipid exudation, a feature not appreciated in patients with untreated choroidal melanoma. Lastly, RPE adenomas/adenocarcinomas are associated with an underlying CHRPE in 22 percent of cases. This is an extremely rare finding in choroidal melanomas and is presumed to be incidental.

Widefield color fundus photography can help document the darkly pigmented nodular lesion. FA shows early hyperfluorescence with late iso- or hyperfluorescence, often with leakage or staining. EDI-OCT evaluation of thinner lesions, or at the margin of thicker lesions, documents localization to the RPE. It
often demonstrates high reflectivity, retinal invasion and a “derby hat” appearance with a vertical elevation at the edge of the lesion.21 B-scan ultrasonography shows dome-shaped or abruptly elevated “derby hat” lesions, typically with medium or high internal reflectivity.21 Distinguishing between RPE adenoma/adenocarcinoma and choroidal melanoma is particularly important given the prognostic implication, as RPE adenoma/adenocarcinoma has only been reported to metastasize in a single case in the literature.56

If FNAB is required for diagnostic confirmation, cytopathology demonstrates pleomorphic pigmented cells in a solid or vacuolar pattern with large melanosomes, compared to spindle cells with smaller melanosomes seen more commonly in uveal melanoma. Immunohistochemistry results are typically positive for CAM 5.2, AE1/AE3 and vimentin in most cases, but can also overlap with uveal melanoma results and be positive for HMB-45, Melan-A and S-100 in some cases.21 Cytopathology must be viewed in light of the clinical examination as results of RPE adenoma/adenocarcinoma FNAB have been misdiagnosed as other lesions prior to enucleation revealing the correct diagnosis.21

Suprachoroidal Hemorrhage

Suprachoroidal hemorrhage is a rare entity thought to occur secondary to rupture of a posterior ciliary artery associated with hypotony, systemic vascular risk factors, anticoagulation and at-risk choroidal vasculature. While most commonly occurring in the intraoperative or immediate postoperative period, spontaneous suprachoroidal hemorrhage secondary to Valsalva can rarely occur.57 There tends not to be diagnostic confusion in the setting of diffuse hemorrhage, but a localized hemorrhage can appear as a focal pigmented lesion and be mistaken for a choroidal melanoma.57,58 One subtle clinical finding often seen with suprachoroidal hemorrhage is overlying radial choroidal folds. Suprachoroidal hemorrhage also tends to have more ill-defined margins than choroidal melanoma or nevus (Figure 8, A).

There tends not to be diagnostic confusion in the setting of diffuse hemorrhage, but a localized hemorrhage can appear as a focal pigmented lesion and be mistaken for a choroidal melanoma.

History is important in distinguishing the lesions, as most suprachoroidal hemorrhages occur in the intraoperative and postoperative course and have been associated with filtering surgery, cataract surgery, keratoplasty and pars plana vitrectomy at differing rates.59,60 In addition to recent surgery, patients may present with a dull pain that is uncommon with choroidal melanoma unless associated with necrotic tumors and scleritis. Typically, localized suprachoroidal hemorrhages will show some degree of resolution within weeks to months, so close observation may also reveal the diagnosis.

Multimodal imaging is helpful in diagnosing a localized suprachoroidal hemorrhage. FAF typically shows isoa autofluorescence in the area of the lesion as the overlying RPE is often intact, but the choroidal folds may be well highlighted as linear, mildly hyper- or hyperautofluorescent streaks (Figure 8, B). Both FA and ICGA demonstrate a normal retinal and choroidal circulation overlying the area of hemorrhage and can show areas of hypofluorescence from choroidal folds.61 EDI-OCT of thinner suprachoroidal hemorrhages can be critical to the diagnosis by documenting the hyporeflective hemorrhage being located between the sclera and the choroid. B-scan ultrasonography may demonstrate heterogenous internal reflectivity, and lesion thickness varies based on the amount of hemorrhage.60

In conclusion, a multitude of pigmented choroidal lesions and simulating conditions exist, and overlapping or atypical clinical features can result in diagnostic confusion. Clinical examination is paramount, but patient history and multimodal imaging may be critical in narrowing the differential diagnosis to distinguish and properly manage these lesions.

(Ed. note: The list of citations is available with the online version at reviewofophthalmology.com.)

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Surgery in the Advanced Uveitic Glaucoma Patient

Doing surgery on these patients requires a different approach than you might use for other glaucoma patients. Here’s help.

Keith Barton, MD, FRCP, FRCS, FROphthD
London

Uveitic glaucoma is a diverse disease. Patients with advanced disease may present with open or closed angles—the latter sometimes acute, sometimes chronic. Acute angle closure obviously requires an urgent response, but for me, chronic angle closure is more a predictor of the chronicity of the problem, rather than something to manage differently from open angle glaucoma.

When managing an advanced uveitic glaucoma patient, the job of the glaucoma specialist is twofold. First, in the short term you need to relieve any existing angle closure. Second, you need to take intraocular pressure out of the equation so that elevated IOP doesn’t restrict the management of chronic inflammation.

In terms of removing IOP from the equation, I believe it’s crucial to understand that you shouldn’t reduce steroid treatment just to accomplish this. That’s a false economy. The patient should be able to use whatever treatment is needed to address the uveitis, as determined by the patient’s uveitis specialist. For that reason, an advanced uveitic glaucoma patient often needs to undergo glaucoma surgery such as trabeculectomy or have a tube shunt implanted. We won’t be successful in every case, but a glaucoma surgeon who does trabs and tubes on a regular basis will be very adept at managing this.

The Importance of Surgery
Performing a less-invasive procedure, such as a MIGS surgery, may seem like an attractive option—perhaps performing a Kahook Dual Blade goniotomy or an iStent, on the basis that these may be enough to avoid more invasive operations. However, these procedures aren’t intended to treat severe disease. In advanced uveitic glaucoma patients, a MIGS procedure is unlikely to resolve the problem; it simply kicks the can down the road. That’s a real concern, because in advanced glaucoma, there’s an opportunity cost for doing this: You’re leaving the patient exposed to further vision deterioration over the long term.

The reality is, when managing an advanced uveitic glaucoma patient, the glaucoma specialist’s job is to take pressure out of the equation as much as is possible. In advanced cases, that requires a trabeculectomy or a tube implant. If your patient has advanced angle closure and/or advanced optic disc and visual field damage, you probably have only one opportunity to fix it. By the time you get to the next opportunity, it’s too late—the glaucoma has progressed further. The patient with a paracentral defect has lost central vision, and a patient with an advanced central defect is really in trouble. That’s why you need to achieve definitive control as quickly as possible.

I think it’s important to get away from the idea that glaucoma surgery is something that doesn’t last forever—the idea that you’ll try one thing and then another until the patient reaches the target pressure. Baerveldt...
implants and trabeculectomies last a very long time, and they give you the opportunity to achieve definitive control from early on.

The glaucoma specialist in this situation must have a range of glaucoma surgeries at his or her disposal. Doctors who say, “I only do this procedure or that procedure” aren’t offering what many of their patients need. That may sound a bit harsh, but it’s reality.

Managing Angle Closure

If you have an open angle that’s completely clean and pigment free, you may be tempted to believe that the patient’s pressure rise is caused by steroid responsiveness rather than by the uveitis. However, if you find a lot of synechiae in the angle, you know the angle has been severely compromised. And if you find a lot of synechiae and the pressure is episodic—sometimes high and then normal again—you know that the situation probably will not settle down. That means the patient is more likely to need surgery in the long term.

Acute angle closure in uveitis is something that’s particularly troublesome to me. It’s not that common, but it’s very severe and we often fail to treat it effectively. There are three types of angle closure in uveitis: pupil block; chronic synechial angle closure; and forward movement of the lens-iris diaphragm.

The first type of angle closure, pupil block, is the biggest management challenge. It may relate to a pre-existing narrow angle or coincidental angle closure; relative pupil block from fibrin obstructing the pupil; or absolute pupil block caused by posterior synechiae. We’re all familiar with primary angle closure, which is due to relative pupil block, but in uveitis, the pupil block is absolute, which is very different. Because the iris is ballooning against the cornea, this isn’t just a closed angle occluding the trabecular meshwork; this is an angle that’s completely zipped shut with sticky aqueous and iris, right up against the cornea.

The second type of angle closure in uveitis is chronic angle closure, associated with peripheral anterior synechiae, secondary to inflammation (e.g., nodules in the angle, neovascularization, and/or a cyclitic membrane). (See example, facing page.) For me, chronic anterior synechiae in the angle is primarily a marker of chronicity; it tells me that there’s more than just a steroid response going on here. The patient doesn’t have high pressure just because of one acute attack—a problem has existed for a long time. As noted earlier, this patient is more likely to need surgery in the long term.

There’s a popular idea that this problem may be relieved by goniosynechialysis. Actually, goniosynechialysis doesn’t work very well in these patients. For example, a retrospective study conducted in Singapore reviewed the outcomes of goniotomy procedures performed in 31 eyes with glaucoma secondary to anterior uveitis.¹ It found that the eyes that achieved success (defined as an IOP of less than 21 mmHg) had a mean of 0.5 clock hours of peripheral anterior synechiae; the eyes that failed to achieve success had a mean of 2.5 hours of PAS.

In general, there’s very limited data regarding using goniosynechialysis to address this, and certainly no comparative studies showing that it works in the long term. I’m not a fan; this procedure causes a lot of bledding, and I’m not convinced it does anything helpful.

The third type of angle closure seen in these patients is a classic symptom of uveitis: forward movement of the lens-iris diaphragm, leading to central anterior chamber shallowing. In the past, a shallow central anterior chamber was often misdiagnosed as pupil block, but nowadays, most doctors don’t jump to that conclusion.

When you find a very shallow central chamber, it either means the crystalline lens is very large, or

When encountering a uveitic patient with angle closure, the surgeon may be tempted to perform a laser peripheral iridotomy. That doesn’t work well in these patients, because the sticky aqueous prevents the iris from falling back, and the angle doesn’t open. Performing a surgical iridectomy (as shown above) is far more effective.
something is pushing the lens forward. Classically, in uveitis, this could be caused by posterior scleritis or Vogt-Koyanagi-Harada disease. However, in clinical practice you almost never see it associated with these causes. The vast majority of cases I see are the result of vitrectomy for retinal detachment that was done using too much gas; a large, cataractous lens; or, most commonly, the result of aqueous misdirection following previous ocular surgery. (The latter can be addressed via atropine or steroids, or a pars plana vitrectomy if it’s recalcitrant.) So, even though posterior scleritis and VKH have been associated with this, much of the time, the cause is iatrogenic.

**The Iridotomy Dilemma**

One problem with addressing angle closure in a patient with uveitic glaucoma is that most surgeons don’t encounter it very often. So, when they do encounter it, they tend to opt for the treatment that might work well in other situations: laser peripheral iridotomy.

That’s not a good approach in this situation, for a couple of reasons. First, if you perform laser iridotomy, you’re laserig the corneal endothelium. Second, because these eyes are very inflamed, the aqueous is kind of sticky; as a result, the iris often doesn’t fall back following the LPI and the angle doesn’t open. You end up with a patent iridotomy and a closed angle, even though you’ve relieved the iris bombé. For example, one patient I encountered had undergone three LPIs. The LPIs opened up the iris, and the bombé has fallen back; nevertheless, the iris was still completely zipped shut against the cornea, and the angles remain closed.

Not surprisingly, this ineffective treatment comes with an opportunity cost. I’ve seen patients like this in their 40s who only received an LPI and now have no light perception, just because they weren’t adequately treated.

The answer is straightforward: Surgical iridectomy is much more definitive than an LPI. (I prefer to do such an iridectomy using vitrectomy forceps and scissors, which provide good visualization.) Doing this doesn’t just make a bigger hole; once you’ve made the hole, it also allows you to physically open up the angle using a viscoelastic such as Healon GV. In theory, you could do this through an LPI opening, but it has to be done in the operating room, so it makes better sense to create the opening surgically. Once the angle has been physically opened, the fact that you’ve relieved the iris bombé should keep it from closing back up.

Another reason to create the hole surgically is that laser-created holes often close up in uveitic patients. Surgical ones are bigger, so they don’t close up as often. Yes, it’s possible that an LPI will remain open, and sometimes a surgical iridotomy will close, despite being larger than an LPI. But being in the OR to perform the surgical iridotomy also allows you to use viscoelastic to physically open the closed angle, which truly resolves the problem. Just making the hole may not resolve it.

Note that this process isn’t the same as goniosynechialysis. This isn’t about breaking physical adhesions. Goniosynechialysis is increasingly popular, but the evidence suggests that it’s not particularly effective in this type of situation.

**Tubes vs Trabs**

Trabeculectomy has a bad reputation in uveitic glaucoma, while tube shunts have a good reputation. Generally, I’m known as an advocate of tubes for glaucoma surgery, but I tend to do trabeculectomies in uveitics—especially in advanced cases, as long as the patient has no risk factors for failure other than the uveitis itself. For example, if the patient is phakic and hasn’t had any previous ocular surgery, he or she may be a good candidate. In these patients, trabeculectomies generally work well.

One issue here is that both high and low intraocular pressures tend to be more extreme in uveitic glaucoma patients than in POAG patients. The explanation may be that chronic uveitics have a little bit less aqueous than POAG patients—with even less outflow. This leads to a very wide spread of pressures. As a result, you can end up with a trabeculectomy where you have very little drainage, but the pressure is very low indeed.

Our trabeculectomy success rate with these patients has been good. In a study we conducted 15 years ago, mean success, defined as IOP ≤21 mmHg, was about 80 percent at about four years. (Of course, less than 21 mmHg is a fairly low bar these days; in cases of advanced uveitic glaucoma, you really want to be getting the pressure down to 10 mmHg or thereabouts.) The reality is, if you have a uveitic patient with...
We’ve also found that pseudophakes sit more than 10% of the time. Black patients in this situation have a lower success rate. Ethnicity is a possible risk; in my experience, Black patients in this situation have a lower success rate. We’ve also found that pseudophakes fail more often, for reasons we have yet to determine. (In fact, pseudophakia is the only major risk factor we’ve identified.)

In some patients with mild disease, an alternative to trabeculectomy such as the Xen gel stent or PreserFlo microshunt (from Santen) may be a workable alternative. If the uveitic patient has high IOP, mild glaucoma, no trabeculectomy failure risk factors and a relatively healthy disc, I’ll use a Xen implant with mitomycin-C, or an InnFocus Microshunt with mitomycin-C. If the same patient had more advanced glaucoma with significant optic neuropathy, I’d perform a trabeculectomy with MMC. (I don’t do canal-based MIGS in these patients.)

Our group published a report about a series of uveitic patients who received Xens; those patients did pretty well. I’ve subsequently written up a series of these patients treated with PreserFlo which hasn’t been published yet, although we presented the data at the American Glaucoma Society meeting in Washington, D.C., two years ago. One significant difference between these two studies was the composition of the subject pools. The XEN study participants were mostly young Caucasian individuals, who tended to have healthy conjunctiva (at least partly because of their age and limited exposure to glaucoma drops). The subjects in the PreserFlo study were mostly not Caucasian. That made a difference, because we were able to detect an association between ethnicity and outcome in the PreserFlo study; we weren’t able to test for that in the other study.

Given that tube shunts generally work well in uveitic patients, why even consider performing a trabeculectomy in a patient like this, we’ve identified.)

• Predicting the outcome of retinal detachment repair. Investigators from Toronto say that you may be able to use early postop imaging to determine who’ll get the most visual benefit from the detachment repair. The researchers retrospectively analyzed 614 eyes of 614 patients who underwent primary rhegmatogenous retinal detachment repair, and tested their vision, metamorphopsia and anisekonia at three months postop. They also imaged them with spectral-domain OCT and fundus autofluorescence imaging.

Regression analysis found that significant early postop imaging predictors of visual acuity were discontinuity of the external limiting membrane (p<0.01) and presence of retinal vessel printings on FAF (p<0.033). Discontinuity of the interdigitation zone was a significant predictor of metamorphopsia (average of MH+MV (p=0.008) and presence of RVPs was a significant predictor of anisekonia (p=0.04). In the study, the researchers say, “Modifications of surgical techniques aimed to reduce postoperative discontinuity of the outer retinal bands and retinal displacement may improve functional outcomes after retinal detachment repair.” (Lee WW. ARVO Abstract [Paper] PERCEIVE Study Report, 2022)

• Macular atrophy progression in different forms of AMD. Researchers looked into the progression of macular atrophy in patients with AMD. They analyzed two groups: 91 patients without MA at baseline (in order to study time to first MA development in treated and fellow eyes); and 47 patients with a total of four years of follow-up, in order to study the time course and growth rate of MA in treated and fellow eyes.

They found a significant difference in MA incidence and progression in eyes with nAMD treated with anti-VEGF agents compared to fellow eyes exhibiting dry AMD. They say that treated nAMD eyes tended to develop MA more often, and the MA progressed at a faster rate in these eyes compared to fellow dry AMD eyes. (Tsilimbaris M. ARVO Abstract A0455, 2022)

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lectomy? Because in general, trabs get lower pressures, and patients with advanced uveitic glaucoma need a really low pressure. I realize that most surgeons faced with a uveitic glaucoma patient would just implant a tube. But I was doing trabs in uveitic patients many years ago when tube shunts were much less popular. Because my success rate in uveitics with this approach had a good success rate, I never stopped.

Today, of course, my practice does place a lot of tube shunts in our uveitic patients, simply because there’s almost always some kind of risk factor for failure. For example, some of our patients here in London are African, and they scar more easily post-surgery. In those patients, Xens and Microshunts don’t work so well; trabs don’t work so well; even tubes don’t work so well. But tubes seem to work better than the other options, so we have a lower threshold for using tubes. In addition, if a uveitic patient has a single-chamber eye, neovascular glaucoma or juvenile idiopathic arthritis, I just go straight to a tube.

**Which Tube?**

If you’re choosing to implant a tube shunt in a patient with uveitic glaucoma, the next question is, which shunt is most likely to work well? In most cases we opt for either a Baerveldt 350 or a Paul Glaucoma Implant in patients with advanced disease.

Many surgeons are reluctant to implant a Baerveldt 350 in a uveitic glaucoma patient with advanced disease, but if you’re trying to get lower pressures, the evidence is very much in favor of the Baerveldt.5 My experience supports this as well. The Baerveldt 101-350 gives the best pressure control in the long term for many uveitics, and, more recently, the Paul Glaucoma Implant seems to produce similar pressures.

At the same time, there are certain patients in whom we shouldn’t use the Baerveldt 350. For example, I wouldn’t place a 350 in a patient who comes to see me at age 20, who’s had severe uveitis since the age of three. These patients have low aqueous production, and they’ll go from very high pressures to very low pressures very easily. I’d also avoid placing a Baerveldt 350 in a uveitic patient with significant neovascularization, and patients who’ve had multiple cyclophotocoagulation treatments. (I would never use CPC in one of these patients myself, because the ciliary body is already diseased.)

People often say that a Baerveldt 350 is too much for a uveitic patient. In most cases, it’s not—although it’s definitely too much for some uveitics. So, you need to choose the patient carefully. If I think the 350 will be too much, I move to the smaller plates.

In very sick eyes, I tend to use a single-plate Molteno. Studies have shown that the Molteno implant does well in these patients.6 This raises a few eyebrows among the nurses at Moorfields, because today, surgeons rarely use a Molteno. But when I see somebody with severe juvenile idiopathic arthritis, who’s had the disease since early childhood, I prefer to put in a Molteno.

(Admittedly, as treatments for uveitis get better and better, I’m seeing fewer of those very sick eyes.)

**Doing the Right Thing**

Unfortunately, today there are many places where surgeons are avoiding doing trabs and tubes. A patient going to a major center in a major city will probably get the right type of surgery done, but for many of today’s ophthalmologists, this kind of surgery has become alien. They don’t do it on a regular basis. That’s a problem.

If you’re unable to offer a patient with advanced uveitic disease and glaucoma a tube or trabeculectomy, you should refer the patient. The problem is, if you’re a glaucoma specialist and you’re referring glaucoma cases to somebody else, what does that make you? You’re not offering a full range of procedures. Yes, the new procedures are elegant; patients like that and doctors like that. But when you’ve got a disease like advanced uveitic glaucoma to treat, those procedures may not suffice to save the patient’s vision.

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**ABOUT THE AUTHOR**

Dr. Barton is a professor of ophthalmology at University College London and former director of the glaucoma service at Moorfields Eye Hospital. He has consulted for Alcon, Allergan, Ivantis, Carl Zeiss Meditec, Santen Pharmaceuticals, Glaukos, iSta, Laborstories Thea, Advanced Ophthalmic Innovations, Elkos and Shifamed.
An 84-year-old woman presents with redness, pain and discharge in her left eye.

SANIKA UDYAVER, MD, AND MARY STEFANYSZYN, MD

Presentation and Initial Work-up

An 84-year-old Caucasian female was transferred to our institution for left eye redness, pain and discharge. Eight months prior to her presentation, she had a left lower lid abscess which was managed with systemic antibiotic therapy resulting in improvement in symptoms. However, she had a resultant ectropion, for which she underwent surgical repair about one month prior to her presentation. During this procedure, there was notable mucopurulent discharge that was concerning for infection. She was treated with another round of both topical and oral antibiotics. With worsening drainage, conjunctival injection and pain with extraocular muscle movement, she presented to a local emergency room. A CT scan showed orbital cellulitis and myositis, so she was treated with intravenous broad-spectrum antibiotics. An MRI was performed due to her lack of improvement and showed possible abscess formation in the orbit. She was transferred for management of orbital cellulitis.

Medical History

Ocular history was only notable for the above lid abscess and ectropion. Past medical history included hypertension, depression and pyoderma (See Figure 1). Family and social history were unremarkable. Medications included atenolol, amlodipine and sertraline.

Examination

Ocular examination demonstrated visual acuity of 20/30 in the right eye and 20/25 in the left. There was no relative afferent pupillary defect. Intraocular pressures were 16 and 20 mmHg in the right and left eye, respectively. Confrontational visual fields were normal in both eyes. Extraocular motility was full in the right eye, and restricted in all gazes in the left eye. Anterior segment examination of the right eye was normal. Anterior segment examination of the left eye revealed lower lid ectropion with mucopurulent discharge from the inferior fornix, trace lid edema and erythema, and conjunctival injection and chemosis (See Figure 2). Dilated fundus examination was unremarkable in both eyes.

Figure 1 (top). External photograph showing a well-defined pink atrophic plaque on the patient’s right hip, with a central focus of ulceration and drainage, consistent with a clinical diagnosis of pyoderma gangrenosum.

Figure 2 (bottom). External photograph demonstrating lower lid ectropion, mucopurulent discharge and conjunctival injection of the left eye.

What’s your diagnosis? What further work-up would you pursue? The diagnosis appears on p. 72.
Work-up, Diagnosis and Treatment

Repeat CT was obtained to further characterize the orbital process (See Figure 3). CT demonstrated an enhancing mass in the inferolateral left orbit that deformed to the surface of the globe, without frank abscess. MRI further defined this as a soft tissue mass in the left orbit with homogeneous contrast enhancement.

The differential diagnosis of this patient with worsening left eye discharge, conjunctival injection and pain with extraocular muscle motility included infectious, neoplastic and inflammatory etiologies. Infectious causes included bacterial or fungal etiologies. Inflammatory causes included orbital pseudotumor, vasculitis, sarcoidosis or IgG4-related disease. Neoplastic causes, which were less likely, included hematolymphoid tumor, soft tissue tumors or orbital metastasis. Given the patient’s lack of improvement despite prolonged broad-spectrum intravenous antibiotic therapy and history of pyoderma gangrenosum, there was suspicion for inflammatory etiology. A bedside conjunctival biopsy was performed, and intravenous corticosteroid therapy was started.

The patient initially improved on IV steroid therapy and was discharged from the hospital on oral steroids. However, two weeks later, she developed worsening discharge and conjunctival injection. Examination showed possible dellen formation in the inferior cornea. Conjunctival biopsy had shown only nonspecific chronic inflammation, so orbitotomy and biopsy of deeper orbital tissue was performed. This showed palisading granulomatous inflammation and granulomatous vasculitis (See Figure 4).

Laboratory studies revealed elevated CRP (2.6), positive ANCA (1:40, nl <1:20), and positive rheumatoid factor (19). Chest X-ray and chest CT showed a right middle lobe infiltrate with irregular margins. With this constellation of findings, granulomatosis with polyangiitis (GPA) was suspected and the patient was started on intravenous rituximab along with daily trimethoprim-sulfamethoxazole (TMP-SMX) and oral prednisone.

The patient’s symptoms began to improve with this treatment, and her orbital disease remained quiescent after initial rituximab therapy. She continued to have left lower lid ectropion necessitating lower lid reconstruction with a full thickness tarsal graft, and later developed lagophthalmos requiring release of upper eyelid retractors to allow better closure.

Discussion

GPA is an autoimmune disease characterized by granulomatous inflammation of small to medium-sized blood vessels, especially of the sinuses, lungs and kidneys. It’s most commonly found in Caucasian patients in their 40s and 50s, and has no specific gender predilection. GPA is associated with anti-PR3 anti-neutrophil cytoplasmic antibodies (c-ANCA), which have been found in more than 90 percent of patients with the disease and 30 to 50 percent of patients with local disease.

A diagnosis of GPA can be made with high sensitivity (88.2 percent) and specificity (92 percent) with two of five clinical criteria: abnormal urinary sediment; abnormal findings on chest radiograph; oral ulcers; nasal discharge; or granulomatous inflammation on biopsy.

Ophthalmologic involvement has been found in 50 to 60 percent of patients with GPA. Orbital involvement is most common (15 percent of patients), but nasolacrimal involvement, scleritis and peripheral ulcer-
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WILLS EYE

Orbital disease is often thought to be spread from contiguous nasal and sinus disease, demonstrated by CT evidence of orbital masses with nearby sinonasal disease and bony erosion.

GPA has been made, immediate treatment is imperative. Although previously treated with cyclophosphamide, the mainstay of treatment is now rituximab. TMP-SMX has also been shown to prevent relapses and reduce risk of infection in ANCA-associated vasculitis. Both therapies were used in our patient, and showed a favorable outcome.

After successful treatment and remission of active disease, our patient continued to have cicatrizing ectropion due to fat necrosis. She had multiple surgeries to correct the ectropion, which demonstrates the refractory nature of the inflammatory condition.

She was later hospitalized for COVID, and discharged to a rehabilitation facility. During this time, she missed a maintenance infusion of rituximab, and had recurrence of discharge from her left eye as well as recurrence of the necrotic hip lesion. This emphasizes the importance of continued treatment in an inflammatory condition such as GPA.

Orbital biopsy proved to be helpful, the conjunctival biopsy was not as fruitful. Previous studies have also commented on the efficacy of orbital biopsies. In a study of 13 orbital biopsies from patients with known GPA, only 54 percent of cases demonstrated the classic histopathologic triad of vasculitis, tissue necrosis and granulomatous inflammation. In contrast, up to 91 percent of lung biopsies from patients with GPA demonstrate all three features. Deeper tissue biopsy, as in the case of our patient’s orbitotomy, may be the key in finding diagnostic tissue.

In addition to the orbital and possible lung involvement, our patient also presented with a necrotic skin lesion that carried a clinical diagnosis of pyoderma gangrenosum. This lesion was never biopsied, but it also showed clinical improvement on steroid and rituximab therapy. Review of the literature reveals that necrotizing skin rash may be a manifestation of cutaneous GPA. In a study of 244 patients with GPA, 14 percent had skin involvement, including palpable purpura and necrotizing ulcers resembling pyoderma gangrenosum. Interestingly, studies have also shown patients with GPA to have coexisting biopsy-proven pyoderma gangrenosum. Thus, the finding of a skin rash can be evidence of skin manifestation of GPA or another coexisting inflammatory condition.

Once the difficult diagnosis of GPA was made, immediate treatment is imperative. Although previously treated with cyclophosphamide, the mainstay of treatment is now rituximab. TMP-SMX has also been shown to prevent relapses and reduce risk of infection in ANCA-associated vasculitis. Both therapies were used in our patient, and showed a favorable outcome.

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