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INDICATION

IZERVAY™ (avacincaptad pegol intravitreal solution) is indicated for the treatment of geographic atrophy (GA) secondary to age-related macular degeneration (AMD)

IMPORTANT SAFETY INFORMATION

CONTRAINDICATIONS

IZERVAY is contraindicated in patients with ocular or periocular infections and in patients with active intraocular inflammation.

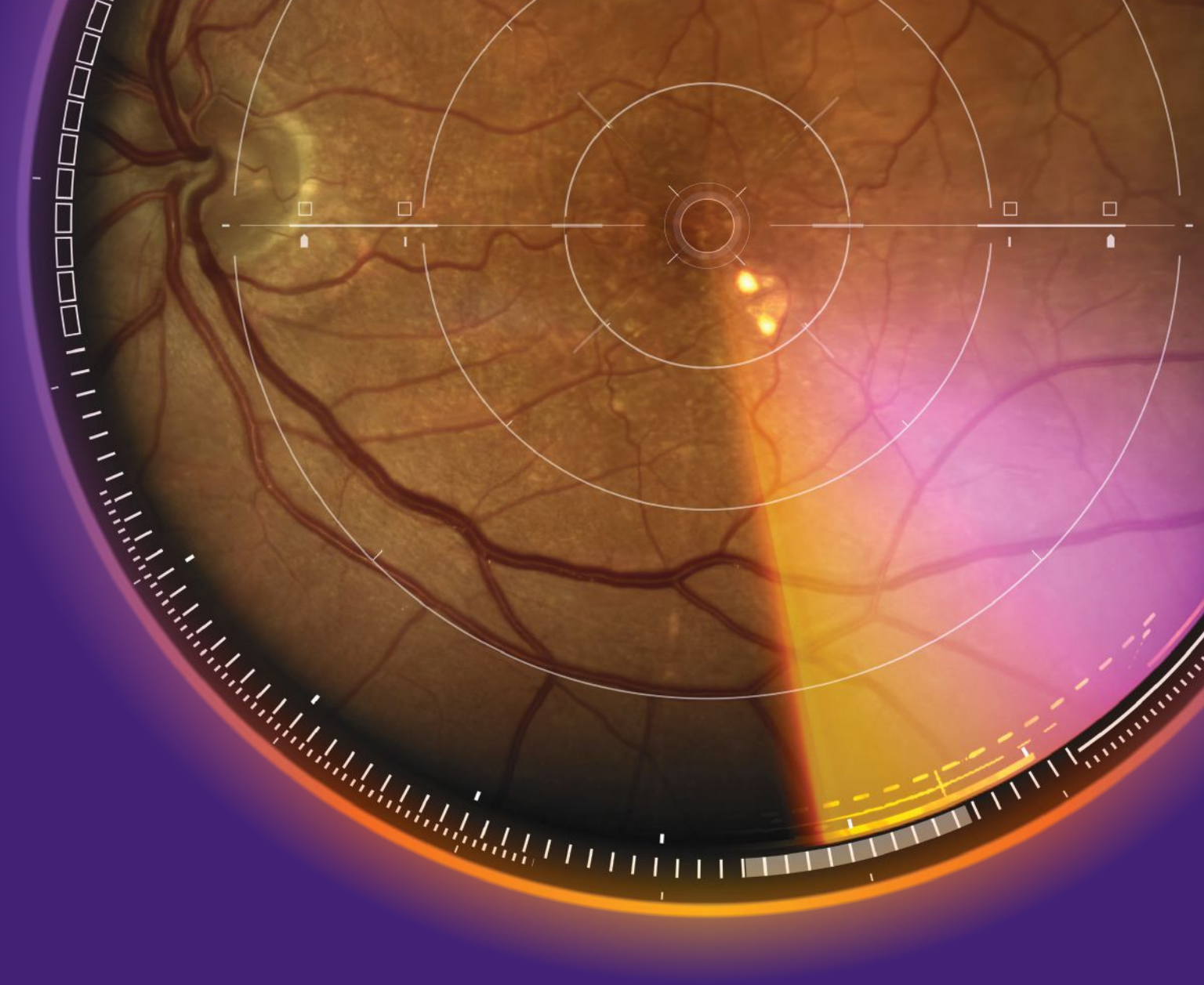
WARNINGS AND PRECAUTIONS

Endophthalmitis and Retinal Detachments

- Intravitreal injections, including those with IZERVAY, may be associated with endophthalmitis and retinal detachments. Proper aseptic injection technique must always be used when administering IZERVAY in order to minimize the risk of endophthalmitis. Patients should be instructed to report any symptoms suggestive of endophthalmitis or retinal detachment without delay and should be managed appropriately.

Neovascular AMD

- In clinical trials, use of IZERVAY was associated with increased rates of neovascular (wet) AMD or choroidal neovascularization (7% when administered monthly and 4% in the sham group) by Month 12. Patients receiving IZERVAY should be monitored for signs of neovascular AMD.



Increase in Intraocular Pressure

- Transient increases in intraocular pressure (IOP) may occur after any intravitreal injection, including with IZERVAY. Perfusion of the optic nerve head should be monitored following the injection and managed appropriately.

ADVERSE REACTIONS

Most common adverse reactions (incidence ≥5%) reported in patients receiving IZERVAY were conjunctival hemorrhage, increased IOP, blurred vision, and neovascular age-related macular degeneration.

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

Image courtesy of Dr. Julie Rodman.

References: 1. Sunness JS, Rubin GS, Applegate CA, et al. Visual function abnormalities and prognosis in eyes with age-related geographic atrophy of the macula and good visual acuity. *Ophthalmology*. 1997;104(10):1677-1691. **2.** Fleckenstein M, Mitchell P, Freund KB, et al. The progression of geographic atrophy secondary to age-related macular degeneration. *Ophthalmology*. 2018;125(3):369-390. **3.** IZERVAY™. Package insert. Northbrook, IL: Astellas Pharma US, Inc.

astellas

IZERVAY™ (avacincaptad pegol intravitreal solution)
Rx only

Brief Summary: This information is not comprehensive. Visit IZERVAYecp.com to obtain the FDA-approved product labeling or call 800-707-4479.

1 INDICATIONS AND USAGE
IZERVAY is indicated for the treatment of geographic atrophy (GA) secondary to age-related macular degeneration (AMD).

2 DOSAGE AND ADMINISTRATION

2.1 General Dosing Information
IZERVAY must be administered by a qualified physician.

2.2 Recommended Dosage
The recommended dose for IZERVAY is 2 mg (0.1 mL of 20 mg/mL solution) administered by intravitreal injection to each affected eye once monthly (approximately every 28 ± 7 days) for up to 12 months.

4 CONTRAINDICATIONS

4.1 Ocular or Periocular Infections
IZERVAY is contraindicated in patients with ocular or periocular infections.

4.2 Active Intraocular Inflammation
IZERVAY is contraindicated in patients with active intraocular inflammation.

5 WARNINGS AND PRECAUTIONS

5.1 Endophthalmitis and Retinal Detachments
Intravitreal injections may be associated with endophthalmitis and retinal detachments. Proper aseptic injection techniques must always be used when administering IZERVAY in order to minimize the risk of endophthalmitis. Patients should be instructed to report any symptoms suggestive of endophthalmitis or retinal detachment without delay, to permit prompt and appropriate management.

5.2 Neovascular AMD
In clinical trials, use of IZERVAY was associated with increased rates of neovascular (wet) AMD or choroidal neovascularization (7% when administered monthly and 4% in the sham group) by Month 12. Patients receiving IZERVAY should be monitored for signs of neovascular AMD.

5.3 Increase in Intraocular Pressure
Transient increases in intraocular pressure (IOP) have been observed after an intravitreal injection, including with IZERVAY. Perfusion of the optic nerve head should be monitored following the injection and managed as needed.

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

- Ocular and periocular infections
- Neovascular AMD
- Active intraocular inflammation
- Increase in intraocular pressure
- Endophthalmitis and retinal detachments

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

The safety of avacincaptad pegol was evaluated in 733 patients with AMD in two sham-controlled studies (GATHER1 and GATHER2). Of these patients, 292 were treated with intravitreal IZERVAY 2 mg (0.1 mL of 20 mg/mL solution). Three hundred thirty-two (332) patients were assigned to sham.

Adverse reactions reported in ≥2% of patients who received treatment with IZERVAY pooled across GATHER1 and GATHER2, are listed below in Table 1.

Table 1: Common Ocular Adverse Reactions (≥2%) and greater than Sham in Study Eye

Adverse Drug Reactions	IZERVAY N=292	Sham N=332
Conjunctival hemorrhage	13%	9%
Increased IOP	9%	1%
Blurred Vision*	8%	5%
Choroidal neovascularization	7%	4%
Eye pain	4%	3%
Vitreous floaters	2%	<1%
Blepharitis	2%	<1%

* Blurred vision includes visual impairment, vision blurred, visual acuity reduced, visual acuity reduced transiently.

8 USE IN SPECIFIC POPULATIONS

8.1 Pregnancy Risk Summary
There are no adequate and well-controlled studies of IZERVAY administration in pregnant women. The use of IZERVAY may be considered following an assessment of the risks and benefits.

Administration of avacincaptad pegol to pregnant rats and rabbits throughout the period of organogenesis resulted in no evidence of adverse effects to the fetus or pregnant female at intravenous (IV) doses 5.1 times and 3.2 times the human exposure (based on AUC) at the maximum recommended human dose (MRHD) of 2 mg once monthly, respectively.

In the U.S. general population, the estimated background risks of major birth defects and miscarriage in clinically recognized pregnancies is 2-4% and 15%-20%, respectively.

Animal Data
An embryo fetal developmental toxicity study was conducted with pregnant rats. Pregnant rats received daily intravenous (IV) injections of avacincaptad pegol from day 6 to day 17 of gestation at 0.1, 0.4, 1.2 mg/kg/day. No maternal or embryofetal adverse effects were observed at any dose evaluated. An increase in the incidence of a non-adverse skeletal variation, described as short thoracolumbar (ossification site without distal cartilage) supernumerary ribs, was observed at all doses evaluated. The clinical relevance of this finding is unknown. Plasma exposures at the high dose were 5.1 times the MRHD, based on Area Under the Curve (AUC).

An embryo fetal developmental toxicity study was conducted with pregnant rabbits. Pregnant rabbits received daily IV injections of avacincaptad pegol from day 7 to day 19 of gestation at 0.12, 0.4, 1.2 mg/kg/day. No maternal or embryofetal adverse effects were observed at any dose evaluated. Plasma exposure in pregnant rabbits at the highest dose of 1.2 mg/kg/day was 3.2 times the human exposure at the MRHD, based on AUC.

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

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

8.4 Pediatric Use
Safety and effectiveness of IZERVAY in pediatric patients have not been established.

8.5 Geriatric Use
Of the total number of patients who received IZERVAY in the two clinical trials, 90% (263/292) were ≥65 years and 61% (178/292) were ≥75 years of age. No significant differences in efficacy or safety of avacincaptad pegol were seen with increasing age in these studies. No dose adjustment is required in patients 65 years and above.

Distributed by: Astellas Pharma US, Inc.
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US-AP-2400227 07/24

SGLT2 Inhibitors Linked to Reduced Glaucoma Risk in Patients with Type 2 Diabetes

A large-scale study suggests these treatments may go beyond glycemic control and have potential ophthalmic benefits.

Patients with type 2 diabetes—of which there are over 462 million worldwide—commonly experience ophthalmic complications, particularly diabetic retinopathy and macular edema. However, glaucoma is a significant comorbidity in adults with diabetes aged 45 and over, with growing evidence to support this association. New anti-diabetic medications, such as glucagon-like peptide-1 receptor agonists (GLP-1RAs), sodium glucose co-transporter 2 (SGLT2) inhibitors and dipeptidyl peptidase 4 (DPP4) inhibitors, have demonstrated some protective effects on ocular complications, including glaucoma, but the literature is sparse. A recent study in *American Journal of Ophthalmology* dove into the impact of SGLT2 inhibitor drugs specifically and discovered patients taking this type of medication had a lower risk of glaucoma, including its subtypes open-angle glaucoma and primary open-angle glaucoma (POAG), than those taking either DPP4 inhibitors or GLP-1RAs.

SGLT2 inhibitors, a relatively newer class of anti-hyperglycemic agents, block the reabsorption of glucose in the kidneys and are shown to reduce weight, lower blood pressure and improve cardiovascular health. Examples include ertugliflozin, empagliflozin and dapagliflozin, all of which were included in this population-based study. The risk of incident glaucoma was compared between this drug class, DPP4 inhibitors and GLP-1RAs.

For the primary analysis, those in the DPP4 group were chosen as the active comparator because, while similarly used as second-line therapy for type 2 diabetes, this class has no known cardiovascular or renal pleiotropic benefits.

Researchers identified 2,355,582 eligible patients with type 2 diabetes from 92 US healthcare organizations. They found patients on SGLT2 inhibitors had a lower risk of glaucoma vs. those on DPP4 meds (overall hazard ratio: 0.815). Among all studied drugs in the class, ertugliflozin (Steglatro, Merck) was associated with the lowest risk of glaucoma, followed by empagliflozin, (Jardiance, Lilly), then dapagliflozin (Farxiga, AstraZeneca).

SGLT2 inhibitor use was also found to confer significant protection against low-tension glaucoma and capsular glaucoma with pseudoexfoliation of lens. Therapy also significantly decreased the risk of POAG and neovascular glaucoma but did not show protective effects against pigmentary glaucoma.

The authors wrote in *AJO*, "the significant reduction in risk of incident glaucoma when compared to other antidiabetic medications in our study suggests that the pathophysiologic mechanism by which SGLT2 inhibitors decrease the risk of glaucoma is likely multifactorial, especially when considering its impact on several different glaucoma subtypes." They suggest it may be best to consider the role of SGLT2 inhibitors in glaucoma risk by subtype, such as for POAG and low-tension glaucoma, in which the benefit is best explained by vascular pathophysiology.

Photo: Merck

SGLT2 inhibitors (*i.e.*, ertugliflozin and empagliflozin) may help lower glaucoma risk in type 2 diabetes patients, new research shows. These medications showed the most efficacy in reducing incidence of open-angle glaucoma and POAG.

"Meanwhile, choroidal blood vessel pathophysiology may be most implicated in angle closure glaucoma," they continued. Ongoing investigations have demonstrated that diabetes patients "have a thicker subfoveal choroid and there is increasing evidence that choroidal expansion contributes to angle-closure physiology." Appropriately controlling this choroidal expansion, such as with SGLT2 inhibitor use, could therefore prevent angle-closure glaucoma, the suggested in their article.

Although they found the results to be encouraging, "prospective studies and clinical trials are needed to validate the findings," the authors concluded.

Eng K, Zebardast N, Boland MV, et al. Sodium-glucose cotransporter 2 inhibitors and glaucoma in patients with type 2 diabetes. Am J Ophthalmol. November 6, 2024. [Epub ahead of print].

Semaglutide Doesn't Increase NAION Risk in General Population, Study Asserts

This was found to be true at one, two and three years of follow-up in patients taking the GLP-1 medication for type 2 diabetes, obesity or both.

A study published over the summer by Hathaway et al. revealed a link between semaglutide—a popular glucagon-like peptide 1 receptor agonist (GLP-1RA) used to treat type 2 diabetes and obesity—and an increased risk of non-arteritic anterior ischemic optic neuropathy (NAION). Since that analysis recruited participants from a single neuro-ophthalmology practice (Massachusetts Eye and Ear in Boston), a separate team of researchers questioned whether these findings apply to broader populations. To investigate, they conducted a population-based real-world study on data from 200 million people across 21 countries within the TriNetX global network to assess whether semaglutide users possess a higher risk of NAION.

The final analysis included Caucasian individuals older than 18 with type 2 diabetes mellitus (T2DM) or obesity, who were further divided into one of three groups for comparison: T2DM-only (n=37,245), obesity-only (n=138,391) and T2DM with obesity (n=64,989). Baseline characteristics, such as age, sex, BMI, hemoglobin A1c, comorbid conditions and medications, were balanced between groups. The researchers then compared the effects of semaglutide with those of various non-GLP-1RA glucose-lowering or weight-loss medications.

Photo: Novo Nordisk

While a single-center study published this past July observed an association between semaglutide and an increased risk of NAION, a recent larger, real-world study failed to find a link between the two.

The results demonstrated that semaglutide use did not increase the risk of NAION development among the general population compared with non-GLP-1RA drugs. This finding was consistent among the T2DM-only group, the obesity-only group and the T2DM with obesity group at one, two and three years of follow-up.

"Our findings contrast with those of Hathaway et al. probably because of the differences in the study populations and designs," the study authors explained in their paper for *Ophthalmology*. They noted that while the prior study "involved patients referred to a single major medical center in a city with a high degree of medical sophistication, our study included individuals from a more general clinical setting." Additionally, they pointed out that "differences in population characteristics and drug prescription preferences between single institutions and global databases may contribute to varying results," as can differences in healthcare systems across regions and countries.

Considering these findings observed in a large, real-world cohort, the researchers concluded that "avoidance of semaglutide based solely on concerns regarding the risk of NAION may not be warranted, as its potential benefits for blood glucose control and cardiovascular health likely outweigh its potential risks."

Chou CC, Pan SY, Sheen YJ, et al. Association between semaglutide and non-arteritic anterior ischemic optic neuropathy: a multinational population-based real-world study. Ophthalmology. November 2, 2024. [Epub ahead of print].

IN BRIEF

E-Cigarette Use Increases Uveitis Risk, Study Finds. Studies have identified increased levels of proteins associated with oxidative stress in the sputum of e-cigarette users. These proteins have been linked to the onset of uveitis, suggesting that **those who vape nicotine may be more susceptible to developing this condition.** A new study in *Ophthalmology* investigated the potential association and indeed found an elevated risk of uveitis among this patient cohort.

The study authors used the TriNetX database, comprising data from more than one hundred million patients across various regions, to identify patients aged ≥18 with and without a recent history of e-cigarette usage. Their analysis included 419,325 e-cigarette users and 419,325 comparators, with a similar racial distribution between groups (including patients of Asian, Black or African and white ethnicities).

The results showed that **e-cigarette users demonstrated a heightened risk of developing uveitis when compared to non-users,** with a hazard ratio (HR) of 2.53. Age stratification in subgroup analyses revealed a heightened risk for uveitis among e-cigarette users in the age groups of 18 to 39 years (HR: 2.59), 40 to 64 years (HR: 2.20) and those aged 65 and above (HR: 3.15). Additionally, this risk persisted throughout four years of follow-up, indicating **the effect of e-cigarette use on uveitis risk is both short- and long-term.**

Traditional cigarette use was also found to increase uveitis risk (HR: 1.28), but not as significantly as e-cigarette use. Additionally, patients with a history of both e-cigarette and cigarette use had a higher uveitis risk than those only using traditional cigarettes.

These findings warrant further investigation, especially considering only case reports have previously documented an association between uveitis and e-cigarette use, the researchers argued. They concluded that **"clinicians caring for patients with e-cigarette history should be aware of the potentially increased risk of new-onset uveitis."**

Hsu AY, Wang YH, Hsia NY, Lai CT. Risk of uveitis among e-cigarette users: a multi-institutional TriNetX study. Ophthalmology. November 8, 2024. [Epub ahead of print].

Severe Dry Eye Raises Risk of Corneal Ulcer Fivefold

It's been shown that severe dry eye disease (DED) can predispose a patient to corneal ulceration, which can then lead to loss of vision—even when treated appropriately. In a new study published in *Ophthalmology*, researchers sought to understand the demographic factors and ocular surface disease associated with corneal ulcers.

A total of 1,910,340 Medicare beneficiaries were included. Corneal ulcers were associated with female sex, white race, dry eye with concurrent cicatrizing conjunctivitis or Sjögren's syndrome and open-angle glaucoma among others.

White subjects had 1.5 to two times the odds of having corneal ulcers compared to Black and Hispanic individuals, although the authors noted in their paper that prior studies found the opposite relationship and their findings may have undercounted non-white subjects.

Women had slightly higher odds (1.1) of developing a corneal ulcer compared to men, especially those older than age 75, possibly due to autoimmune diseases. According to the authors, autoimmune diseases are more common in women and can exacerbate DED, which may partially explain their higher risk of ulcers, as well as the impact of estrogen on the ocular surface.

Overall, patients with DED had 5.38 times higher odds of developing corneal ulcers than those without dry eye. "Evaluation of ocular surface and tear film parameters and appropriate escalation of therapy are essential," the authors wrote.

As mentioned earlier, Sjögren's syndrome and cicatrizing conjunctivitis are both significantly associated with corneal ulcers. "The increased risk for corneal ulcers could be explained by the increased activity of matrix metalloproteinases on the ocular surface, which can lead to damage of the lacrimal ducts and gland," the authors wrote.

To the authors' knowledge, this is the first study to reveal significant racial differences in corneal ulcer prevalence and the potential role of underlying Sjögren's syndrome in compounding the risk of developing corneal ulcers among individuals with DED. Further studies are still needed to evaluate the severity of corneal ulcers based on these risk factors and identify possible pathogenic mechanisms that increase the risk.

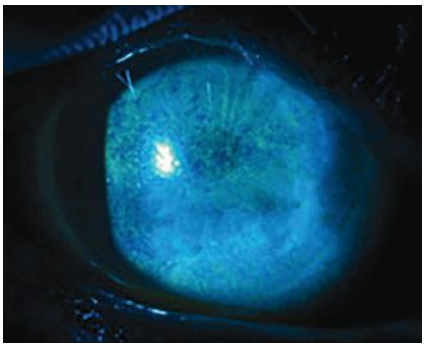

Photo: Ben Gaddie, OD

In Sjögren's patients, increased activity of matrix metalloproteinases on the ocular surface can damage the lacrimal ducts and gland and ultimately increase the risk for corneal ulcers.

Hwang J, Li G, Sommi A, et al. Demographic and ocular comorbidities in elderly individuals with corneal ulcers. Ophthalmology. November 7, 2024. [Epub ahead of print].

Meta-analysis Favors Oral Azithromycin Over Doxy for MGD

A recent systemic review and meta-analysis compared oral doxycycline and oral azithromycin for managing meibomian gland dysfunction (MGD). It revealed a better safety profile for the latter, with equivalent efficacy in reducing disease signs.

Four trials and a quasi-experimental study involving 612 eyes with MGD were included. The primary outcomes assessed were symptom score, sign score and overall clinical response. Some individual results showed that "azithromycin led to greater improvement in conjunctival redness and corneal staining, in addition to MG secretion," the authors wrote in their paper for *Clinical Ophthalmology*. "However, it's important to note the high heterogeneity in the results, indicating substantial variability among the studies."

After controlling for differences among the studies, the researchers found no significant difference in sign scores between doxycycline and azithromycin, but at follow-up less than six months later, azithromycin showed superiority over doxycycline in sign scores. Azithromycin did show a better safety profile, while some on doxycycline experienced gastrointestinal issues.

"These findings suggest that azithromycin has an early and potentially more potent anti-inflammatory effect on the signs of MGD," the authors wrote. "This early effect appears to be maintained, and azithromycin remains as effective as doxycycline after six months of therapy."

Duration of the regimen is also a factor. The researchers noted in their paper that "oral doxycycline may require a longer therapeutic course to achieve a similar level of effectiveness," while "the treatment regimen for the oral azithromycin varied between five to 21 days among the included studies with slightly different doses."

While the underlying causes of the high heterogeneity among the study designs remain poorly understood, it is plausible that variations in dosage, frequency and duration across the included studies may have contributed to the pooled results being influenced, the authors explained. Another factor that may have influenced the results is the early effect of azithromycin on the sign score in the initial two to three months.

Further investigations with larger sample sizes are needed to obtain a more comprehensive understanding of the long-term outcomes pertaining to the use of oral azithromycin in MGD, the authors concluded.

Bukhari ZM, Alsudais AS, Bshnaq AG, et al. Oral azithromycin vs. oral doxycycline in the treatment of meibomian gland dysfunction: a systemic review and meta-analysis. Clin Ophthalmol. November 21, 2024. [Epub ahead of print].

Four to Eight Hours Post-Cataract Surgery is Optimal Time to Measure IOP, Study Finds

A comprehensive meta-analysis suggests this is the ideal window for obtaining the most accurate readings and can help avoid missed spikes.

Recommendations on the optimal time to measure IOP following cataract surgery are vague, ranging from within the first 24 hours for high-risk patients, to 48 hours post-op in low-risk patients. Without specific guidance, timing has become a matter of convenience for the surgeon, which could lead to missed IOP spikes if done too soon or too late. A considerable amount of research exists with data accounting for IOP measurements taken at different time points following uncomplicated cataract surgery, and a new study published in the journal *Vision* reports meta-analysis results suggesting the best time to measure IOP may be within the first four to eight hours following surgery.

This study included 57 randomized clinical trials published between 1992 and 2023, from which they derived a total of 6,318 participants and 7,089 eyes (43.7% male; mean age 68.4). The most significant decrease in IOP from baseline was in postoperative hour one (-2.08), while hour two had a non-significant increase (+.081). Post-op hours four, six and eight were the only timepoints to show a significant increase in IOP (+1.38, +0.83 and +0.93, respectively). There was no significant change in IOP on post-op day one and a non-significant decrease on day two (-0.36). Researchers conducting this meta-analysis therefore concluded that the data supports post-op hours four to eight as the optimal IOP measuring timepoints to avoid missed IOP spikes.

The authors wrote in their paper that measuring IOP sooner than two hours may be misleading, "as IOPs were found to be lower than baseline, likely related to surgical techniques to manage wound closure following aspiration of ophthalmic viscosurgical devices (OVD). The results indicated that a continuous decrease in IOP at three, seven and 30 days post-op is expected and consistent with evidence that retained OVD is unlikely to be causative after two to three days."

Significant variability of perioperative medications were also observed in the meta-analysis. The most common pre-op medications were antibiotics or NSAIDs, and—for those who did report the administration of medications intraoperatively—the most common were found to be antibiotics, carbachol and/or steroids. A combination of antibiotics, steroid and/or NSAID were used postoperatively in a majority of the studies.

"These medication combinations have been shown in some studies to have a small effect on IOP in the immediate days following cataract surgery," the study authors noted. "Ten studies reported the use of an IOP-lowering medication, which included carbonic anhydrase inhibitors, beta-blockers, prostaglandin analogs and alpha agonists. These medications were used either prophylactically to prevent IOP elevations, to lower IOP in patients who were actively experiencing a dangerous spike or as routine treatment for glaucoma patients. Despite these medications having peak effects between two and eight hours post-administration, they did not seem to prevent the IOP spikes noted from four to eight hours later."

One limitation noted by the authors was the variability in the quality scoring of the examined studies, which may risk bias assessment due to unclear blinding. "However, as the current literature only offered a small number of relevant publications, all were included, irrespective of their quality score," they said.

It's also worth highlighting that none of the studies included in this meta-analysis mentioned patient position during IOP measurement. "This is important to note as clear corneal thickness, astigmatism and patient position can potentially affect IOP measurements," they wrote.

In conclusion, this study provides more specific guidance for when IOP should be measured, with caution not to do so prior to the four-hour timepoint when spikes became significant. "Continuous practice assessment to determine factors that optimize patient-reported outcomes and experiences in the context of evidence-based quality care may be the key to best practice recommendations," the authors concluded in *Vision*.

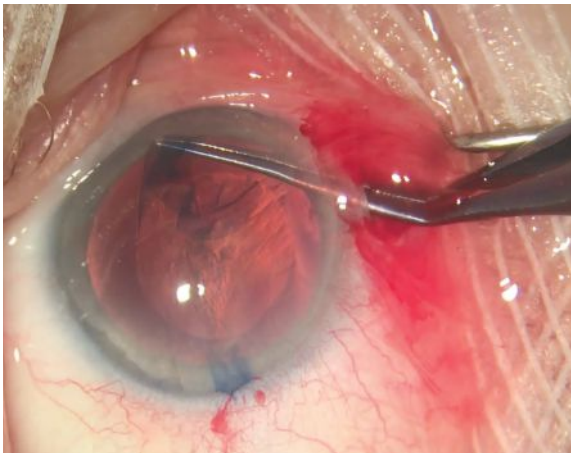

Photo: Christina Tran, BS, and Leonid Skorin, Jr., DO, OD

A recent meta-analysis of 57 clinical trials suggests the optimal time to measure IOP after cataract surgery is between four to eight hours post-op. Hours four, six and eight had an increase of IOP from baseline of +1.38, +0.83 and +0.93, respectively. With data from over 6,300 patients, the study highlights the risks of missing these spikes, should IOP be measured too soon following surgery.

Herspiegel WJ, Yu BE, Algodi HS, et al. Optimal timing for intraocular pressure measurement following phacoemulsification cataract surgery: a systematic review and a meta-analysis. Vision. November 8, 2024. [Epub ahead of print].

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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.

(The Rick Bay Foundation for Excellence in Eyecare Education is a nonprofit, tax-exempt organization under section 501(c)(3) of the Internal Revenue Code.)

RRD Likelihood About Threefold Greater with Topical Pilocarpine

The recent introduction of topical pilocarpine agents for improved near vision in presbyopes has generated interest in a potential new modality of vision correction, but also raised concerns about rhegmatogenous retinal detachment (RRD) risk. A new retrospective study in *American Journal of Ophthalmology* examined risk in those using the drug for presbyopia and development of this rare adverse event.

An aggregated EHR research network was used to identify individuals over 40 who received topical pilocarpine (1.25% or any dose with exclusion of other indications) for the first time; controls were presbyopia patients on artificial tears.

After propensity score matching, the three-month risk of RRD was significantly higher in the pilocarpine group (0.53%) vs. controls (0.25%) by roughly twofold. This disparity was echoed in six-month risk data, with elevated levels in the study group of 0.60% vs. 0.31% for controls. At one year, RRD risk increased in the pilocarpine group to 0.78% and stayed relatively stable at 0.33% in the control group. Pilocarpine posed a 3.14-fold increased risk of RRD vs. controls after adjusting for demographics and comorbidities. Additional risk factors included male sex, myopia (twofold risk), vitreous degeneration (twofold risk), lattice degeneration (fourfold risk) and pseudophakia (threefold risk).

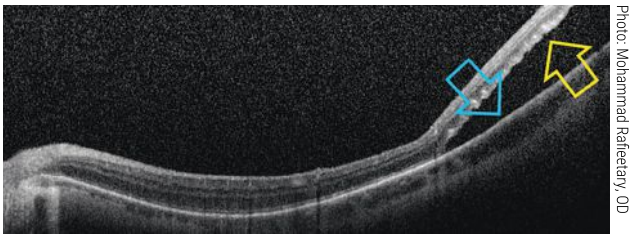

Photo: Mohammad Rafieetary, OD

Ciliary muscle contraction and rotation due to pilocaprine use may exert traction and stretching on the peripheral retina and result in retinal breaks near the ora serrata.

The authors stress the importance of these results, as the GEMINI I and II Phase III clinical trials of Vuity (Allergan) did not report any RRD cases with 1.25% pilocarpine; however, both included only 750 patients, a level not sufficient to reflect uncommon adverse events, the researchers say. As well, those with history of cataract surgery, myopia of >4.00D or certain pre-existing ocular conditions were excluded, thus not reflecting real-world risk.

The authors conclude by recommending that those who start pilocarpine with pre-existing risk factors of myopia, lattice degeneration or pseudophakia undergo a comprehensive dilated retinal exam before starting treatment.

Elhusseiny AM, Chauhan MZ, Jabbehdari S, et al. Using real-world data to assess the association of retinal detachment with topical pilocarpine use. Am J Ophthalmol. November 5, 2024. [Epub ahead of print].

VA Might Not Be Best Measure for IRD Progression

Researchers in Australia assessed change in retinal structure and function over 10 years in individuals with rod-cone dystrophies (RCDs), as well as the symmetry of progression between eyes and factors affecting the rate of progression. Their study, published in *Ophthalmology Science*, found that at 10-year follow-up, only 35% of participants with RCD met the FDA minimal clinically important difference of 15 letters (0.30 logMAR), emphasizing the slow rate of progression measured using visual acuity (VA). The authors wrote in their paper, "This highlights the need for further examination of distinct patterns of decline within and between genetic subgroups, which is crucial for modeling long-term progression."

Twenty-three participants attended follow-up (mean age 63, 48% female), with 20 classified as having RCD and three re-classified as having cone-rod dystrophy based on genetic diagnosis. In advanced disease, both dystrophies show extensive photoreceptor loss, making it difficult to distinguish between rod-dominant and cone-dominant phenotypes.

At 10 years, only 60% of RCD patients showed progression of ≥15 letters in one or both eyes. Between the eye with poorer vs. better VA at baseline, high symmetry in disease progression was observed for visual field loss, and moderate interocular symmetry in disease progression was observed for VA and ellipsoid zone (EZ) width. Baseline values influenced progression for VA and percentage change in Goldmann visual field area, while total percentage change in EZ width did not differ across baseline values.

"To better understand inter-eye asymmetry, we need larger longitudinal studies to explore factors influencing differences in progression rates between eyes," the researchers concluded.

Britten-Jones AC, Luu CD, Jolly JK, et al. Longitudinal assessment of structural and functional changes in rod-cone dystrophy: a 10-year follow-up study. Ophthalmol Sci. November 5, 2024. [Epub ahead of print].

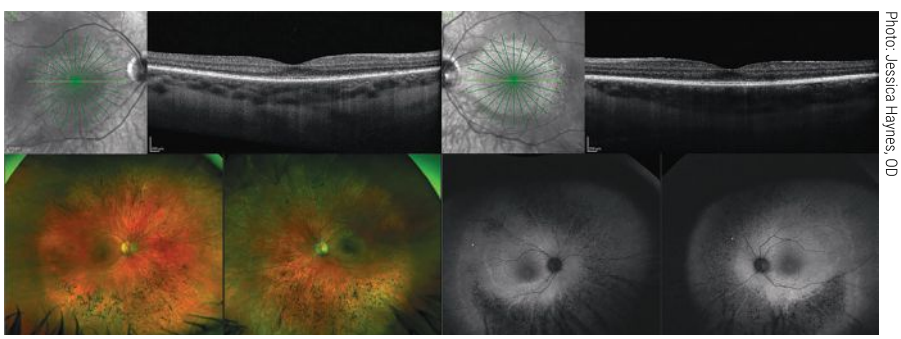

Photo: Jessica Haynes, OD

Despite experiencing structural decline over 10 years, several patients with both autosomal-recessive and autosomal-dominant rod-cone dystrophy also maintained stable visual function.


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FEATURES

REVIEW OF OPTOMETRY • Vol. 161, No. 12 • DECEMBER 15, 2024

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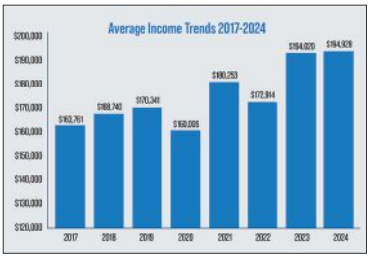

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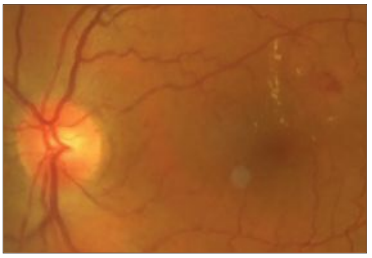

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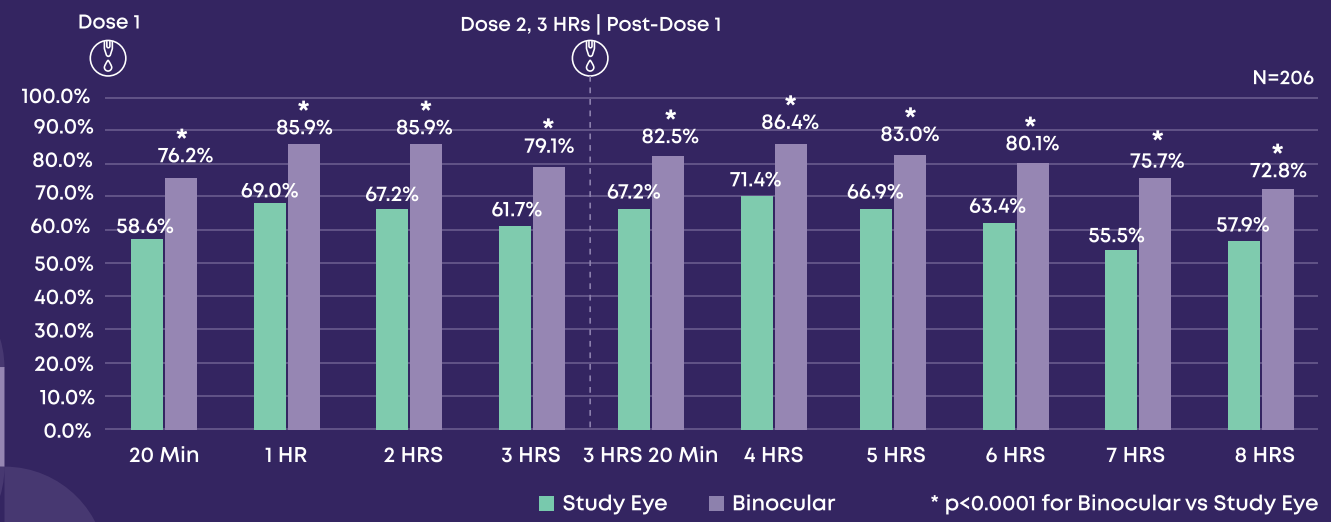
Data from a pooled analysis of two Phase 3, randomized, double-masked, vehicle-controlled clinical studies, NEAR-1 and NEAR-2, Participants (n=613) aged 45 to 64 years old with presbyopia were randomized to either QLOSI n=309 or placebo (n=304) in these two studies and treated for 2 weeks. The primary endpoint of the study was a comparison of the number of participants demonstrating a gain from baseline of 3 lines or more (>= 15 letters) in BDCVA at 40 centimeters without a loss of 1 line or more (>= 5 letters) in BDCVA at 4 meters.

Functional Near Vision (DCNVA 20/40 or Better) - Day 15



Important Safety Information

Indication and Usage
Qlosi™ is indicated for the treatment of presbyopia in adults.

Contraindications
Hypersensitivity

Warnings and Precautions
Advise patients to not drive or operate machinery if vision is not clear (e.g., blurred vision). Exercise caution in night driving and other hazardous occupations in poor illumination. Rare cases of retinal detachment have been reported with miotics. Examination of the retina is advised in all patients prior to initiation of therapy.

Advise patients to seek immediate medical care with sudden onset of flashes of lights, floaters, or vision loss. Qlosi™ is not recommended to be used when iritis is present. Qlosi™ should not be administered while wearing contact lenses. Remove lenses prior to the installation of Qlosi™ and wait 10 minutes before reinsertion. Avoid touching the tip of the vial to the eye or any other surface.

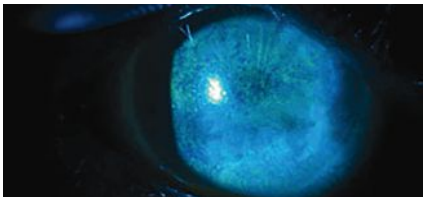
Adverse Reactions
The most common adverse reactions (5% to 8%) are instillation site pain and headaches. For more information, see the full Prescribing Information.

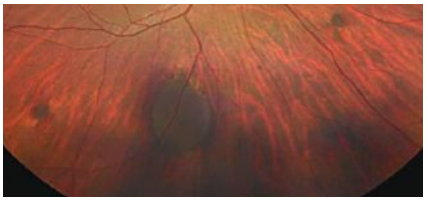
References

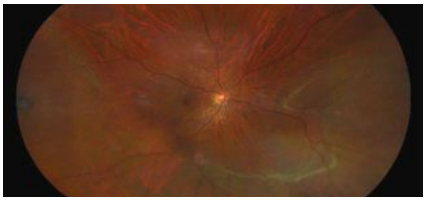
1. Grzybowski, A., Kapitanovaite, L., & Zemaitiene, R. (2024). TOC. Advances in Ophthalmology Practice and Research, 4(4), 3–9. https://doi.org/https://doi.org/10.1016/j.aopr.2024.09.001
2. Holland, E., Karpecki, P., Fingeret, M., Schaeffer, J., Gupta, P., Fram, N., Smits, G., Ignacio, T., & Lindstrom, R. (2024, February). Efficacy and safety of CSF-1 (0.4% pilocarpine ... Clinical Therapeutics.https://www.clinicaltherapeutics.com/article/S0149-2918(23)00478-2/fulltext
3. Xu, R., Thibos, L., & Bradley, A. (2016). Effect of Target Luminance on Optimum Pupil Diameter for Presbyopic Eyes. Optometry and Vision Science, 93(11), 1409–1419.

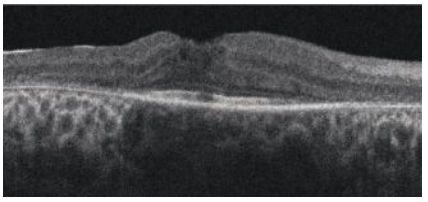
Please see full prescribing information here:
www.qlosi.com/prescribing-information

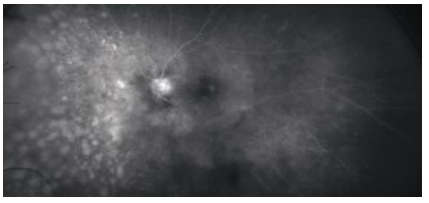
DEPARTMENTS

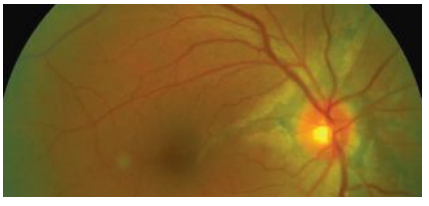












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BY JACK PERSICO
EDITOR-IN-CHIEF
OUTLOOK

The Pursuit of Happiness

Optometry has its share of challenges, but practitioners report consistently high levels of satisfaction with their profession.

We share our annual income survey this month, and there's a lot in the data to be enthused about. The average income reported by the 422 optometrists who participated came in just shy of $200,000. Admittedly, that number obscures the wide range of results within various subgroups of survey respondents (see the article for details), but even practitioners on the lower end of the scale are making well into the six figures. It's true that the personal debt one must accrue in order to create such earning potential is formidable, but with the prospect of a 40-year career ahead of them, ODs who are able to weather their cash-strapped early days are in for a very satisfying trajectory.

Some practice-owning ODs put up truly eye-popping income numbers this year, too—a few told us they hit the seven-figure mark. That's admittedly atypical, but there was also a healthy spread of readers reporting incomes in the $300,000 to $500,000 range. It takes a ton of work and self-sacrifice, but private practice optometry truly is a gateway to upper income tiers that few professions can match.

Of course, money isn't everything. The recurring theme among optometrists who work for someone else (and typically have a lower income ceiling as a result) was gratitude for the favorable quality of life this choice allows them. "I feel like if I wanted to earn more I could, but currently I like my work-life balance," wrote one respondent, a comment echoed by many.

I think what that sentiment gets at is the notion of autonomy—the ability to call the shots for yourself, at least to some extent. In that light, the high level of satisfaction among optometrists who work as employees makes sense. When you make an informed choice about how you want to spend your days, money is just one factor out of many. Among survey respondents, 65.2% of employed ODs reported that they were either "somewhat" or "very" satisfied with their professional earnings, and the result wasn't tremendously higher for those who are self-employed: 68.8%. In fact, satisfaction remained consistently around that same level for many subgroups, including full-time (67.5%) and part-time workers (64.3%), plus each age/experience bracket.

Where we did see some notable separation, however, was along gender lines. In optometry as with the wider workforce, women earn less than men. As such, 61.2% of female ODs reported they were satisfied with their compensation vs. 72.7% for their male counterparts. Still, that's a sizable majority of women who told us they're satisfied with their incomes even in light of the professional and cultural headwinds that keep their earnings below the average.

None of this is meant to gloss over the real frustration that many readers did express about their earnings. Much of the anger in the candid comments about these hardships centered on complaints about forces beyond one's control: inflation, insurers, bosses or, quite often, all three. So, if you're among those who felt a bit shortchanged this year, spend some of 2025 trying to carve out a better path for yourself. Even if it doesn't lead to a big windfall, the feeling of acting on your own behalf can sometimes be its own reward. ■

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Nilson, Robert 10.18.2024

PROVIDER
"Good morning, Bob. How can I help you today?"

PATIENT
"I've been noticing a bit of eye strain, especially after working on the computer."

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BY PAUL M. KARPECKI, OD
CHIEF CLINICAL EDITOR

Be Instrumental in OSD

There's so many more procedures than just punctal plugs.

Last month I discussed the plethora of ocular surface disease (OSD) treatments available today, and this month we're sticking with OSD by taking a look at the procedures most optometrists routinely perform. There are several of these as well, and they go well beyond punctal occlusion. Let's dive into all the surgical options and see which ones can greatly help your patients.

IES/NTT Conference

This past month, I co-chaired the Intrepid Eye Society/New Technology and Treatments Conference in Nashville. There were nearly 200 attendees and the Intrepid Eye Society members who served as faculty, along with Ben Gaddie, OD, and Marc Bloomenstein, OD, brought incredible clinical and practice insights. One that struck me was the importance of not only participating in advanced OSD procedures, but even the process required, via instrumentation.

Perception is Reality

These high-demand, advanced procedures serve over 150 million people with meibomian gland dysfunction, dry eye and/or blepharitis. The use of instruments, as Mark Schaeffer, OD, pointed out during the amniotic membrane and instrumentation workshop we shared—like lid expressors or bandage lens forceps, rather than our fingers—are far more impressive to the patient and a better model a patient-pay or insurance-covered procedure. So, start with good instrumentation, which can also decrease complications and increase efficiency. For example, bandage lens forceps prevent stabbing the conjunctiva with sharp jewelers forceps or removing delicate epithelium in the case where the bandage lens is adherent.

Procedures Aplenty

The first procedure that comes to mind due to its long history is punctal occlusion. Impressive recent innovations like tapered 180-day dissolving punctal plugs (Oasis Medical) and cross-linked hyaluronic acid lacrimal occlusion, have provided superior results and a far more positive patient response.

> **Start with good instrumentation, which can also decrease complications and increase efficiency.**

Newer intense pulsed light (IPL) devices that use self-cooling heads (Espancione, Essilor Instruments) remove the need for face gel, practically eliminate the risk of burning a patient, eliminate the "snapping elastic band" pain, treat more skin types and are equally effective in my experience of over 3,000 cases.

A new system involving radiofrequency energy called the Darwin (Oculus) is on the market and, in 2025, an IPL from Lumibird is seeking FDA approval.

Low-level light therapy (LLLT) has allowed doctors to avoid having to surgically remove or inject chalazion. LLLT involves two or three treatments and is very effective on hordeola and early chalazia without the addition of IPL. Perhaps this is due to endogenous heat measured in the lower eyelid 25 minutes after application.[1]

Biofilm removal options include microblepharoexfoliation (*e.g.* BlephEx, NuLids), Optivize (BlephEx) or Rinsada. You can also do a quick biofilm over the meibomian gland orifices with an eyelid debrider (Bruder Healthcare) after a dry eye exam. While this doesn't have the same biofilm-removing capability of microblepharoexfoliation or irrigation, it certainly delivers an impressive patient response, which further emphasizes how valuable this process is.

For everting the eyelids to provide foreign body removal, concretion removal or meibography, instruments like the Meivertor (Bruder Healthcare) greatly improve efficiency and a professional appearance. Keep in mind that most instruments can easily be sanitized with bead-sterilizer.

Finally, there is amniotic membrane therapy with the use of ProKera corneal bandages (BioTissue) forceps for removal, dry amnion forceps for applying amnion to the cornea and contact lens and bandage contact lens forceps (all provided by Bruder). Amnion placement itself is a major opportunity in appropriate patients, such as those that don't respond to topical therapy or have neurotrophic keratitis. Innovations such as CAM360 (BioTissue) that provide ProKera without the ring, Apollo (Atlas Medical) dehydrated amnion that maintains significant healing components or lyophilized or freeze-dried (Oculus Biologics) have continued to allow optometrists to better service our patients.

So, when looking at surgical options, consider the incredible opportunity in front of you that involves advanced ocular surface disease. ■

1. Pult H. Low-level light therapy in the treatment of meibomian gland dysfunction. Invest Ophthalmol Vis Sci. 2020;61(7):99.

About Dr. Karpecki

Dr. Karpecki is director of cornea and external disease at the Kentucky Eye Institute in Lexington, KY. He is the Chief Clinical Editor for *Review of Optometry* and chair of the New Technologies & Treatments conferences. A fixture in optometric clinical education, he consults for a wide array of ophthalmic clients, including ones discussed in this article. Dr. Karpecki's full disclosure list can be found in the online version of this article at www.reviewofoptometry.com.

IYUZEH™ (latanoprost ophthalmic solution) 0.005% is the first and only preservative-free latanoprost for patients with open-angle glaucoma (OAG) and ocular hypertension (OHT).

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Michael Chaglasian, OD, FAAO

Dr. Chaglasian is a paid consultant of Thea Pharma Inc.

INDICATIONS AND USAGE

IYUZEH™ (latanoprost ophthalmic solution) 0.005% is a prostaglandin F2α analogue indicated for the reduction of elevated intraocular pressure in patients with open-angle glaucoma or ocular hypertension.

IMPORTANT SAFETY INFORMATION

CONTRAINDICATIONS

Known hypersensitivity to latanoprost or any other ingredients in this product.

WARNINGS AND PRECAUTIONS

IYUZEH may cause changes to pigmented tissues. Most frequently reported changes are increased pigmentation of the iris, periorbital tissue (eyelid), and eyelashes. Pigmentation is expected to increase as long as IYUZEH is administered. Iris pigmentation is likely to be permanent. Eyelid skin darkening and eyelash changes may be reversible.

IYUZEH may cause gradual change to eyelashes including increased length, thickness, and number of lashes. These changes are usually reversible upon discontinuation of treatment.

IYUZEH should be used with caution in patients with a history of intraocular inflammation (iritis/uveitis) and should generally not be used in patients with active intraocular inflammation.

IYUZEH should be used with caution in aphakic patients, in pseudophakic patients with a torn posterior lens capsule, or in patients with known risk factors for macular edema.

Reactivation of herpes simplex keratitis has been reported during treatment with latanoprost. IYUZEH should be used with caution in patients with a history of herpetic keratitis.

Contact lenses should be removed prior to the administration of IYUZEH and may be reinserted 15 minutes after administration.

ADVERSE REACTIONS

The most common adverse reactions (5% to 35%) for IYUZEH are: conjunctival hyperemia, eye irritation, eye pruritus, abnormal sensation in eye, foreign body sensation in eyes, vision blurred, and lacrimation increased.

DRUG INTERACTIONS

The combined use of two or more prostaglandins or prostaglandin analogs including IYUZEH is not recommended. It has been shown that administration of these prostaglandin drug products more than once daily may decrease the IOP lowering effect or cause paradoxical elevations in IOP.

Please see full Prescribing Information at www.iyuzeh.com and Brief Summary on the next page.

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Théa
let's open our eyes

iyuzeh™

(latanoprost ophthalmic solution) 0.005%

HIGHLIGHTS OF PRESCRIBING INFORMATION

This brief summary does not include all the information needed to use IYUZEH safely and effectively. See full prescribing information for IYUZEH.

Initial U.S. Approval: 2022

----------INDICATIONS AND USAGE----------

IYUZEH is a prostaglandin F2α analogue indicated for the reduction of elevated intraocular pressure in patients with open-angle glaucoma or ocular hypertension.

----------CONTRAINDICATIONS----------

Known hypersensitivity to latanoprost or any other ingredients in this product.

----------WARNINGS AND PRECAUTIONS----------

Pigmentation: Topical latanoprost ophthalmic products, including IYUZEH have been reported to cause changes to pigmented tissues. The most frequently reported changes have been increased pigmentation of the iris, periorbital tissue (eyelid), and eyelashes. Pigmentation is expected to increase as long as latanoprost is administered.

The pigmentation change is due to increased melanin content in the melanocytes rather than to an increase in the number of melanocytes. After discontinuation of latanoprost, pigmentation of the iris is likely to be permanent, while pigmentation of the periorbital tissue and eyelash changes have been reported to be reversible in some patients. Patients who receive treatment should be informed of the possibility of increased pigmentation. The long-term effects of increased pigmentation are not known.

Iris color change may not be noticeable for several months to years. Typically, the brown pigmentation around the pupil spreads concentrically towards the periphery of the iris and the entire iris or parts of the iris become more brownish. Neither nevi nor freckles of the iris appear to be affected by treatment. While treatment with IYUZEH can be continued in patients who develop noticeably increased iris pigmentation, these patients should be examined regularly.

Eyelash Changes: Latanoprost ophthalmic products, including IYUZEH may gradually change eyelashes and vellus hair in the treated eye; these changes include increased length, thickness, pigmentation, the number of lashes or hairs, and misdirected growth of eyelashes. Eyelash changes are usually reversible upon discontinuation of treatment.

Intraocular Inflammation: IYUZEH should be used with caution in patients with a history of intraocular inflammation (iritis/uveitis) and should generally not be used in patients with active intraocular inflammation because inflammation may be exacerbated.

Macular Edema: Macular edema, including cystoid macular edema, has been reported during treatment with latanoprost ophthalmic products, including IYUZEH. IYUZEH should be used with caution in aphakic patients, pseudophakic patients with a torn posterior lens capsule, or in patients with known risk factors for macular edema.

Herpetic Keratitis: Reactivation of herpes simplex keratitis has been reported during treatment with latanoprost. IYUZEH should be used with caution in patients with a history of herpetic keratitis and should be avoided in cases of active herpes simplex keratitis because inflammation may be exacerbated.

Contact Lens Use: Contact lenses should be removed prior to the administration of IYUZEH and may be reinserted 15 minutes after administration.

----------ADVERSE REACTIONS----------

The following adverse reactions have been reported with the use of topical latanoprost products and are discussed in greater detail in the prescribing information:

- Iris pigmentation changes
- Eyelid skin darkening
- Eyelash changes (increased length, thickness, pigmentation, and number of lashes)
- Intraocular inflammation (iritis/uveitis)
- Macular edema, including cystoid macular edema

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

In the two clinical trials conducted with IYUZEH (latanoprost ophthalmic solution) 0.005% comparing it to XALATAN the preserved 0.005% latanoprost reference product, the most frequently reported ocular adverse reactions were conjunctival hyperemia and eye irritation (Table 1).

Table 1. Adverse Reactions

	Adverse Reactions [n (%)]	
Symptom/Finding	**IYUZEH (n=378)**	**XALATAN (n=358)**
Conjunctival hyperemia	129 (34)	133 (37)
Eye irritation	72 (19)	112 (31)
Eye pruritus	57 (15)	58 (16)
Abnormal sensation in eyes	51 (14)	52 (15)
Foreign body sensation in eyes	44 (12)	36 (10)
Vision blurred	28 (7)	30 (8)
Lacrimation increased	19 (5)	14 (4)
Photophobia	13 (3)	17 (5)

----------POSTMARKETING EXPERIENCE----------

The following adverse reactions have been identified during post-approval use of topical latanoprost products. 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. The reactions, which have been chosen for inclusion due to either their seriousness, frequency of reporting, possible causal connection to ophthalmic latanoprost products, or a combination of these factors, include:

- Nervous System Disorders: Dizziness; headache; toxic epidermal necrolysis
- Eye Disorders: Eyelash and vellus hair changes of the eyelid (increased length, thickness, pigmentation, and number of eyelashes); keratitis; corneal edema and erosions; intraocular inflammation (iritis/uveitis); macular edema, including cystoid macular edema; trichiasis; periorbital and lid changes resulting in deepening of the eyelid sulcus; iris cyst; eyelid skin darkening; localized skin reaction on the eyelids; conjunctivitis; pseudopemphigoid of the ocular conjunctiva.
- Respiratory, Thoracic and Mediastinal Disorders: Asthma and exacerbation of asthma; dyspnea
- Skin and Subcutaneous Tissue Disorders: Pruritis
- Infections and Infestations: Herpes keratitis
- Cardiac Disorders: Angina; palpitations; angina unstable
- General Disorders and Administration Site Conditions: Chest pain

----------DRUG INTERACTIONS----------

The combined use of two or more prostaglandins, or prostaglandin analogs including IYUZEH is not recommended, and administration of these prostaglandin drug products more than once daily may decrease the IOP lowering effect or cause paradoxical IOP elevations.

----------USE IN SPECIFIC POPULATIONS----------

Pregnancy: There are no adequate and well-controlled studies of IYUZEH administration in pregnant women to inform drug-associated risks.

Lactation: It is not known whether this drug or its metabolites are excreted in human milk. Because many drugs are excreted in human milk, caution should be exercised when IYUZEH is administered to a nursing woman. The developmental and health benefits of breastfeeding should be considered along with the mother's clinical need for IYUZEH and any potential adverse effects on the breastfed child from IYUZEH.

Pediatric Use: The safety and effectiveness of IYUZEH have not been established in pediatric patients.

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

----------OVERDOSAGE----------

Intravenous infusion of up to 3 mcg/kg of latanoprost in healthy volunteers produced mean plasma concentrations 200 times higher than during clinical treatment with latanoprost ophthalmic solution and no adverse reactions were observed. IV dosages of 5.5 to 10 mcg/kg caused abdominal pain, dizziness, fatigue, hot flushes, nausea, and sweating.

----------HANDLING THE CONTAINER----------

IYUZEH is a sterile solution that does not contain a preservative supplied in a single-dose container. The solution from one individual container is to be used immediately after opening for administration to one or both eyes. Since sterility cannot be maintained after the individual container is opened, the remaining contents should be discarded immediately after administration. Open a new single-dose container every time you use IYUZEH.

Manufactured for: Thea Pharma Inc. Waltham, MA.

U.S. Patent N°. 8,637,054.
Revised: 04/2023

Théa
let's open our eyes

Listen to the CHRPE

Accurate detection of these unique pigmented fundus lesions can provide critical life-long care.

Q A 40-year-old presented to me with multiple atypical congenital hypertrophy of the retinal pigment epithelium (CHRPE) lesions and no systemic diagnosis. I know that CHRPEs can be a benign finding in most patients, but when should I be concerned?

A CHRPEs can be idiopathic or be associated with Gardner's syndrome, a variant of familial adenomatous polyposis (FAP). "The goal is to recognize the unique presentation of these CHRPEs and know when to facilitate appropriate testing and referral," says Alek Karthikeyan, OD, of Rochester, NY. "These patients are at high risk of early death from colon cancer."

What to Look For?

There are three main variations of the condition, the first and most common being *solitary CHRPE*. This lesion represents hypertrophy and hyperplasia of the RPE cells and is typically unilateral and not associated with any systemic conditions.[1] The second are *grouped CHRPE*, also known as "bear tracks." These lesions represent an increase in the pigmentation within the melanin granules of the RPE cells and are typically unilateral, multifocal and confined to a single quadrant of the retina.[1] "There is a common misconception that bear tracks are associated with Gardner's; however, these lesions have no systemic associations and are benign in nature," Dr. Karthikeyan says.

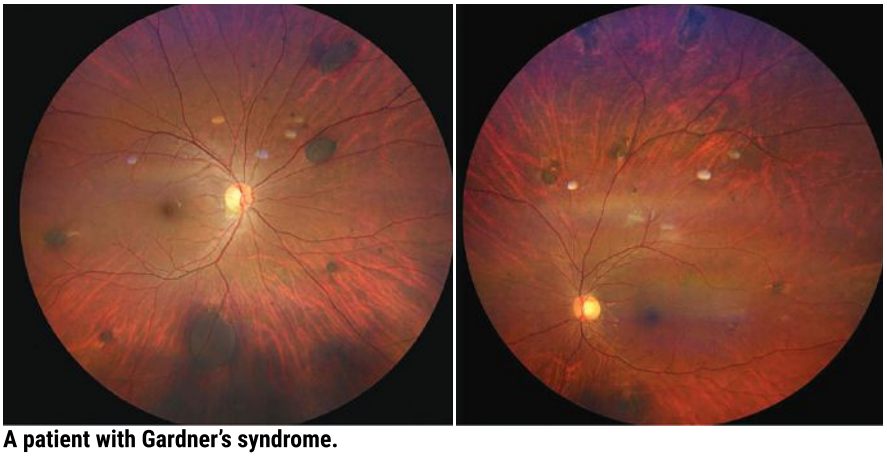
The last and least common presentation are *CHRPE associated with FAP*. These lesions are bilateral, multifocal and extend into different quadrants. They often have a "pisciform" appearance with irregular depigmented borders, as seen in this patient's fundus. These CHRPE are the earliest and most common extracolonic manifestations of FAP.[2] The presence of four or more CHRPE is highly specific for this systemic pathology.

Next Steps

When these suspicious lesions are identified on exam, Dr. Karthikeyan says it's imperative to do a deep dive in the patient's family history and review of systems for any gastrointestinal symptoms. Upon further questioning, he identified that the patient's father and brother both died of cancer. Additionally, the patient also reported routine hematochezia (blood in stool). All these findings lined up with a slam dunk diagnosis. This patient hadn't seen a doctor in a long time, so an emergent referral was made to a primary care provider within our health system. He was quickly referred to a gastroenterologist for a colonoscopy and related testing, but was lost to follow up.

The pathologic sign of FAP is the development of hundreds to thousands of polyps within the colon and rectum. These will inevitably transform into colon cancer if left untreated (7% risk by age 21, increasing to 87% by age 45 and then 93% by age 50).[3] Gardner's syndrome is a variant of FAP, where there are additional extracolonic manifestations, such as CHRPE, desmoid tumors, osteomas and dental abnormalities, to name a few. When 30 or more polyps are detected, removal of the colon and rectum may be recommended. According to Dr. Karthikeyan, the ultimate goal is to prevent development of colon cancer and associated malignancies.

ODs play a critical role in detecting atypical CHRPEs early in patients with Gardner's syndrome and setting a precedent in addressing this disease process. Trust your gut when you see these lesions, and facilitate appropriate referrals to potentially add years to your patients' lives. ■



A patient with Gardner's syndrome.

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3. Yen T, Stanich PP, Axell L, et al. APC-Associated polyposis conditions. In: Adam MP, Feldman J, Mirzaa GM, et al., eds. GeneReviews [Internet]. Seattle (WA): University of Washington, Seattle. www.ncbi.nlm.nih.gov/books/NBK1345/. Last updated May 12, 2022. Accessed September 1, 2024.

About Dr. Ajamian **Dr. Ajamian** is board certified by the American Board of Optometry and serves as Center Director of Omni Eye Services of Atlanta. He is president of the Georgia State Board of Optometry and general CE chairman of SECO International. He has no financial interests to disclose.

BY MONTGOMERY VICKERS, OD

CHAIRSIDE

It's Opposite Day

Time to change things up in an unconventional way.

The urban legend goes something like this: my first year in optometry school, on my very first physiological optics test, I scored what is widely considered the lowest score in the history of physiological optics. One of the cadaver heads in anatomy lab scored better than I did.

Two weeks later, on our second test, I scored the highest score in the class. The professor (who, out of respect, shall remain nameless… not to mention I can't remember who it was), called me in for a meeting and stated that some students just get it quick and others take time to understand the complexities of the course. He wanted me to explain how I turned the ship around so quickly.

My answer was: "The first test, I worked on the problems and wrote down my answer. The second test, I worked out the problems, figured out the answer and wrote down the opposite."

In our profession's self-destructive race to accept less money for our services and our optical solutions, my gut tells me that instead of just writing down the answers, maybe it's time to consider the opposite.

It's time to be creative. As I used to tell my kids, "It's Opposite Day. Now, do NOT clean your room."

Now, OK, I don't want to paint every single individual doctor with the same stroke, but I think we can all admit that creativity is not the first word that pops into anyone's mind when they consider an optometrist. Our training makes us more left-brained, analytical, habit forming, linear and precision-seeking.

To us, being creative means we just cannot bring ourselves to finally throw out those old frame bars we had when we first opened our office.

To us, being creative might mean we finally ask for extra ketchup for our fries after years of therapy.

To us, being creative in the office means we show up three minutes later than we have for 37 years… once.

To us, being creative means we think a major change in the office décor is a new doormat. We take the old one home, of course.

So, yes, we have our challenges. I mean, what can we do? On one side, computerization and AI very possibly could replace the need for a patient to actually walk into your office. On the other side, we will accept lower and lower reimbursements just so we can get someone to actually walk into our office, even if we barely break even when we see them.

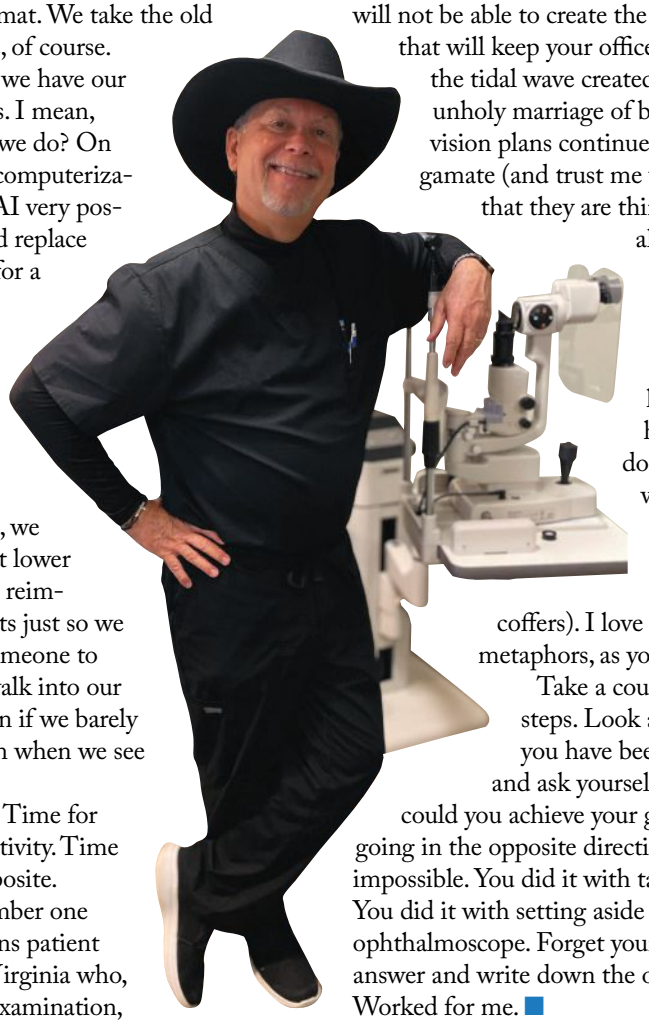
People! Time for some creativity. Time to get opposite.

I remember one contact lens patient in West Virginia who, after his examination, asked me for a copy of his contact lens prescription because it would be "cheaper" to get them somewhere else. My answer was: "How could it be cheaper somewhere else? In my office, the contact lenses are free."

After his mind was blown, I continued: "The contact lenses are free. My contact lens evaluation fee is $300."

I'll admit this did not work, but at least I was thinking outside the box, right?

If you are not reviewing how you have always done things in your office and thinking what you could do that is the opposite of what you do now, you will not be able to create the new norms that will keep your office afloat as the tidal wave created by the unholy marriage of big tech and vision plans continue to amalgamate (and trust me when I say that they are thinking way ahead and looking at doing things the opposite of how they have been doing things while we sit back and enrich their war coffers). I love mixed metaphors, as you can see.



Take a couple of baby steps. Look at one path you have been taking and ask yourself, how could you achieve your goal by going in the opposite direction? It's not impossible. You did it with taking PDs. You did it with setting aside your direct ophthalmoscope. Forget your obvious answer and write down the opposite. Worked for me. ■

About Dr. Vickers

Dr. Vickers received his optometry degree from the Pennsylvania College of Optometry in 1979 and was clinical director at Vision Associates in St. Albans, WV, for 36 years. He is now in private practice in Dallas, where he continues to practice full-scope optometry. He has no financial interests to disclose.

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†In a chronic dry eye patient usage study, participants from a variety of socioeconomic backgrounds answered questions about their experience with iVIZIA lubricant drops. In the study, 203 chronic dry eye patients, 28-80 years old, switched from their dry eye artificial tears to iVIZIA for a month.[1]
‡To limit blurriness when using contact lenses, remove contacts, apply drops, then insert contacts.

Reference: 1. Thea Data on File.

Théa
let's open our eyes

BY PAMELA H. SCHNELL, OD, AND MARC B. TAUB, OD, MS, EdD

Modify Your Exam with the Modified Thorington

This quick test can cue the practitioner in to subtle vertical deviations that can evade detection on cover test.

We have reviewed a number of tests in this column, most of which we all learned in optometry school but perhaps don't use on a daily basis. For this month's offering, we thought we would look at a test that is less well-known—one that you may not have seen outside of a lab course at some point—but one that is incredibly easy to run and highly useful: the Modified Thorington test.

Thorington Use

The main purpose of the Modified Thorington test is to measure ocular deviation. While most of us perform cover tests or perhaps phorias as a routine part of our comprehensive eye exams, we often use these tests to look only for horizontal deviations. Cebrian et al. compared distance heterophoria on two separate occasions by two examiners in 110 subjects aged 18 to 32 years using four different tests: cover test, von Graefe, Maddox rod and Modified Thorington.[1] The Modified Thorington showed good intra-examiner repeatability and the best inter-examiner reliability.

Here, we will also discuss how the Modified Thorington can be used not only to measure horizontal misalignments, but also subtle vertical ones, which often have a large impact on patients' quality of life.

The set-up for the Modified Thorington is as easy as it gets. You only need a few items to run it: the Modified Thorington card itself (*Figure 1*), a Maddox rod (*Figure 2*) and your transilluminator (a penlight will also work, but the transilluminator fits nicely into the card). The patient holds the Maddox rod in front of their right eye, with the striations oriented appropriately for the direction of deviation that you want to measure. Recall that when the patient looks through the Maddox rod, they will see a line oriented perpendicular to the direction of the striations, so hold the striations horizontally to measure lateral phorias and vertically to measure vertical ones. Holding the card at 40cm from the patient, shine the light through the hole in the center of the card (*Figure 3*). Since they are only seeing the line with one eye, they are performing a monocular fixation in a binocular field type of test; thus, the eyes' natural deviation will manifest. Ask the patient to report where the line formed by the Maddox rod crosses the scale printed on the card. Whatever they report is their deviation at that moment. The direction of deviation (eso, exo, hyper, hypo) is conveniently printed on the card.

While we can measure ocular deviation in multiple ways in the exam room, the Modified Thorington is quick and simple, as well as allowing for a relatively unrestricted measurement of phorias or tropias. This is extremely useful for patients who may not be comfortable in the phoropter or for whom you want a more precise measurement than your cover tests provide.

The following case illustrates the use of the Modified Thorington in a

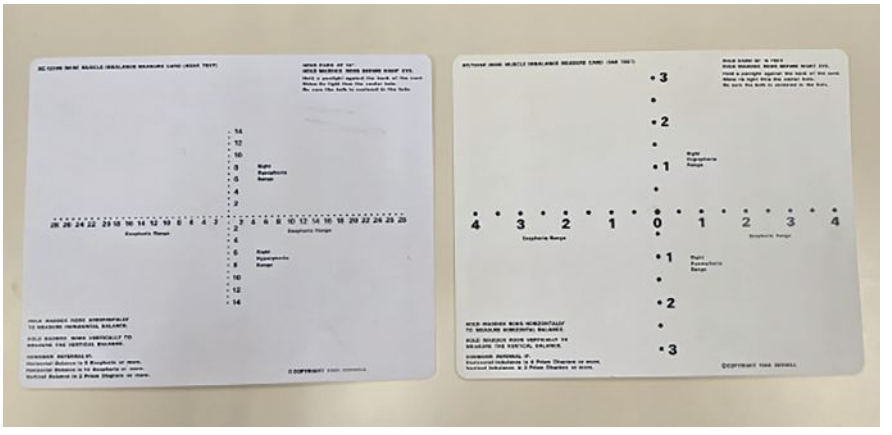


Fig. 1. Modified Thorington cards. On left, near card for use at 40cm. On right, distance card for use at 10 feet.

About Drs. Taub and Schnell

Dr. Taub is a professor and co-supervisor of the Vision Therapy and Pediatrics residency at Southern College of Optometry (SCO) in Memphis. He specializes in vision therapy, pediatrics and brain injury. **Dr. Schnell** is a professor at SCO and teaches courses on ocular motility and vision therapy. She works in the pediatric and vision therapy clinics and is co-supervisor of the Vision Therapy and Pediatrics residency. Her clinical interests include infant and toddler eye care, vision therapy, visual development and the treatment and management of special populations. They have no financial interests to disclose.

Fig. 2. Maddox rod. With this orientation, a vertical line will appear to the patient, allowing testing of horizontal deviation.

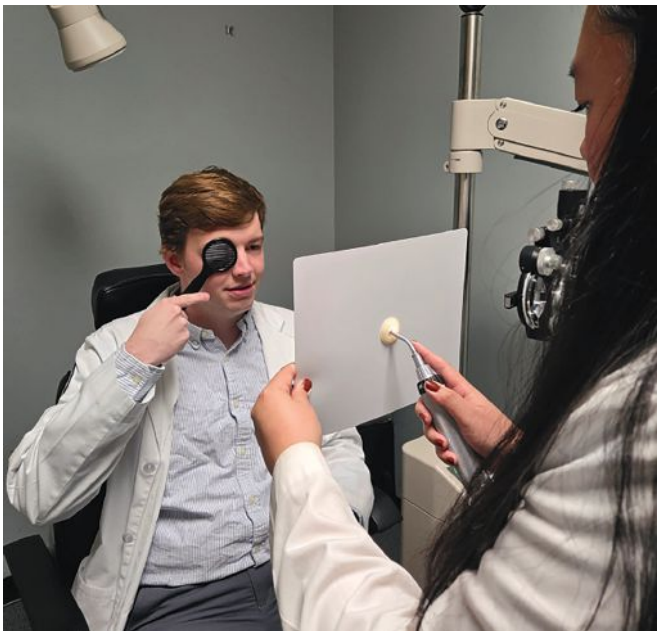


Fig. 3. Set-up for testing with the Modified Thorington card.

patient we saw recently. Shout-out to our fourth-year intern, Payton Lock, who thought of the Modified Thorington test for this patient and uncovered some subtle findings that made all the difference.

Case Report

A nine-year-old girl presented to the Vision Therapy & Rehabilitation Service with a history of an eye turn diagnosed at an examination in the Pediatric Service earlier the same month. She was in fourth grade but was reading at a third grade level. Her grades were As and Bs except in reading, in which she was getting a C. She and her mother reported that she turned her head to the left and had daily frontal headaches. She skipped words when reading, but the patient reported that this was due to comprehension. She also reported being clumsy and bumping into things often, stating that she "bumps her head all the time." Her exam from five years prior, which was the last time she was seen, did not show the presence of an eye turn.

At the primary care pediatrics exam, she was given +0.50D OU for full-time use, so all testing performed was completed through those lenses. Her visual acuity was 20/20-2 OD, OS, OU at distance and near. Extraocular motilities, fields by confrontation and pupils were normal. Stereo was measured at 30 sec of arc. The cover test was 6^ intermittent alternating exotropia at distance and 18^ intermittent alternating exotropia at near. The control score, a measure of the turn that takes into account the patient's ability to "control" the intermittent exotropia, was 1. This indicated that there was "no exotropia unless dissociated, recovers in one to five seconds." The near point of convergence was 7/10cm, 8/11cm and 8/11cm, and accommodative amplitudes were 16.00D OD, OS. The quality-of-life questionnaire was a 37. As a reminder, anything over a 20 is a red flag for a binocular vision issue.

Based on the patient's control of the intermittent exotropia and the severity of the headaches, Payton decided to pull out the Modified Thorington, as she had a hunch that there might be a small vertical deviation present. Sure enough, the distance measurement showed a 4^ exophoria and a 2^ right hyperphoria. The near showed a 16^ exophoria and a 5^ right hyperphoria. To assess the impact of the convergence stress on the hyperphoria at near, we trialed 2^ base-in prism in each eye and retested. This time, the hyperphoria was reduced to 1^ right hyperphoria.

With the use of the Modified Thorington test, we were able to assess this patient's vertical deviation appropriately. Since we were planning to start the patient in vision therapy to address the intermittent alternating exotropia and the small amount of base-in prism had such a huge impact on the hyperphoria, we decided to hold off on prescribing the vertical prism. As we move through the therapy program, we will address both the horizontal and vertical issues to enable the patient to look at near targets without the headache burden.

This case resulted in a great outcome from such a quick check. The Modified Thorington can help identify subtle vertical deviations that evade even the most experienced clinician on cover test and, as a bonus, this test can easily be performed by a paraoptometric technician. We use the test fairly often in clinical care and can recommend both its ease of use and its benefits for your patients. ■

1. Cebrian JL, Antona, B, Barrio A, et al. Repeatability of the Modified Thorington card used to measure far heterophoria. Optom Vis Sci. 2014;91(7):786-92.

BY JEROME SHERMAN, OD, SHERRY BASS, OD, AND DIANA DOSCAS, OD

YOU BE THE JUDGE

Imaging: Friend or Foe?

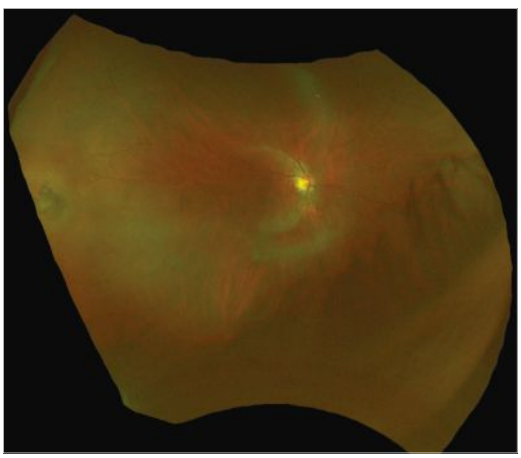
This case documents a misdiagnosis of UWF photos on five visits over a six-year span.

The intriguing topic of imaging in malpractice allegations was first mentioned in the December 2023 You Be the Judge article entitled "Maybe Too Thin?" This case was about a fashion model on Plaquenil (hydroxychloroquine, Sanofi) for rheumatoid arthritis for only about 30 months who unexpectedly developed toxic maculopathy in both eyes. The first eyecare clinician to evaluate the patient when she was on Plaquenil for 15 months appropriately performed a comprehensive exam including OCT, which was normal and interpreted as such. About a year later, the patient was evaluated by a different eyecare clinician in a different practice who also appropriately performed a comprehensive exam including OCT.

When malpractice allegations ensued, a review of all the records, emphasizing the all-important spectral-domain OCT (SD-OCT) findings, revealed that only the SD-OCT performed by the second eye clinician, which was interpreted as normal, was clearly abnormal and characteristic of Plaquenil-induced toxic maculopathy OU.

Hence, the normal OCT on the first visit shielded the first clinician from successful malpractice allegations but provided irrefutable evidence that the second clinician deviated from the existing standard of care by misinterpreting the SD-OCT, which resulted in irreversible loss of vision and culpability of malpractice. We can conclude that imaging (the OCT) was a friend for the first doc and a foe for the second.

In this new case below, ultra-widefield (UWF) fundus imaging clearly documents a misdiagnosis that recently resulted in a large settlement for the plaintiff.



Lesion at nine o'clock was diagnosed as CHRPE on this visit and subsequent visits.

Case

A 50-year-old myopic man presented for routine care including a new spectacle prescription and updated contact lenses. The health history and previous eye history were unremarkable. The 7D myope was evaluated by the same ophthalmic clinician on five occasions over a six-year period. UWF Optos images were obtained on each visit. The patient never complained of flashes but mentioned occasional floaters in the right eye during the last two visits. A posterior vitreal detachment was noted by the eye clinician in the right eye, and a possible risk of retinal detachment was explained to the patient. The patient never complained of field loss on any of these visits.

On the first visit, the eye doc diagnosed a CHRPE (congenital hypertrophy of the retinal pigment epithelium) lesion in the periphery of the right eye. The location of the lesion was not noted, and a drawing or sketch of the lesion was not included. With minor changes in the prescription, the patient's visual acuity (VA) was improved to 20/20 in each eye on all five visits. The CHRPE lesion was noted on all subsequent examinations. The patient was dilated on three of the five visits and refused dilation on the other two. Several months after the last visit, the patient began complaining of decreased vision in the right eye, was referred to a retinal specialist and was diagnosed with an inferior retinal detachment OD. The retinal specialist noted that "the primary break was temporal." The retinologist did not identify any CHRPE lesions in either eye.

You Be the Judge

Given the facts presented thus far, consider the following questions:

- Was the lesion the primary eye clinician imaged and documented on several occasions a CHRPE?
- Was the temporal retinal break that eventually enlarged to a retinal detachment misdiagnosed as a CHRPE lesion?
- If the lesion was correctly diagnosed as a retinal break years earlier, would the outcome be different?
- Can experts for the eye clinician present any meaningful arguments for the defense?

About Drs. Sherman and Bass

Dr. Sherman is a Distinguished Teaching Professor at the SUNY State College of Optometry and editor-in-chief of *Retina Revealed* at www.retinarevealed.com. During his 53 years at SUNY, Dr. Sherman has published about 750 various manuscripts. He has also served as an expert witness in 400 malpractice cases, approximately equally split between plaintiff and defendant. Dr. Sherman has received support for *Retina Revealed* from Carl Zeiss Meditec, MacuHealth and Konan. **Dr. Bass** is a Distinguished Teaching Professor at the SUNY College of Optometry and is an attending in the Retina Clinic of the University Eye Center. She has served as an expert witness in a significant number of malpractice cases, the majority in support of the defendant. She serves as a consultant for ProQR Therapeutics.

• Were the UWF images in this case friend or foe for the primary eye clinician?

Our Opinion

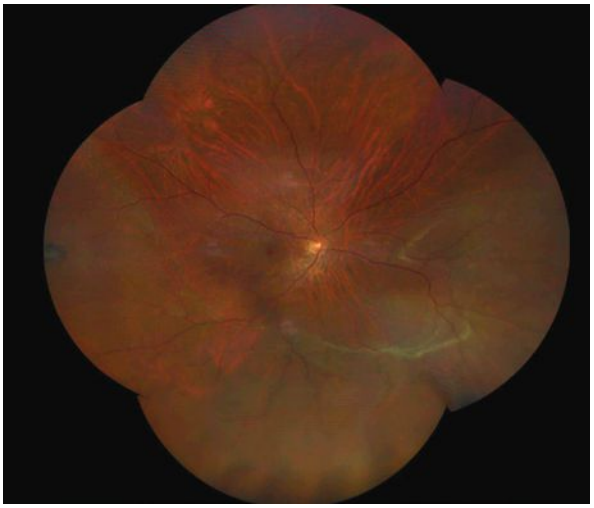
One of us (JS) was requested to review all the records with emphasis on the multiple UWF images. I concluded that the temporal retinal break that was imaged with the UWF device was repeatedly misdiagnosed by the eye clinician as a CHRPE lesion. The delay in diagnosis and subsequent delay in treatment resulted in the need for a scleral buckle and pars plana vitrectomy. Although the combined procedure was successful from a surgical point of view, this essential intervention then resulted in a cataract in the right eye, which required removal. A secondary cataract, a posterior capsular opacification, developed, which will require treatment. The patient also developed cystoid macula edema (CME) as a result of the combined surgical intervention and an epiretinal membrane. The CME has required a combination of steroid drops, perhaps for a prolonged period of time, which increases the risk of infection in the right eye and other side effects. I opined that the retinal break could have been diagnosed on the first visit and treated successfully with cryotherapy or laser six years earlier.

I asked my new associate, DD, to review the images, as I have done in previous cases. Dr. Doscas immediately diagnosed the lesion as a retinal tear in the temporal retina of the right eye.

The Defense

Two highly respected MD experts with impressive credentials and publications reviewed the case files and reached the following conclusions. Both acknowledged that the lesion documented with UWF Optos images was not a CHRPE but a retinal break and, hence, misdiagnosed by the primary eyecare clinician. One of these experts stated, "CHRPE is a benign condition, showing lesions with flat, hyperpigmentation. CHRPE is an uncommon but not rare retinal condition with a prevalence of about 1% to 2%. I believe that Dr. X incorrectly diagnosed CHRPE due to the presence of pigmentation seen around the retinal tear."

This expert added, "It should be noted that asymptomatic retinal breaks such as seen in this case have only a 5% chance of developing retinal detachment […] Had the patient been referred out to a retinal specialist, it is entirely possible that no treatment would have been offered, particularly since the tear was already partially self-demarcated (*i.e.*, pigment was present around some of the tear). Had laser treatment and or cryotherapy been opted for, there is roughly a 10% failure rate due to development of recurrent retinal tears. There is a roughly 3% to 10% chance of developing epiretinal membrane after either of these treatments."



UWF image taken the day the detachment was diagnosed by the retina surgeon. The lesion at nine o'clock was diagnosed as a retinal tear that resulted in the retinal detachment.

I (JS) have no substantive disagreement with either physician in their summary of the surgeries and care rendered by others prior to and subsequent to these surgeries, save perhaps for the care rendered by the defendant, which both experts appear to have avoided. My opinion remains that the failure to diagnose the retinal tear initially and over several years subsequently resulted in the need for these surgeries. If the primary eyecare clinician met the standard of care and did not misdiagnose the retinal tear as a CHRPE lesion, the tear could have been treated successfully with laser or cryo and avoided both surgeries.

Fortunately, the patient is left with normal near central vision but does demonstrate loss of perhaps 6% of his macula vision, as documented with the Humphrey Visual Field Analyzer. There remains, and will forever, superotemporal peripheral vision loss in the right eye. There is also metamorphopsia, or distortion of vision where straight lines appear to bend or curve. This annoying distortion will likely last forever. The macular pucker, or epiretinal membrane scarring, is a result of the retinal detachment surgery, which could have been avoided if the correct diagnosis was arrrived at initially and treated with laser or cryo.

The agony, pain, suffering and other stress-related issues associated with the surgery, as well as costs not covered by insurance, including a $2,000 toric intraocular lens, all relate to the wrong diagnosis.

Follow-up

In a Midwestern state where this all occurred, both sides agreed to mediation rather than going to trial. We have no experience with mediation in malpractice cases and cannot comment on how this approach works. The bottom line in this case was that the patient was awarded an amount well into six figures.

Hence, the UWF images were not a friend but a foe to this primary eyecare clinician. The three authors are all fans of UWF imaging, but the images must be correctly interpreted to avoid such disasters. ■

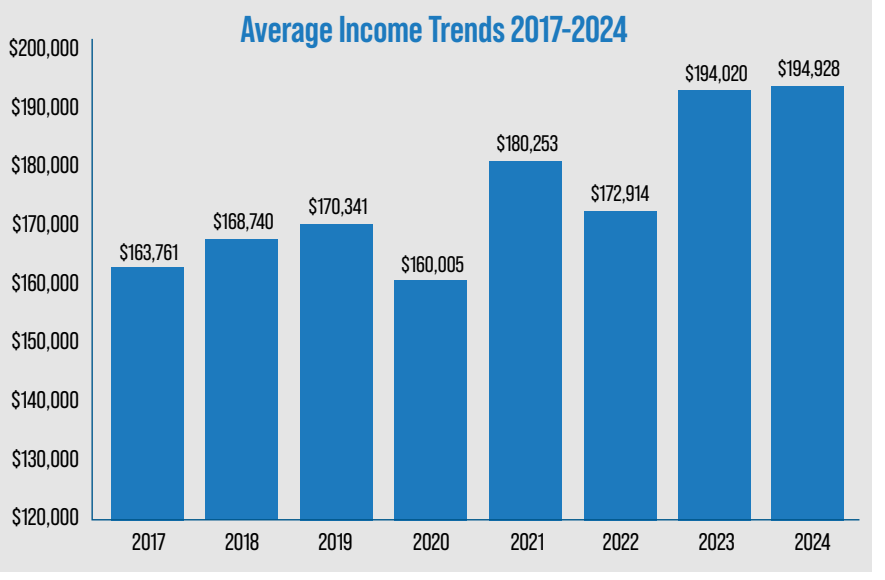
ABOUT THE CO-AUTHOR

Dr. Doscas graduated from SUNY College of Optometry in 2023. She completed her residency training in primary care optometry and ocular disease at VA Hudson Valley and is currently employed at a private practice in White Plains, NY.

2024 INCOME: HIGH TIMES FOR PRIVATE PRACTICE ODs

Being your own boss brings in the bucks, our survey shows, but job satisfaction runs deep among those who favor the work-life balance of an employment contract.

BY JACK PERSICO
EDITOR-IN-CHIEF



Each November, as we all begin to take stock of the year that's winding down, *Review of Optometry* surveys its readers on their anticipated financial performance over the previous 12 months. In the aggregate, optometry is doing great: posting average annual incomes just shy of $200,000 per doctor. However, if you split the group in any meaningful way—employed vs. self-employed, young vs. old, men vs. women—you reveal a wide range of earnings, and they don't always track with what one might consider a fair outcome.

"I feel optometrists are not paid as well as we should be compared to other doctors," wrote one OD from the Mid-Atlantic region, who practices in a commercial setting. "I had a lot of debt and did not feel my salary (especially starting out) was enough to compensate. Perhaps school overall is too much, considering what we make on the outside. Plus, I've had to increase patients per hour to help with income."

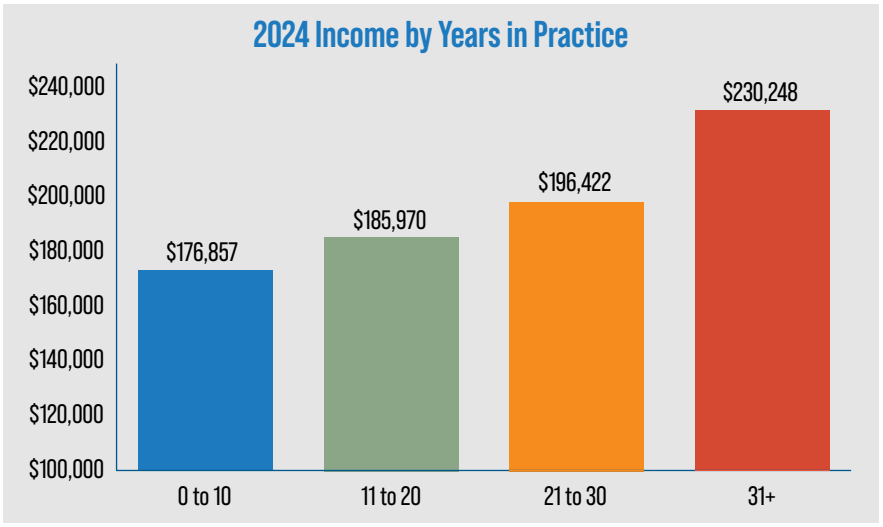
Even though the average income among this year's pool of 422 respondents—an impressive $194,928—is virtually identical to last year's, the data in our annual survey continues to highlight the greater opportunities afforded by private practice. Senior ODs also typically earn more than younger ones, even though that's not always an accurate reflection of effort or expertise. Plenty of bright young optometrists are in the "paying their dues" phase of their careers right now.

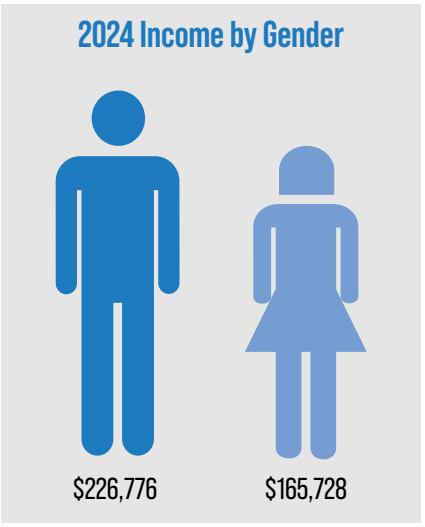
"It's my first year practicing and I have what I would think is a great salary, but I haven't even started paying student loans ($230K) and my cost of living is quite high," wrote one young OD. "Rent prices are insane. I'm worried for my financial future/retirement."

Geographic area can swing the numbers notably too, with the lowest and highest regions adjacent to each other. And, most frustratingly, the gender divide continues to persist—even when accounting for part-time status.

As always, be mindful that while we ask the same survey questions, the responses come from different individuals each year, making trend analysis tricky. The results here offer an illuminating look at the profession but aren't considered statistically rigorous, particularly in year-over-year comparisons.

With that caveat in mind, let's dig in.





Profits for Private Practitioners

Self-employed ODs who responded to our survey reported average earnings of $243,650 in 2024, while those in an employed setting received salaries of $156,819 on average, representing a 55% advantage for those who take the plunge into entrepreneurship.

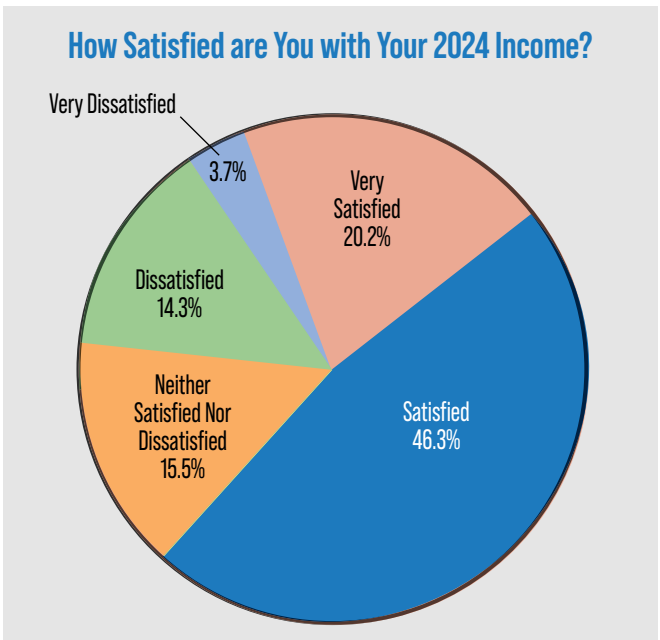
But, of course, higher earnings also add more stress to maintain the practice and one's income level.

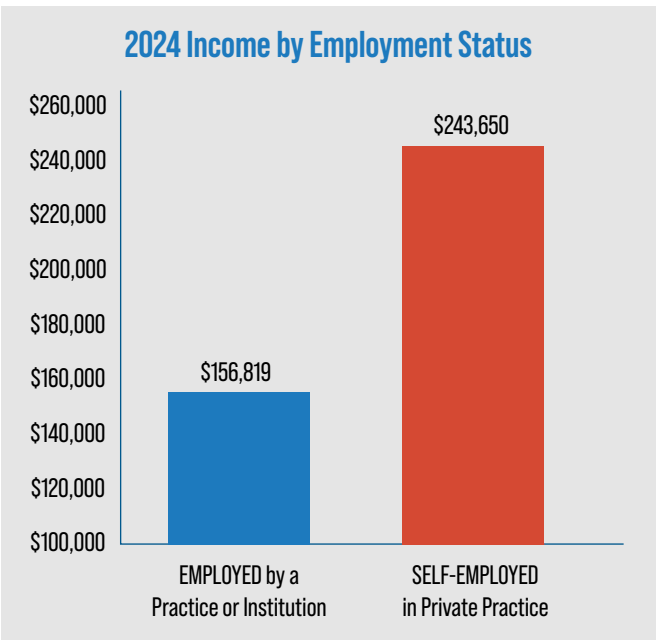
"I'm very worried about increasing cost of goods and decreasing reimbursements for my practice (as well as increasing cost of living), as I won't always be able to just 'work more hours' to balance out the books and maintain personal health and enjoyment," wrote one reader from the Northeast.

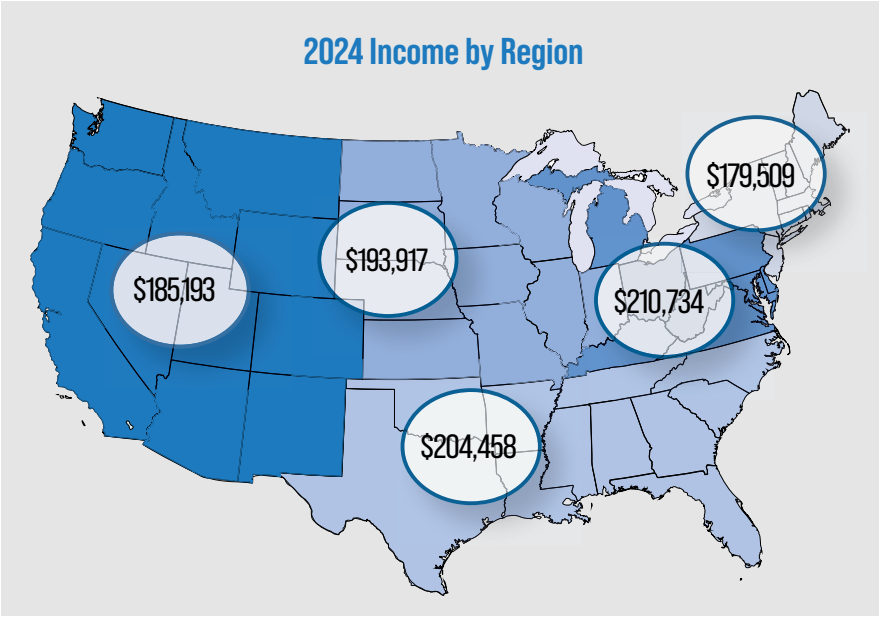
"I spend a great deal of time trying to maintain a high volume of patient visits and to maintain an excellent level of quality care," wrote Brian Kahn, OD, who practices in the South. "I have learned from ophthalmology how to obtain this level of productivity and net income."

The grind can easily lead to burn-out. "The net income is excellent, though I am seeking partnership since it's a lot of work to get this income—it wears me out," a self-employed OD from the West wrote. Some point to lifestyle choices they've made as decisive factors. "I am happy with the income because my husband and I chose not to have children," wrote a solo private practitioner from the Northeast. "Otherwise, I'd be quite stressed by the rather poor daily life-work balance that I have."

Savvy ODs know how to work the advantages of self-employment to their advantage. "I'm currently purchasing the commercial real estate where I practice to build equity with payments instead of losing it to rent," said reader Connor Smallwood, OD. Still, self-employment is an uphill climb. "I went from being employed to self-employed in a new state, and it's slower than I thought it would be," writes a solo







private practitioner from the West. "I'm going to work part-time for another practice until mine builds up."

Employed ODs take comfort in having a steady paycheck and no entrepreneurial hassles, but are at the mercy of their practice owners. "I work way too hard for very little compensation," said one employed OD. "My employer asks us to make sacrifices for the good of the business. I work 60 to 80 hours a week right now. I don't have any spare time to work any additional jobs to increase my revenue." This was echoed by many readers who expressed frustration at being squeezed by inflation on one end and stagnant paychecks on the other.

Turning to seniority, we see that well-established optometrists earned at least $50,000 more on average than younger ones, as those with 31+ years on the job reported income of $230,238 vs. $176,857 among ODs who've been in the workforce for 10 years or less.

The proportion of respondents who work part-time has been going up steadily. In 2018, just 9% of readers worked part time; this year, 15% do. Average earning within these groups were $204,523 among full-timers and $137,364 for part-time workers.

Women were twice as likely as men to report part-time employment status, and, as expected, this shows up in the disparity in earnings between the genders: $226,776 for men and $165,278 for women on average. However, even among readers of the same employment status, women earned less: female full-time ODs reported incomes of $179,039; among male ODs, it was $228,492.

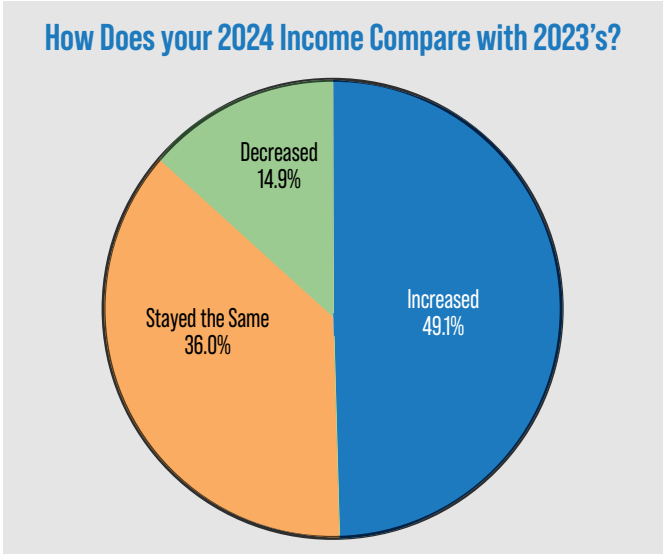
Another factor at work: The women ODs in our survey also skewed younger than the men, and higher earnings accrue later in one's career. The "years in practice" percentage breakdown by gender was as follows:

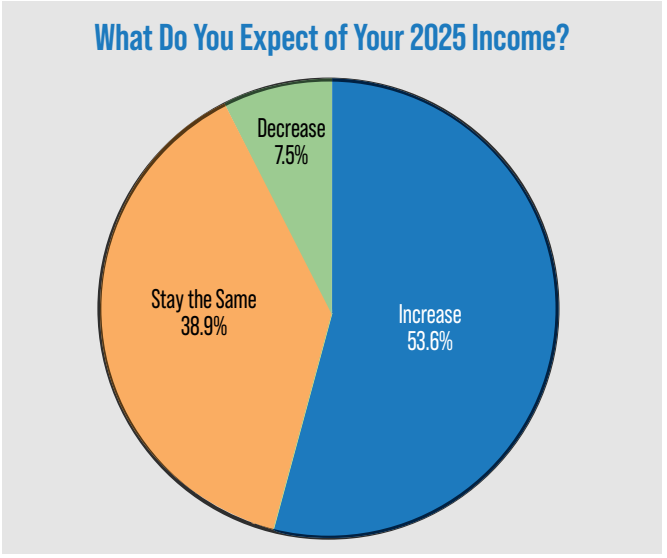
	Women	*Men*
0-10 yrs	27.1%	19.3%
11-20 yrs	37.1%	30.5%
21-30 yrs	25.8%	21.8%
31+ yrs	10.0%	28.4%

One last piece of the puzzle: The breakdown of the self-employment category decisively favored male ODs, who comprised 59% of the group. Since earnings correlate with both self-employment and years in practice—and those categories remain dominated by men—the earnings of female optometrists continue to lag behind. In time, we expect a narrowing of this gap as the workforce continues to shift to a predominantly female one over time.

Stresses and Satisfactions

In the aggregate, nearly 15% of readers reported a decline in income in 2024





vs. 2023—never a welcome sight—and another 36% told us their incomes stayed the same, which is also dispiriting to many. "As a corporate sublease owner, the opening of all these other corporate locations has been horrible for business," wrote one self-employed OD. "My goal was to work very hard for a few years, save a lot and then leave. Now I'm working there longer because other jobs still don't pay as much, and I'm not making as much as before."

Besides competition, ODs also have to constantly battle an insurance landscape that's not conducive to their financial success or professional aspirations. "Frequently, patients change medical insurances and that prevents ODs from practicing medical optometry," noted Spencer Moy, OD, a solo private practitioner from the Northeast. "Essentially, the only entry to care is an eyeglass plan. I refuse the play that game." Performing what amounts to a medical exam on the scale of a vision exam's compensation structure is a source of ire for many. "The most frustrating thing is that you have to do a diabetic exam with a vision plan that pays $35 dollars," a Southern OD wrote. "Vision insurance should just be for refraction."

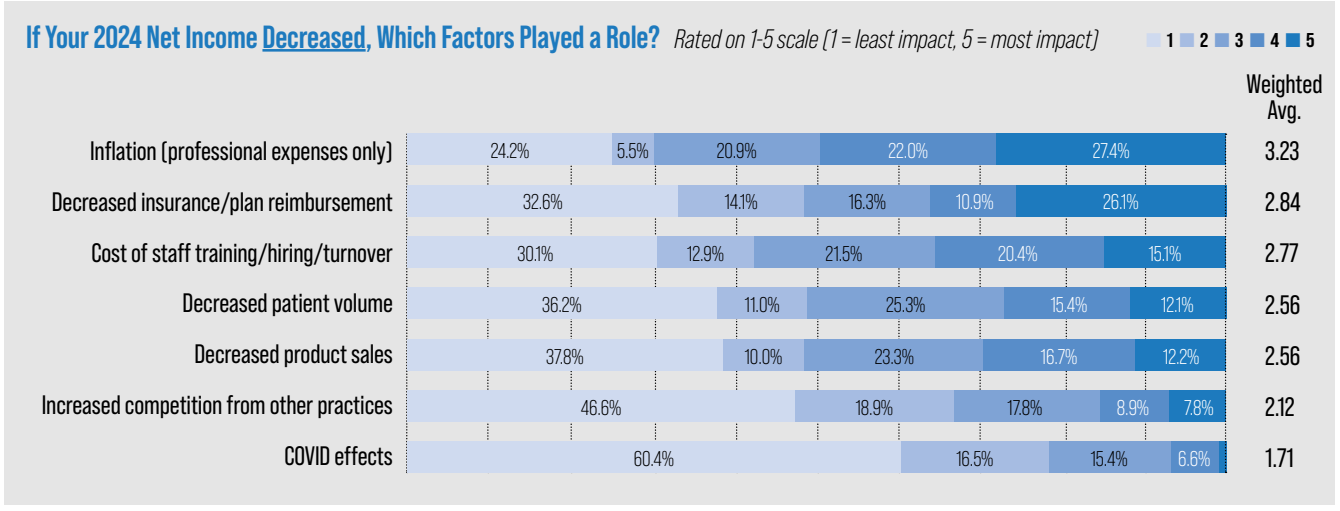
Macroeconomic forces also took a toll, as readers whose incomes declined ranked inflation the #1 factor contributing to it—and of course there's the double-whammy of having to weather rising costs for one's professional inventories but also personal expenses, too. "I'm still making the same as I was seven years ago, but inflation has made that money useless," lamented one private practitioner from the Northeast.

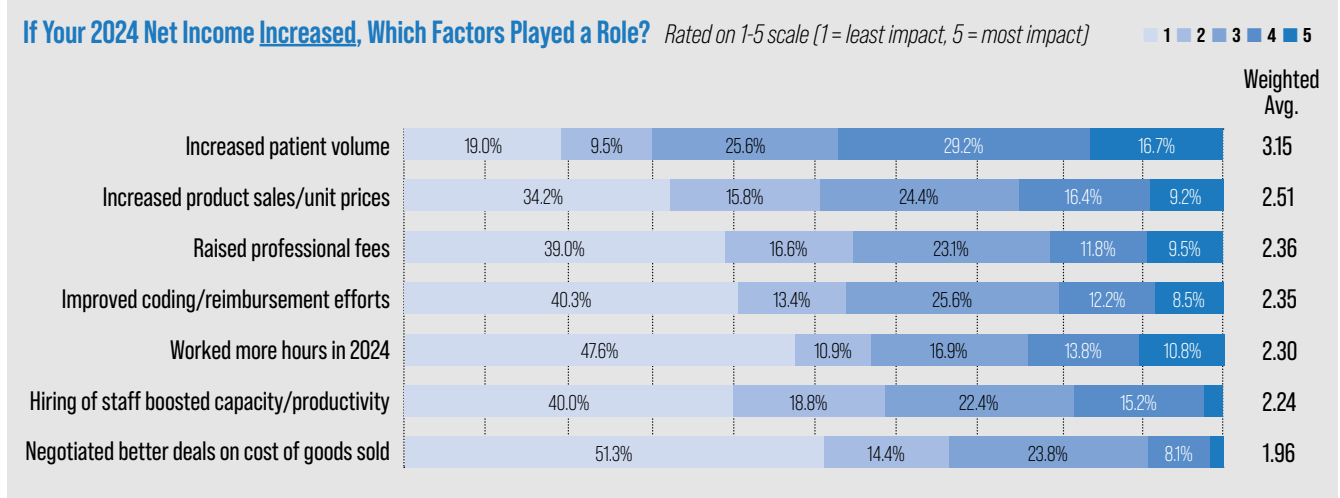
Still, amid these often-difficult circumstances for many, there's a deep well of satisfaction with what the practice of optometry provides; only 18% of respondents said they are dissatisfied with their compensation.

"I chose to work in a practice setting that allows me to put patients first," one survey respondent wrote. "I did not select this job for best income." Said another, "I feel like if I wanted to earn more I could, but currently I like my work-life balance."

One optometrist whose income dropped in 2024 nevertheless reported that he was "very satisfied" with his income. "I dumped all discount vision plans, reduced my workload to 3.5 days a week and now my associates work a little more," he wrote.

As one reader put it, "I can make enough to help support my family doing a job I love." Sometimes, it's as simple as that. ■





tyrvaya®
(varenicline solution)
nasal spray 0.03 mg

FOR THE SIGNS & SYMPTOMS OF DRY EYE DISEASE

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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 next page and the full Prescribing Information at Tyrvaya-pro.com.

Reference: 1. Tyrvaya. Prescribing Information. Oyster Point Pharma.

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tyrvaya®
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INDICATIONS AND USAGE

TYRVAYA® (varenicline solution) nasal spray is a cholinergic agonist indicated for the treatment of the signs and symptoms of dry eye disease.

ADVERSE REACTIONS

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

In three clinical trials of dry eye disease conducted with varenicline solution nasal spray, 349 patients received at least 1 dose of TYRVAYA. The majority of patients had 31 days of treatment exposure, with a maximum exposure of 105 days.

The most common adverse reactions reported in 82% of TYRVAYA treated patients was sneezing. Other common adverse reactions that were reported in >5% of patients include cough (16%), throat irritation (13%), and instillation-site (nose) irritation (8%).

USE IN SPECIFIC POPULATIONS

Pregnancy: Risk Summary: There are no available data on TYRVAYA use in pregnant women to inform any drug associated risks. In animal reproduction studies, varenicline did not produce malformations at clinically relevant doses.

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

Data: *Animal Data*: Pregnant rats and rabbits received varenicline succinate during organogenesis at oral doses up to 15 and 30 mg/kg/day, respectively. While no fetal structural abnormalities occurred in either species, maternal toxicity, characterized by reduced body weight gain, and reduced fetal weights occurred in rabbits at the highest dose (4864 times the MRHD on a mg/m^2 basis).

In a pre- and postnatal development study, pregnant rats received up to 15 mg/kg/day of oral varenicline succinate from organogenesis through lactation. Maternal toxicity, characterized by a decrease in body weight gain, was observed at 15 mg/kg/day (1216 times the MRHD on a mg/m^2 basis). Decreased fertility and increased auditory startle response occurred in offspring at the highest maternal dose of 15 mg/kg/day.

Lactation: Risk summary: There are no data on the presence of varenicline in human milk, the effects on the breastfed infant, or the effects on milk production. In animal studies varenicline was present in milk of lactating rats. However, due to species-specific differences in lactation physiology, animal data may not reliably predict drug levels in human milk.

The lack of clinical data during lactation precludes a clear determination of the risk of TYRVAYA to an infant during lactation; however, the developmental and health benefits of breastfeeding should be considered along with the mother's clinical need for TYRVAYA and any potential adverse effects on the breastfed child from TYRVAYA.

Pediatric Use: Safety and efficacy of TYRVAYA in pediatric patients have not been established.

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

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EXPECTING THE UNEXPECTED: AN OVERVIEW OF CATARACT SURGERY COMPLICATIONS

It is important for optometrists to maintain clinical expertise and to be equipped to handle these situations.

BY GLEB SUKHOVOLSKIY, OD
TACOMA, WA

With the current state of healthcare, optometrists are heavily involved in the comanagement of patients undergoing cataract surgery. Whether working with ophthalmologists in surgical practices or managing patients postoperatively in their own clinics, optometrists often share the burden of successful outcomes and patient satisfaction. It is of great importance, thus, for us to be well-versed in the complexities of postsurgical care and to be acutely aware of not only the common postoperative complications but also of how certain intraoperative issues may affect postoperative care and outcomes.

Intraoperative Complications

When seeing patients for their post-op appointments after cataract surgery, it is important to understand that not every surgery goes the same way. While most if not all patients get an intraocular lens (IOL) in place of their cloudy natural lens, the path to that IOL placement can often be vastly different. Without paying close attention to the surgical note, it is difficult to be fully aware of the hardships the surgeon faced during the procedure. Often, the result is excellent despite a challenging surgery. Though sometimes, signs of intraoperative complications may be present.

Posterior capsular rupture is a dreaded but relatively common intraoperative issue, with an occurrence rate of 0.45% to 5.2%.[1,2] While it is impossible to always anticipate capsular rupture, recognizing the risk factors and careful planning reduces the possibility of it occurring. Those factors include the presence of posterior polar cataracts, pseudoexfoliation or very dense cataracts.[2] Previous retinal surgeries or intravitreal injections may also increase the risk.[3] A lens may be nicked accidentally during a retinal procedure, resulting in minor damage to the posterior capsule, which may not manifest into a problem until the stress of manual manipulation during the cataract surgery. Poor patient cooperation can also result in a capsular rupture, as eye movement during procedure creates an unstable surgical environment.

There are three main difficulties that may present with posterior capsular rupture: difficulty with IOL fixation, anterior vitreous prolapse and loss of lens material into vitreous.[4] If vitreous comes forward anteriorly during the surgery, anterior vitrectomy is performed. Postoperatively, it is common to see white residue of intracameral steroid used to better visualize vitreous during the vitrectomy.[5] If there is any concern for lenticular material in the vitreous, retinal specialist should be involved as soon as possible to determine if additional surgery is needed. The longer the lens material remains in the vitreous, the higher the risk of posterior complications, such as cystoid macular edema.[6] If the IOL was placed properly, patients can still do well after vitrectomy and lens fragment removal.

If capsular integrity is compromised, placement of the IOL into the bag

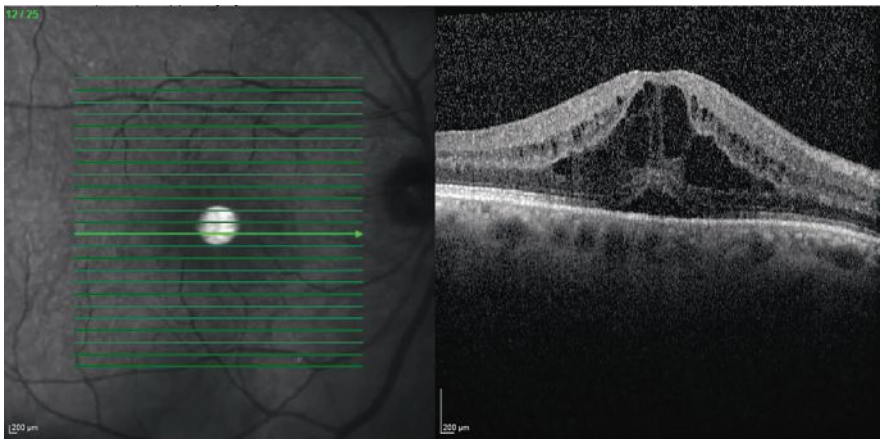
About the author **Dr. Sukhovolskiy** is a staff optometrist at Pacific Cataract and Laser Institute, practicing in Tacoma, WA. He has no financial disclosures.

may not be possible. The IOL can still be fixated using primary or reverse optic capture (IOL optic being secured on one side of the capsule and haptics on the opposite side), or by placing a three-piece IOL in the sulcus. If there is not enough remaining capsular support for these options, scleral fixation may be considered. Unfortunately, with posterior capsular compromise, placement of premium IOLs may not be possible. This can be very frustrating to patients who were planning on receiving either a toric or a presbyopia-correcting IOL, only to be told after the surgery that they received a spherical single-focus IOL due to an intraoperative complication. As always, it is better to discuss a possibility of such scenario prior to surgery to avoid greater patient dissatisfaction.

It is not uncommon to see various ***iris defects*** postoperatively. They may present at transillumination defects, iris atrophy and/or pigmentary dispersion. These can arise from iris prolapse that needed to be swept back in during the surgery or from use of mechanical iris dilation tools in cases when pharmacological pupil dilation was not adequate. History of alpha-1 blockers increases the risk of floppy iris syndrome.[7] Any patient known to take such medication would benefit from gentle hydrodissection and a more expert surgeon.

A rare, but visually threatening, surgical complication is ***suprachoroidal hemorrhage***. It is thought to result from reduced intraocular pressure (IOP) during surgery, resulting in choroidal effusion with subsequent choroidal or ciliary vessel rupture.[8] Though not always, suprachoroidal hemorrhage usually has an acute onset during the surgery. Anterior chamber shallowing, increased IOP, loss of red-light reflex and pain are common signs and symptoms of suprachoroidal hemorrhage.

Management of this condition involves immediate re-pressurization of the eye to increase IOP, even if the surgery is not complete.[9] Depending on the severity of the hemorrhage, the surgeon will determine further course of action.



Cystoid macular edema should always be ruled out if best-corrected vision postoperatively does not meet preoperative potential.

Postoperative Complications

Let's review the potential situations that could occur in your post-cataract patients.

Wound leaks. These present early in the postoperative period and are incredibly concerning.

Signs of a wound leak include shallow anterior chamber, low IOP and a positive Seidel sign.[10]

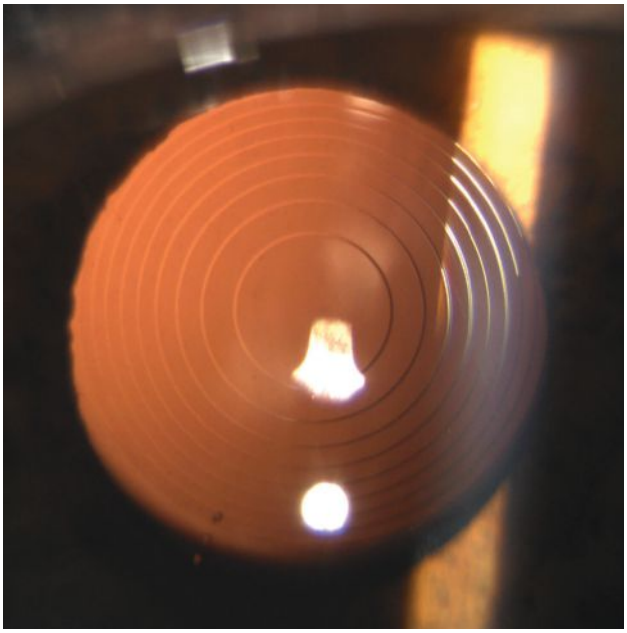
Slow wound leaks in eyes with relatively deep anterior chambers can be observed closely. Wound scarring usually seals the leak over a course of a few days. Scarring can be facilitated by stopping the use of anti-inflammatory medication (steroids), switching the patient to an antibiotic that is less friendly to the ocular surface and placing a bandage contact lens over the eye.[11] Aqueous suppressant eye drops may be used in conjunction.

If the intraocular pressure is very low, anterior chamber is shallow and/or the leak is more severe in scale, surgical intervention may be needed. Each surgeon may have their own process, but some common interventions range from "hydrating the wound" (creating artificial corneal edema around the incision to allow for better seal) or placing one or more sutures to hold the wound closed until the scarring occurs (some sutures would need to be removed a few weeks later).[12] Note that a tight suture may temporarily induce significant astigmatism, which resolves once the suture is removed.

Endophthalmitis. Inflammation of the aqueous and vitreous fluids due to an infection with bacteria or fungus after cataract surgery is a rare but severely sight-threatening complication.[13] Symptoms of endophthalmitis include pain, redness and gradual loss of vision. Signs include prolific white blood cell reaction in aqueous and vitreous, as well as severe conjunctival hyperemia.[14] Acute endophthalmitis presents within a few days to a few weeks after cataract surgery. Delayed-onset endophthalmitis can present over six weeks after surgery. Antimicrobial treatment needs to be started promptly. Cultures can aid diagnosis and choice of drug.

Residual refractive error. Technological advancements in the field of cataract surgery and the ability to achieve more and more precise refractive outcomes have brought with them the sky-high expectations from both patients and optometrists. It is important to understand that refractive surprises still occur about 12% to 15% of the time and are much more likely in patients with long or short axial lengths, previous corneal refractive surgery, irregular astigmatism (*e.g.*, from keratoconus, corneal scarring or anterior basement membrane dystrophy), mature cataracts or poorly managed ocular surface disease and long-term previous contact lens wear (especially rigid gas-permeable lenses).[15]

Much should be done to optimize these contributing factors prior to



Diffractive extended depth-of-focus IOLs are more likely to cause dysphotopsias than single focus IOLs.

surgery, but a perfect refractive outcome is never guaranteed. Despite knowing and understanding this truth, patients may be disappointed with their vision if their refractive target is not met. Thankfully, there are options to improve their visual outcome. IOL exchange and corneal refractive surgery such as LASIK or PRK can be performed in cases of significant residual refractive error. Procedure choice may depend on the amount of refractive surprise, corneal thickness, ocular surface health, type of IOL used and time elapsed since initial surgery, among other factors. A consultation with the surgeon is in order, though sometimes it may be prudent to wait a few weeks for refractive error to stabilize. Waiting too long is not ideal, as IOL exchange becomes significantly more difficult after three to six months due to capsular fibrosis.[16]

An unexpectedly significant amount of astigmatism after surgery could be a result of toric IOL rotation. Checking the toric IOL axis to make sure it matches the planned axis is recommended within one to two weeks after cataract surgery. If toric IOL rotation is suspected, the patient can be sent back to the surgeon for the IOL to be rotated to the intended axis. Rarely, unexpected postoperative increase in astigmatism can be surgically induced by the creation of a corneal incision and resolve on its own over the course of a few weeks.

IOL decentration. This can be a result of zonular weakness from previous trauma or pseudoexfoliation, or IOL implantation issues, such as capsular rupture or failure of haptic to be positioned properly in-the-bag.[17] A surgeon may choose to insert a capsular tension ring to compensate for the uneven force distribution among the zonules or address whatever other issue is causing the decentration.

Corneal edema. Cataract surgery is the most common cause of this condition. Corneal edema is associated with endothelial cell loss during phacoemulsification. Excess phacoemulsification power damages endothelial cells. Prolonged surgery may cause more stress to the cornea. Narrow anterior chamber and denser cataracts would increase the risk of corneal edema.

Viscoelastic substances may be used during the surgery to protect the endothelium, especially in eyes with preexisting endothelial damage or high risk of it during the surgery. Endothelial damage results in stromal edema, where most of the swelling occurs in the posterior cornea, often with resulting haze and endothelial folds. Another type of corneal edema, called microcystic edema, involves more anterior cornea. Microcystic edema is usually a result of elevated IOP. It is possible to see both types of edema in the same eye. Generally, corneal edema resolves over a few days. Rarely is it present a week after surgery. If stromal edema persists long-term (weeks or months), significant endothelial decompensation likely occurred. A consult with a corneal specialist should be considered.

Elevated IOP.[18] Causes of elevated postoperative IOP range from retained viscoelastic to steroid response to inflammation. It is important to identify the likely cause and select appropriate treatment. While retained viscoelastic is the most common cause of increased IOP at post-op day one, IOP that rises three to four weeks after surgery is likely due to steroid response.[19]

In most cases, a temporary addition of IOP-lowering medication is all that is needed to keep IOP under control. With inflammatory causes, increased anti-inflammatory treatment may be helpful. In cases where steroid response is suspected, reducing steroid administration frequency or switching to a milder steroid would be advised.

Cystoid macular edema (CME). The rate of this occurring following cataract surgery is under 2%.[20,21] Patients with diabetes or macular pathology (*e.g.*, epiretinal retinal membrane, previous macular edema) are more prone to CME development. Patients who develop CME are also more likely to be male, younger than age 65, Black, smokers and those with a history of uveitis.[22]

Treatment of CME may require a stepwise approach. First, steroid and NSAID drops (such as ketorolac or diclofenac) can be used. In a majority of cases without other comorbidities, this treatment is successful. Improvement and resolution of CME may take six to eight weeks. After the macula appears dry on OCT, medications can be tapered. Sub-tenon's Kenalog (triamcinolone, Bristol-Myers Squibb) or intravitreal steroid (Ozurdex; dexamethasone intravitreal implant, Allergan) can be considered if topical medications do not elicit a response.[23,24]

Retinal detachment. One of the more vision-threatening complications of cataract surgery is retinal detachment, occurring after around 0.5% of surgeries.[25] Younger age, male sex and longer axial length are significant risk factors. The increased risk of retinal detachment persists for up to 10 years after cataract

surgery.[26] Discussing this risk with patients is important, as is providing thorough education on symptoms of retinal detachment so that patients can seek care promptly.

Posterior capsular opacification (PCO). The diagnosis and management of PCO is rather straightforward. Nd:YAG laser capsulotomy can be performed, resulting in improvement with very little risk for the patient.[27,28] If there is any chance of IOL exchange being needed in the future, the posterior capsule should be preserved.

IOL exchange is significantly more difficult after YAG capsulotomy and IOL options may also be limited due to increased difficulty of securing a new lens in the eye without the support of the posterior capsule. This is especially important if patients have a refractive surprise or they are not fully satisfied with their presbyopia-correcting IOL. In those cases, consultation with the surgeon should take priority over the YAG procedure.

Dysphotopsias. Presence of these can be extremely bothersome to patients despite excellent visual outcome.[29] Dysphotopsias occur because of light reflecting off the IOL onto the retina in a way that results in patients seeing unwanted visual phenomena. Dysphotopsias can be positive or negative in presentation.

Positive dysphotopsias are often described as light arcs, flashes, starbursts, halos or a shimmer. The hypothesized mechanism of positive dysphotopsias is stray light reflected off the IOL and concentrated on a specific area of the retina.[30] Two factors associated with a higher risk of positive dysphotopsias are higher index of refraction of acrylic IOLs (the most commonly used IOL material currently), and the square IOL edge design of many modern IOLs (meant to reduce the rate of PCO formation).[31,32] Most post-surgical dysphotopsias improve on their own over several weeks due to the process of neuroadaptation. The only management for most of these patients involves education and encouragement. For more symptomatic cases, pharmacologic miotic therapy such as brimonidine 0.15% or pilocarpine 0.5% may help.

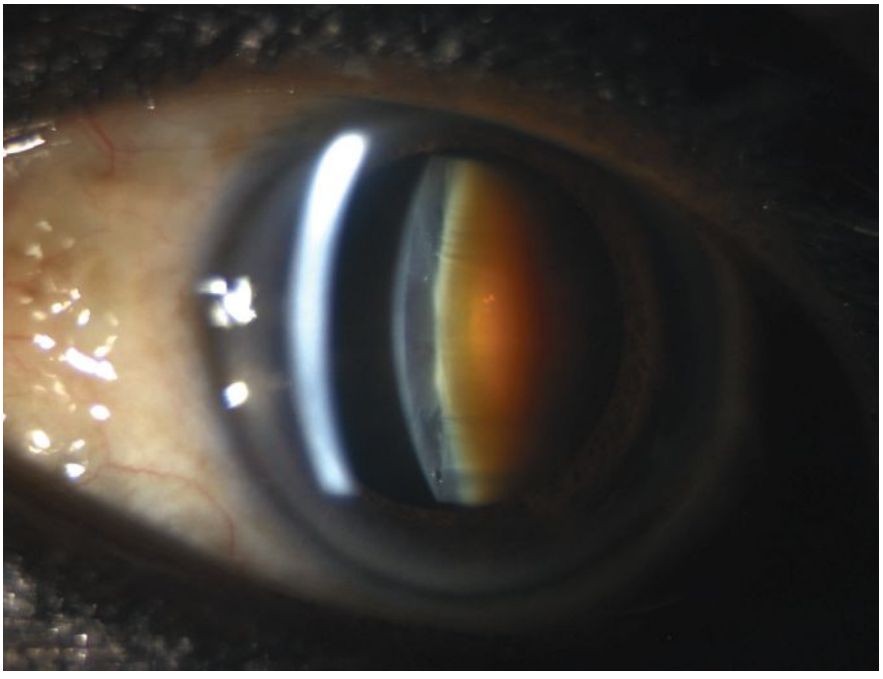
If positive dysphotopsias do not improve with time (three to six months) or miotic therapy, surgical consult should be considered. Surgical treatment typically involves exchanging an IOL for one with a lower index of refraction (silicone or polymethyl methacrylate material), rounder edges, or a larger effective optic.[33]

Negative dysphotopsias are typically described as a dark peripheral "arc" or "crescent." Some patients report a line or linear shadow, while others report a "strand of hair." It is mostly noticed in the temporal field of vision. Light interacting with the sharp edge of the IOL at a specific angle results in a shadow on the nasal retina, affecting temporal visual field.[34] The vast majority of symptomatic patients note significant improvement in symptoms or a complete resolution within three to six months. If negative dysphotopsias continue to be bothersome and show no signs of improvement, surgical intervention may be considered.

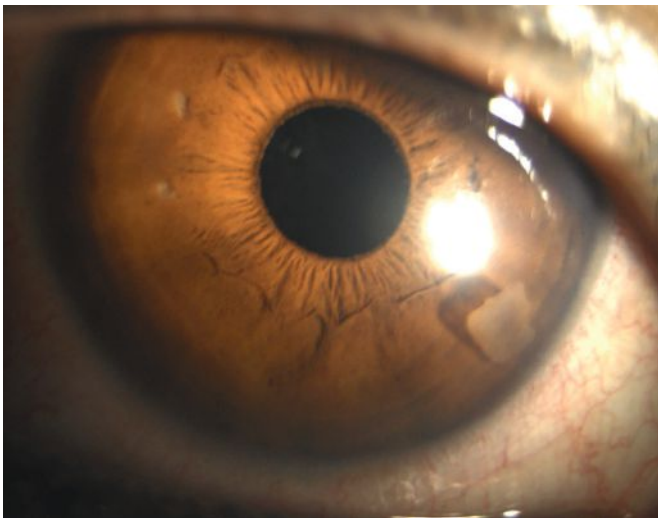
Reverse optic capture of current IOL (optic of the IOL is lifted above the capsulorhexis, while the haptics remain in the bag) or placement of a three-piece IOL in the sulcus are the most effective treatments options.[35] Both of these procedures result in a more anterior IOL position, thus changing the angle at which the light interacts with the IOL edge. It is important to warn the patient that changing the position of the IOL more anteriorly will also slightly change the refractive outcome.

Presbyopia-correcting IOLs. Patients who receive these IOLs may have higher expectations and lower tolerance for imperfections given the high additional cost and the "premium" product label. The most common cause of dissatisfaction in patients with multifocal implants is residual refractive error, followed by dry eye, glare and halos.[36] Quality of vision and severity of dysphotopsias is usually more favorable with extended depth-of-focus IOLs, but uncorrected near vision is better with multifocal IOLs. Myopic residual refractive error can be enhanced with corneal refractive surgery. Significantly hyperopic outcomes may benefit more from an IOL exchange.

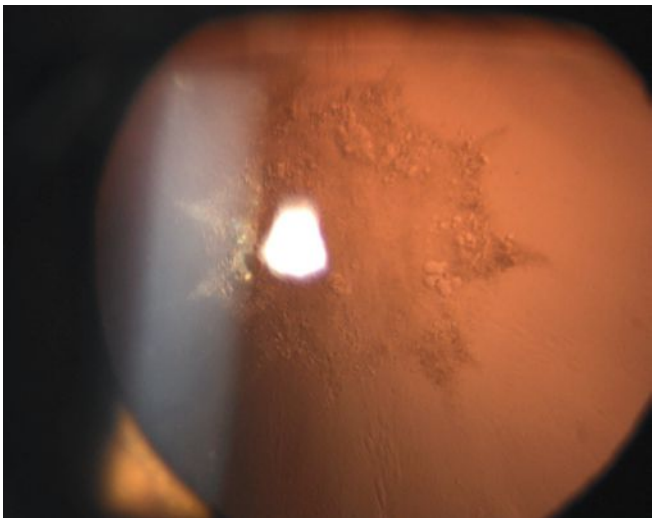
Despite an otherwise perfect result, some patients just do not tolerate the optics of presbyopia-correcting IOLs, reporting blurry vision and/or significant dysphotopsias. In the absence of



Patients with dense cataracts are at higher risk of posterior capsular rupture.



Small nuclear fragment in anterior chamber.



Posterior subcapsular cataracts increase the risk of PCO.

other significant issues, an exchange for a single-focus IOL should be considered. Waiting two to three months for neuroadaptation to occur is prudent, but waiting longer than six months will make an IOL exchange more difficult. Referral should be made back to the surgeon in that time frame.

Takeaways

Even though cataract surgery has been around for quite a while, it continues to evolve. While surgical complications are not desired, they happen. It is important for ODs to maintain clinical expertise, continue providing excellent perioperative care and work together with ophthalmologists to achieve great patient outcomes and satisfaction. ■

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ADVANCES IN REFRACTIVE SURGERY YOU MAY HAVE MISSED

Get familiar with these new and emerging procedures to better counsel patients desiring spectacle freedom.

BY BRADLEY DANIEL, OD
EDMOND, OK

Refractive surgery is a constantly evolving field, with new techniques and technologies emerging at a rapid pace. As primary eyecare providers, it's crucial to stay up to date with these advancements to provide the best possible care and guidance to our patients. In this article, I'll explore some of the latest developments in refractive surgery, from topography-guided LASIK to SMILE and more. Additionally, I'll offer a glimpse into the future of refractive surgery, highlighting the exciting advancements currently being developed.

Topography-Guided LASIK: Personalized Precision

Traditional LASIK surgery revolutionized vision correction by reshaping the cornea using excimer laser technology rather than a scalpel. However, it primarily focused on correcting the overall curvature of the anterior cornea, while leaving behind subtle imperfections on the corneal surface that are known to cause higher-order aberrations (HOAs). These aberrations could lead to visual disturbances like glare, halos or reduced contrast sensitivity, particularly in low-light conditions.

The advent of wavefront-guided LASIK marked a significant leap forward. By using advanced technology to create a detailed map of the eye's unique optical characteristics, surgeons can now tailor the laser treatment to address not only the major refractive errors but also pre-existing corneal irregularities that contribute to complex astigmatic patterns. This personalized approach led to improved visual outcomes, with many patients experiencing sharper vision and reduced night-vision disturbances.

Building upon this foundation, topography-guided LASIK represents the next frontier in LASIK technology. In addition to the wavefront data, this technique incorporates a high-resolution 3D mapping of the cornea's surface. This allows surgeons to identify and correct even more subtle irregularities on the corneal surface, even at the time of the surgery, further enhancing visual acuity (VA) and reducing the risk of postoperative visual complications.

Topography-guided LASIK differs from traditional and wavefront-guided LASIK in the following ways:

Customization. Traditional LASIK employs a standard ablation pattern based on the patient's refractive error. Conversely, topography-guided LASIK uses detailed corneal mapping to create a personalized ablation profile that addresses both lower-order aberrations and HOAs unique to each eye (*Figure 1*).[1] This 3D mapping of the corneal surface allows for precise measurement of the curvature, irregularities and other characteristics of the cornea. By analyzing this data, the surgeon can identify and address specific areas of irregularities on the corneal surface that may be affecting vision quality.[1]

Wavefront-guided LASIK uses a wavefront map that shows how light travels through the entire eye, including the cornea, lens and other structures. This map is like a detailed blueprint of the eye's optical system, revealing not only the shape of the cornea but also any irregularities or distortions in how light passes through the eye. It has been demonstrated that topography-guided LASIK resulted in a greater reduction of

About the author

Dr. Daniel specializes in ocular disease and refractive surgery at Edmond Regional Eye Associates in Edmond, OK, having received advanced clinical training in the diagnosis and management of ocular disease. He is also certified in laser vision correction, anterior segment laser procedures and other minor surgical procedures. Dr. Daniel is a fellow of the American Academy of Optometry, as well as a diplomate of the American Board of Optometry. He has no financial disclosures.

TABLE 1. FDA-APPROVED SYSTEMS FOR TOPOGRAPHY-GUIDED ABLATION[1]

System Name	Manufacturer	Topography System	Key Features
Contoura Vision	Alcon	Topolyzer Vario (Placido-based)	- Uses WaveLight EX500 excimer laser - Specific FDA algorithm for treatment planning - Combines topography and manifest refraction data - Iris registration/eye tracking called "cyclorotation" compensation
Navex (Advanced Vision Excimer Laser System)	NIDEK	OPD-Scan III (Placido-based with wavefront aberrometry)	- Combines topography-guided and wavefront-guided treatments - Allows for customized ablation profiles
iDesign Refractive Studio	Johnson & Johnson Vision	Integrated system (Hartmann-Shack wavefront sensor with corneal topographer)	- Primarily known for wavefront-guided treatments - Offers topography-guided capabilities - High-resolution aberrometry
Amaris	Schwind	Keratron Scout (Placido-based)	- Offers both topography-guided and wavefront-guided treatments - Features fast ablation speeds - Includes eye-tracking technology
Mel 90	Zeiss	Atlas 9000 (Placido-based)	- Provides topography-guided treatment options - Features CRS-Master software for treatment planning - Includes eye-tracking capabilities

HOAs compared to wavefront-guided LASIK.[2]

Precision. The ability to analyze the fine intricacies of the corneal surface at both a quantitative and qualitative level has ushered in a new era for topo-guided LASIK. This advancement allows for enhanced accuracy in reshaping the cornea by precisely pinpointing areas of irregularity.[1] It translates to improved visual outcomes, particularly in low-light settings where glare and halos are minimized.[2-6] Research has also shown that topo-guided LASIK results in superior contrast sensitivity and reduced night vision symptoms compared to wavefront-optimized LASIK.[3] The personalized approach of topo-guided LASIK minimizes risk of overcorrection or undercorrection, promoting better long-term stability and reducing the need for enhancement procedures.[4] Due to its ability to address subtle corneal irregularities more effectively, topo-guided LASIK typically results in fewer retreatments than wavefront-optimized LASIK.[4]

Vision outcomes. Especially for patients with significant HOAs, topo-guided LASIK offers several potential benefits in terms of vision:

• *Improved VA:* Topography-guided LASIK can help patients achieve sharper vision and enhanced contrast sensitivity, particularly those with HOAs that affect visual quality beyond lower-order aberrations such as nearsightedness or farsightedness.[3]

• *Reduced glare and halos:* Topography-guided LASIK demonstrates superior night vision outcomes compared to wavefront-guided procedures, primarily due to its more conservative tissue ablation approach. By removing less stromal tissue and maintaining more of the cornea's natural shape, this technique minimizes induced HOAs that typically cause night vision disturbances.[4]

• *Enhanced visual quality:* Patients often report a subjective improvement in overall visual quality after topography-guided LASIK, including reduced eye strain, clearer night vision and richer color perception.[5]

• *Undercorrection/overcorrection:* Topo-guided LASIK can help minimize the risk of undercorrection or overcorrection, which can occur when the ablation pattern is not perfectly aligned with the cornea's irregularities. This can result in better long-term visual outcomes and reduce the need for additional procedures.[4]

One thing topography-guided and wavefront-guided LASIK have in common is their excellent safety profiles. Both techniques present minimal risk of significant complications, and studies have shown no significant difference in the incidence of major adverse events or vision-threatening complications between the two.[5] Both procedures also have minor side effects, resulting in dry eye or temporary visual disturbances that typically resolve within a few weeks postoperatively.[5]

Requirements for Topo-Guided Ablation

These systems approved by the FDA typically have specific criteria required to ensure optimal treatment outcomes (*Table 1*).[6] While exact parameters may vary between laser platforms, the general principles remain consistent across systems. These criteria often include:

Astigmatism axis alignment: For patients with higher degrees of astigmatism (typically ≥2.00D), the difference in the astigmatic axis between manifest refraction and topographic data should be minimal, often not exceeding 5° to 10°.

Lower astigmatism considerations: In these cases (generally <2.00D astigmatism), a slightly larger discrepancy between manifest and topographic astigmatic axes may be acceptable, often up to 10° to 15°.

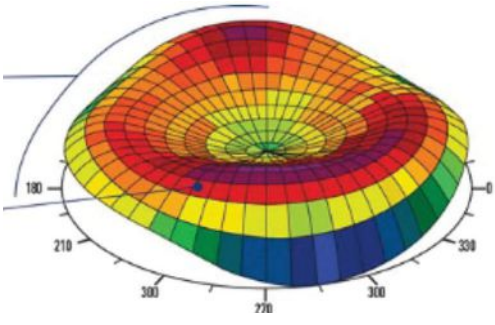

Photo: Alcon

Fig. 1. Contoura Vision's advanced corneal mapping technology captures 22,000 unique elevation points per eye, creating detailed 3D topographic maps for customized LASIK treatments.

Astigmatic power consistency: The difference in astigmatic power between manifest refraction and topographic data should be relatively small, typically not exceeding 0.75D to 1.00D.

In essence, topography-guided LASIK has evolved beyond simply reshaping the cornea; it now also refines its surface texture. This meticulous customization often results in a more natural visual experience, with many patients reporting vision surpassing what they achieved with glasses or contact lenses.[1]

The evolution of LASIK from traditional to wavefront-guided and now topography-guided demonstrates the ongoing pursuit of precision and personalization in vision correction. As technology continues to advance, we can anticipate even more refined techniques that will further improve visual outcomes and expand the possibilities for patients seeking optimal vision.

SMILE: Minimally Invasive Vision Correction

Small incision lenticule extraction (SMILE) is the newest FDA-approved refractive laser surgery for common refractive errors (*Figures 2* and *3*).[7] At present, candidacy for SMILE requires patients to have myopia within the range of -1.00D to -10.00D. The procedure can also treat astigmatism up to -3.00D within the FDA-approved parameters.[8] This procedure has many key differences that make it unique. It is a completely different way of performing refractive surgery than the current methods. Only one laser is used during the entire process, unlike the various forms of LASIK.[9]

During the SMILE procedure, a femtosecond laser (VisuMax, Carl Zeiss Meditec) is used to create a small, arc-shaped incision on the corneal surface. The same laser then creates a thin disc of corneal tissue, called a lenticule, within the cornea stroma. The surgeon then carefully removes the lenticule through the small incision, reshaping the cornea and correcting the refractive error.

Because the incision made in SMILE is significantly smaller than the flap created in LASIK, there are many benefits, including better corneal biomechanics. However, potential drawbacks include a higher cost compared to LASIK, a narrower range of treatable refractive errors, a slightly longer recovery time, an increased risk of night aberrations and more limited enhancement options.[9]

SMILE has become an established form of refractive surgery as of late in the US and has been for even longer worldwide. Boasting excellent visual outcomes with a good safety profile, this procedure is a viable treatment option for myopia and myopic astigmatism in the absence of any corneal surface disorder.

Let's review some of the unique features of SMILE:

Minimally invasive. SMILE involves a much smaller incision than LASIK, reducing the risk of complications and potentially improving healing time. Initially, the lenticule was extracted by lifting an epithelial flap similar to LASIK, then evolved to a single clear peripheral 2mm corneal incision.[8]

Intrastromal. SMILE's intrastromal approach, where the lenticule is created and extracted within the cornea, preserves the integrity of the anterior stroma, the cornea's strongest layer. With a cap thickness fixed at 120µm, SMILE maintains most of the biomechanically important anterior stromal tissue. Research shows the posterior 60% of the stroma is 50% weaker than the anterior 40% of the corneal stroma.[7,11] This translates to enhanced biomechanical stability, potentially reducing the risk of post-surgical ectasia and promoting faster visual recovery.[12] Furthermore, by sparing the anterior stroma, SMILE minimizes the chance of damaging corneal nerve fibers believed to be associated with postoperative dry eye.[10,13]

All-in-one. SMILE offers a significant advantage in surgical efficiency by using a single femtosecond laser for both the incision and lenticule creation. This streamlined approach eliminates the need for an excimer laser, effectively optimizing operating room space and resource allocation.[9]

The Future of SMILE

Recent research suggests promising developments in SMILE technology, with ongoing studies exploring its potential applications beyond current indications. While the procedure has shown encouraging results for treating hyperopia in early studies, its expansion into broader refrac-

Photo: Carl Zeiss Meditec

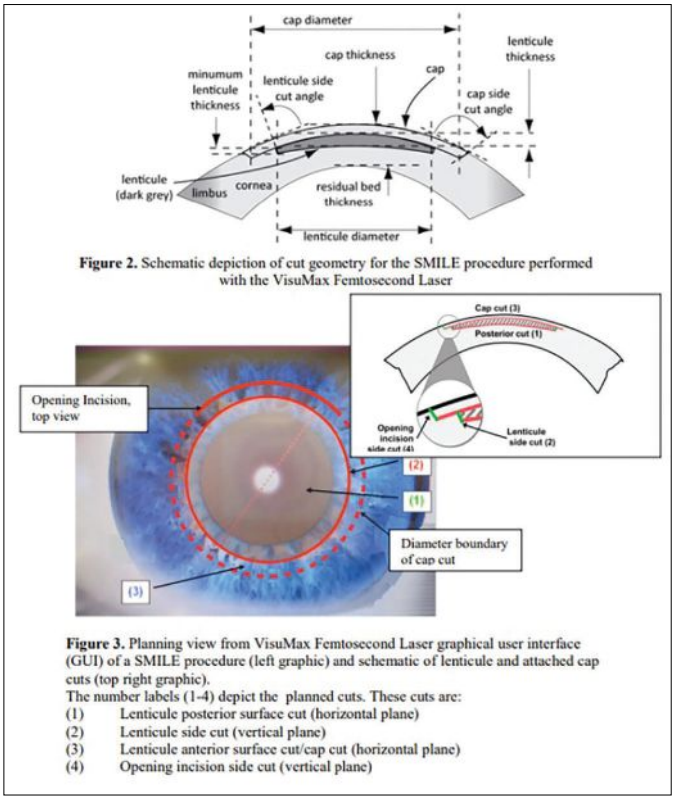

Figure 2. Schematic depiction of cut geometry for the SMILE procedure performed with the VisuMax Femtosecond Laser

Figure 3. Planning view from VisuMax Femtosecond Laser graphical user interface (GUI) of a SMILE procedure (left graphic) and schematic of lenticule and attached cap cuts (top right graphic).
The number labels (1-4) depict the planned cuts. These cuts are:
(1) Lenticule posterior surface cut (horizontal plane)
(2) Lenticule side cut (vertical plane)
(3) Lenticule anterior surface cut/cap cut (horizontal plane)
(4) Opening incision side cut (vertical plane)

Figs. 2 and 3. These images illustrate the key components of the SMILE procedure; the top diagram shows the schematic cross-section of cut geometry, detailing the lenticule dimensions and corneal parameters. The lower image displays the VisuMax Femtosecond Laser graphical user interface during surgery, showing the planned circular incision pattern and the four sequential laser cuts required to create and extract the lenticule.

tive corrections awaits further clinical validation and regulatory approval. The emergence of new variants demonstrates the continued evolution of this technology, pointing to future refinements in refractive surgery techniques.

While SMILE may offer a safe treatment option for a broader range of hyperopia compared to LASIK, it is important to note that it currently lacks FDA approval for this specific indication. Due to its relative novelty, long-term studies are scarce. However, a promising prospective study involving 93 eyes treated with SMILE for hyperopia demonstrated encouraging results, with 95% achieving uncorrected VA of 20/40 or better and maintaining good corneal stability after 12 months.[14] These results suggest that SMILE could be a viable treatment for hyperopia in the future, pending further research and regulatory approval. In Europe, SMILE is currently being performed on up to +6.00D of hyperopia and 5.00D of cylinder.[7]

A new SMILE variant, SILK (smooth incision lenticule keratomileusis, uses a different femtosecond laser that creates a smaller lenticule.[15] While not yet FDA-approved, SILK offers promising advancements as a future modification of the SMILE procedure.

The core of SILK is the Elita femtosecond laser (Johnson & Johnson Vision), operating at an unprecedented 10MHz level compared to the kilohertz levels of existing systems. This high-speed operation combined with low-energy settings (<50nJ) results in exceptionally smooth lenticule creation. Key features include real-time adjustment for pupil centration, cyclotorsion control and overlapping spots for nearly dissection-free lenticule removal.

The Elita laser's capacity for real-time adjustments based on pupil centration and cyclo-rotation is particularly noteworthy. This could enhance refractive outcomes and streamline lenticule removal, potentially leading to more predictable results and shorter surgical times.

As SILK progresses through clinical trials and regulatory approval processes, its role in refractive surgery practices remains to be determined. Rigorous clinical studies will be crucial to fully understand its long-term efficacy, safety profile and potential advantages over established refractive procedures.

PRK: The Comeback Kid

Photorefractive keratectomy (PRK), once overshadowed by LASIK, is experiencing a resurgence in popularity. This renaissance is driven by several factors, including improved surgical techniques, advanced laser technology and a growing recognition of its benefits for certain patients. Below, we will highlight some of these recent innovations and the advantages of PRK.

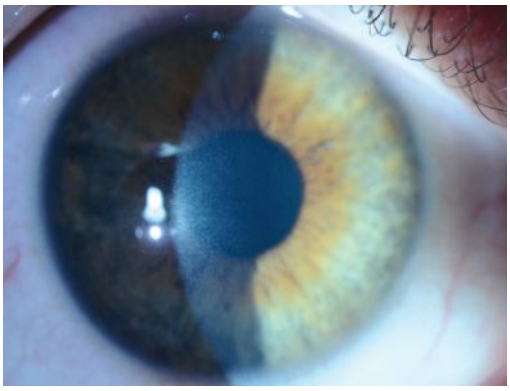

Photo: Christopher J. Rapuano, MD

Fig. 4. Many of the newer PRK techniques reduce risk of postoperative corneal haze formation.

Transepithelial PRK (T-PRK). Traditional PRK, while effective, involves the burden of requiring manual or alcohol-assisted removal of the corneal epithelium before laser ablation. This step, though necessary, could lead to potential complications and discomfort. Alternatively, T-PRK has revolutionized this process by using the excimer laser to precisely ablate the epithelium, making the procedure less invasive and potentially more comfortable for patients.

Some advantages of T-PRK include:

• *Reduced complication risk:* Eliminating manual or chemical epithelial removal minimizes the risk of infection, corneal haze (scarring), postoperative discomfort, dry eye and other complications associated with traditional/alcohol-assisted PRK (*Figure 4*).[16]

• *More uniform ablation surface:* The laser creates a smoother, more uniform ablation surface, which can lead to better visual outcomes and reduced risk of irregular astigmatism.[17]

• *Potentially faster visual recovery:* Due to much less re-epithelialization required from T-PRK, patients often return to normal activities sooner and have better VA in the early postoperative period compared to traditional PRK.[16,17]

Topography-guided PRK. This represents a significant advancement in bringing customizable refractive surgery to a broader patient population. This variant of PRK has emerged as a significant refinement in corneal refractive procedures, offering enhanced precision in treating both regular ametropia and irregular astigmatism. Modern excimer laser platforms have evolved to support this advancement, featuring sophisticated eye-tracking systems that compensate for involuntary eye movements and ensure precise ablation delivery.

This technique uses high-resolution corneal topography data to generate a customized ablation profile, effectively addressing not only refractive errors but also corneal surface irregularities that may be undetectable or untreatable with traditional wavefront-guided or wavefront-optimized approaches. Enhanced ablation speeds in contemporary laser systems reduce corneal exposure time, potentially contributing to more predictable outcomes and faster healing.

The fundamental principle underlying topography-guided treatments is the integration of anterior corneal surface data with refractive error measurements to create a more comprehensive treatment plan. By combining wavefront- and topography-guided approaches, surgeons can develop personalized ablation profiles based on each patient's unique corneal characteristics. This integrated approach allows for simultaneous correction of lower-order aberrations and regularization of the corneal surface, potentially mitigating HOAs associated with corneal irregularities.

Other prospects for PRK include:

Expanded candidacy. Due to its ability to treat a wider range of refractive errors and corneal conditions, PRK remains an attractive option for patients who are

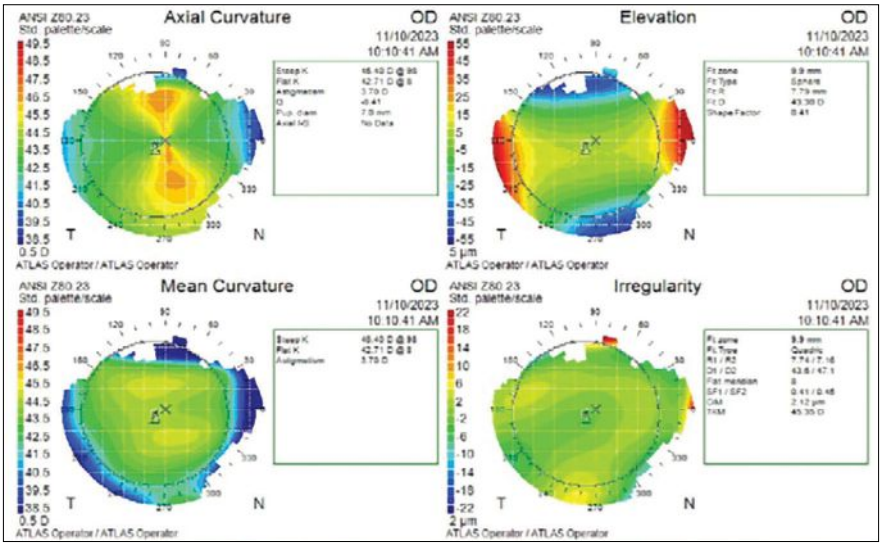

Fig. 5. Preoperative corneal topography of the right eye was obtained prior to PRK. The left eye (not pictured) won't be operated on, as its inherent manifest refraction of -1.50D provides good near vision. To ensure patient adaptation to monovision, a contact lens trial was conducted before surgery simulating the anticipated post-op refractive outcome.

not suitable candidates for LASIK or other corneal refractive procedures. One example is patients with thinner corneas: by avoiding the creation of a corneal flap, PRK preserves more corneal tissue, making it a safer option for these individuals.

The long-term efficacy and safety of PRK in patients with thin corneas have been investigated with promising results. One study found PRK to be safe and effective in patients with corneas thinner than 500µm, noting stable refractive outcomes and no cases of ectasia over a 10-year follow-up period.[18]

PRK may also offer advantages for patients with pre-existing dry eye syndrome or those at higher risk of developing dry eye after refractive surgery. The procedure preserves more corneal nerves than LASIK, potentially resulting in less severe and shorter-duration dry eye symptoms postoperatively.

Research from 2015 comparing dry eye symptoms and tear film parameters after PRK and LASIK found that while both procedures induced dry eye symptoms initially, the PRK group showed faster recovery and better tear film stability at six months post-op.[19]

Reduced risk of flap-related complications. By eliminating the need for a corneal flap, PRK avoids potential flap-related complications associated with LASIK, such as flap dislocation, striae or epithelial ingrowth. This makes PRK an attractive option for patients with active lifestyles or those in professions with a higher risk of eye trauma.

Treatment of irregular astigmatism. PRK, especially when combined with topography-guided treatments, has shown significant efficacy in managing irregular astigmatism, a condition that can be challenging to treat with traditional refractive surgery techniques.

• *Post-trauma or post-surgical irregularities:* A 2020 study on the use of topography-guided PRK for treating irregular astigmatism following radial keratotomy demonstrated significant improvements in both uncorrected and corrected VA, as well as reductions in HOAs.[20]

• *Keratoconus:* In mild to moderate cases, topo-guided PRK combined with corneal crosslinking (the "Athens Protocol") has shown promising results in keratoconus (more on this later). One study reported long-term stability and improved visual outcomes in keratoconic eyes treated with this approach.[21]

• *Decentered ablations:* For patients with decentered ablations from previous refractive surgeries, topography-guided PRK can help regularize the corneal surface. One study from 2018 demonstrated the efficacy of this approach in treating highly aberrated eyes with significant visual symptoms.[22]

Expanded range for hyperopia treatment. While PRK has traditionally been associated with myopic corrections, advancements in laser technology and treatment protocols have expanded its application to hyperopic treatments.

• *Higher hyperopic corrections:* Modern PRK techniques can effectively treat higher degrees of hyperopia compared to earlier iterations. Research from 2020 that evaluated outcomes of PRK for hyperopia up to +6.00D reported safe and effective results with good long-term stability.[23]

• *Hyperopic astigmatism:* PRK has shown efficacy in treating compound hyperopic astigmatism. A study reporting on the long-term outcomes of PRK for compound hyperopic astigmatism demonstrated stable refractive results and high patient satisfaction over a 10-year follow-up period.[24]

• *Presbyopic hyperopes:* For presbyopic patients with hyperopia, PRK can be combined with monovision or blended vision techniques. Recent research exploring the outcomes of hyperopic PRK with monovision reported high levels of spectacle independence and patient satisfaction.[25]

These expanded applications underscore PRK's versatility in modern refractive surgery. By offering effective treatment options for irregular astigmatism and a wider range of hyperopic corrections, PRK continues to play a crucial role in addressing complex refractive cases and providing tailored solutions for patients who may not be candidates for other procedures.

PRK vs. LASIK: Long-term Outcomes

Multiple studies have shown that the long-term outcomes of PRK are comparable to LASIK in terms of VA, refractive stability and patient satisfaction. A nine-year follow-up study from 2015 comparing long-term outcomes of LASIK and PRK for myopia found no significant difference in any of those three parameters between the two procedures.[26] Another study from the same

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LIGHT ADJUSTABLE LENS INDICATIONS FOR USE AND IMPORTANT SAFETY INFORMATION

INDICATIONS: The Light Adjustable Lens™ (LAL™) and Light Delivery Device™ (LDD™) system is indicated for the reduction of residual astigmatism to improve uncorrected visual acuity after removal of the cataractous natural lens by phacoemulsification and implantation of the intraocular lens in the capsular bag in adult patients with preexisting corneal astigmatism of ≥ 0.75 diopters and without preexisting macular disease. The system also reduces the likelihood of clinically significant residual spherical refractive errors.

CONTRAINDICATIONS: The Light Adjustable Lens is contraindicated in patients who are taking systemic medication that may increase sensitivity to ultraviolet (UV) light as the LDD treatment may lead to irreversible phototoxic damage to the eye; patients who are taking a systemic medication that is considered toxic to the retina (e.g., tamoxifen) as they may be at increased risk of retinal damage during LDD treatment; patients with a history of ocular herpes simplex virus due to the potential for reactivation from exposure to UV light; patients with nystagmus as they may not be able to maintain steady fixation during LDD treatment; and patients who are unwilling to comply with the postoperative regimen for adjustment and lock-in treatments and wearing of UV protective eyewear.

WARNINGS: Careful preoperative evaluation and sound clinical judgment should be used by the surgeon to decide the risk/benefit ratio before implanting an IOL in a patient with any of the conditions described in the Light Adjustable Lens and LDD Professional Use Information document. Caution should be used in patients with eyes unable to dilate to a pupil diameter of ≥ 7 mm to ensure that the edge of the Light Adjustable Lens can be visualized during LDD light treatments; patients who the doctor believes will be unable to maintain steady fixation that is necessary for centration of the LDD light treatment; patients with sufficiently dense cataracts that preclude examination of the macula as patients with preexisting macular disease may be at increased risk for macular disease progression; and patients at high risk for future vitreoretinal disease that may require silicone oil as part of therapy. The Light Adjustable Lens must be implanted in the correct orientation with the back layer facing posteriorly.

PRECAUTIONS: The long-term effect on vision due to exposure to UV light that causes erythropsia (after LDD treatment) has not been determined. The implanted Light Adjustable Lens MUST undergo a minimum of 2 LDD treatments (1 adjustment procedure plus 1 lock-in treatment) beginning at least 17-21 days post-implantation. All clinical study outcomes were obtained using LDD power adjustments targeted to emmetropia post LDD treatments. The safety and performance of targeting to myopic or hyperopic outcomes have not been evaluated. The safety and effectiveness of the Light Adjustable Lens and LDD have not been substantiated in patients with preexisting ocular conditions and intraoperative complications. Patients must be instructed to wear the RxSight-specified UV protective eyewear during all waking hours after Light Adjustable Lens implantation until 24 hours post final lock-in treatment. Unprotected exposure to UV light during this period can result in unpredictable changes to the Light Adjustable Lens, causing aberrated optics and blurred vision, which might necessitate explantation of the Light Adjustable Lens.

ADVERSE EVENTS: The most common adverse events (AEs) reported in the randomized pivotal trial included cystoid macular edema (3 eyes, 0.7%), hypopyon (1 eye, 0.2%), and endophthalmitis (1 eye, 0.2%). The rates of AEs did not exceed the rates in the ISO historical control except for the category of secondary surgical interventions (SSI); 1.7% of eyes (7/410) in the Light Adjustable Lens group had an SSI ($p < .05$). AEs related to the UV light from the LDD include phototoxic retinal damage causing temporary loss of best spectacle corrected visual acuity (1 eye, 0.2%), persistent induced tritan color vision anomaly (2 eyes, 0.5%), persistent induced erythropsia (1 eye, 0.3%), reactivation of ocular herpes simplex Infection (1 eye, 0.3%), and persistent unanticipated significant increase in manifest refraction error (≥ 1.0 D cylinder or MRSE) (5 eyes, 1.3%).

CAUTION: Federal law restricts this device to sale by or on the order of a physician.

Please see the Professional Use Information document for a complete list of contraindications, warnings, precautions, and adverse events.

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year examined the 20-year outcomes of PRK for myopia, reporting excellent long-term safety and efficacy, with stable refractive results and no significant long-term complications.[27]

Emerging Trends and Future Directions

As PRK continues to demonstrate excellent long-term outcomes comparable to LASIK, researchers and clinicians are exploring refinements and combinations to further enhance its safety and efficacy. Recent developments focus on optimizing treatment protocols, particularly through the integration of complementary therapies and techniques to address specific clinical challenges and expand treatment options for complex cases. Here are a few examples:

Combination therapies. The integration of PRK with complementary procedures has opened new avenues for treating complex corneal conditions and enhancing refractive outcomes. These combination approaches combine the strengths of multiple modalities to address a broader range of visual and structural corneal issues.

PRK with corneal crosslinking (CXL). The combination of PRK and CXL, often referred to as the "Athens Protocol" when performed simultaneously, has shown promising results in managing keratoconus and other corneal ectatic disorders.[28-30]

• *Forme fruste keratoconus:* The combination of PRK with accelerated CXL for patients with forme fruste keratoconus was recently demonstrated to improve visual outcomes and corneal stability compared to PRK alone.[30]

• *Progressive keratoconus:* A long-term study that evaluated the 10-year outcomes of topography-guided PRK combined with CXL for keratoconus reported stable visual and refractive outcomes, demonstrating the technique's potential for managing progressive corneal ectasia.[28,31]

• *Post-LASIK ectasia:* Studies investigating the effectiveness of combined PRK with CXL in treating post-LASIK ectasia show significant improvements in corneal stability and visual outcomes. This approach has shown promise in halting ectasia progression while providing visual rehabilitation for patients with this challenging complication.[32]

PRK with phototherapeutic keratectomy (PTK). The combination of PRK and PTK has shown efficacy in treating corneal surface irregularities alongside refractive errors. This approach was recently evaluated in patients with corneal scarring and concurrent refractive errors, who showed significant improvements in both VA and corneal clarity.[22]

Emerging combination approaches. Several novel combination therapies involving PRK are currently under investigation:

• *PRK with accelerated epithelial healing:* In 2022, researchers began exploring the use of insulin-like growth factor-1 eye drops following PRK to accelerate epithelial healing and reduce postoperative discomfort.[33]

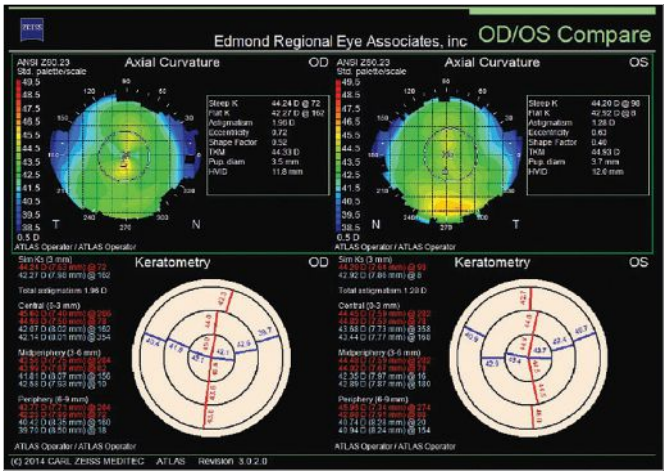

Fig. 6. Preoperative topographies OU before topography-guided PRK with a target of plano sphere OU.

• *PRK with autologous platelet-rich plasma:* Early studies have shown potential benefits of using platelet-rich plasma in conjunction with PRK to enhance corneal wound healing and reduce haze.[34]

These combination therapies represent the cutting edge of refractive surgery, offering tailored approaches for complex cases that may not be suitable for standard procedures. As research progresses, we can expect further refinement of these techniques and the emergence of new combination approaches to address the diverse needs of our patients, potentially improving both visual and structural outcomes.

Takeaways

Refractive surgery is evolving at a remarkable pace, driven by groundbreaking research and technological innovations that could transform the lives of countless individuals by offering them the opportunity to achieve clear, spectacle-free vision and enhance their overall quality of life. Optometrists occupy a unique position at the forefront of patient care. Staying current on the latest refractive surgery techniques and technologies allows clinicians to guide patients toward the most appropriate and effective treatment options. As primary eyecare providers, it is our responsibility to educate patients about the risks and benefits of various procedures, ensuring they make informed decisions based on their needs and visual goals.

Furthermore, collaborating with refractive surgeons fosters a seamless continuum of care, enabling optometrists to provide comprehensive support throughout the patient journey. From pre-op evaluations and patient selection to post-op management and long-term follow-up, ODs play an integral role in optimizing patient outcomes and ensuring their visual well-being.

The future of refractive surgery is undoubtedly bright, with promising new technologies on the horizon. Optometry's practice scope is expanding in a growing number of states, which may even include performing certain refractive surgery procedures. By embracing these advancements, ODs can empower patients to achieve their vision goals and enjoy the freedom of clear and comfortable vision. ■

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STAY LASER FOCUSED ON THE LONG-TERM COURSE

Knowing why SLT, LPI and YAG capsulotomy help your patients beyond the typical postoperative period is just as important as how to perform them successfully.

BY SPENCER JOHNSON, OD, AND DARIN CUMMINGS, OD
PROVO, UT; EPHRAIM, UT

As the scope of optometric practice has expanded, much education and training has been dedicated to the skills necessary to perform these advanced procedures. As important as the how-to is in successfully managing a patient's condition, however, a thorough understanding of when (and when not) to consider a procedure can't be overstated. A laser procedure is a significant event for the patient and, as optometry's involvement grows, we must strive to see it in the context of their long-term care.

Here, we will address indications and contraindications for the three most commonly performed laser procedures: selective laser trabeculoplasty (SLT), laser peripheral iridotomy (LPI) and YAG capsulotomy. This information is pertinent for both optometrists who comanage these procedures as well as the ones who are performing them.

SLT

This in-office medical procedure is employed to help lower the intraocular pressure (IOP). Although it is not fully understood, the theory behind SLT is that one of two things happen:

(1) SLT targets the pigmented chromophores in the trabecular meshwork. The laser emits small bursts of energy that stimulate the contraction of the cells, allowing the aqueous to drain more effectively and ultimately reducing IOP.

(2) SLT causes a biological response in which the macrophages clean out the collector channels, allowing for much easier outflow of aqueous. Due to the very low energy levels used, there is little to no permanent, visible change to the tissue, and thus SLT can be repeated multiple times. Many eyecare professionals now use SLT as a first-line therapy for treating glaucoma, choosing it over traditional pharmacological treatment with IOP-lowering medications, given new research implying more favorable long-term glaucoma outcomes with SLT.[1]

Indications

Consider SLT in the following patients:

- As a primary treatment for patients with open-angle glaucoma (OAG), pseudoexfoliative (PE) or pigmentary glaucoma (PG).
- OAG/PE/PG patients not properly controlled by medical therapy.
- OAG/PE/PG patients that have shown poor compliance to medical treatment.
- OAG/PE/PG patients with allergic reactions and/or poor tolerance to topical medications.
- OAG/PE/PG patients in whom IOP remains above target and/or their disease is progressing.
- Low-tension glaucoma.
- Ocular hypertension.
- For newly diagnosed patients with OAG/PE/PG, this can be offered as a first-line defense instead of using topical therapy.

About the authors

Dr. Johnson is currently a professor at Rocky Mountain University College of Optometry and senior director of The RMU Eye Institute. Dr. Johnson's clinic interests include ocular disease, lasers, contact lenses and advanced optometric procedures. Previously, he was a faculty member at the Oklahoma College of Optometry where he taught courses in neuro-ophthalmic disorders, healthcare systems and epidemiology, as well as trained students in the clinic on lasers and advanced optometric procedures. Prior to his career in academia, Dr. Johnson worked in the refractive surgery industry and owned a private practice. **Dr. Cummings** is founder and owner of the Eye Center of Ephraim in Ephraim, UT, and is also a faculty member and teaches at Rocky Mountain University School of Optometry. His clinical experience includes ocular disease, particularly diabetes, glaucoma, keratoconus, macular degeneration and cataracts. Dr. Cummings is a member of both the Utah and American Optometric Associations and is actively involved in bringing eye care to underserved countries such as the Dominican Republic and Mali, Africa.

Contraindications

SLT is not generally recommended for patients with these types of glaucoma:

- inflammatory
- neovascular
- traumatic
- congenital
- angle-closure glaucoma
- advanced glaucoma

The procedure is also not recommended for glaucoma patients in whom there is poor visualization of the trabecular meshwork secondary to anatomic angle status and/or corneal opacity. Also, do not consider this for patients who cannot sit still or hold their head in position in the slit lamp for the procedure.

If at any time there is a concern that performing SLT would be risking the patients overall health of the eye, then the procedure should not be performed. Careful screening and consideration of the patient's health and ability to keep their head still is recommended.

What glaucoma specialists would like us to know about SLT complications

- Occasionally, there may be some mild soreness, redness or blurred vision in the immediate postoperative period. This may be caused by the SLT gonio lens, its coupling fluid, induced iritis and/or an IOP spike, and may be prophylactically or secondarily treated with a topical nonsteroidal anti-inflammatory or a topical corticosteroid several times per day for two to seven days post-procedure.[2]
- A short-term IOP spike after SLT is not uncommon, is usually temporary and may be prophylactically and/or secondarily treated with a topical α agonist (either apraclonidine 0.5% or brimonidine 0.2%).
- Much less common with SLT vs. its predecessor argon laser trabeculoplasty, the incidence of peripheral anterior synechiae is very low (0% to 2.86%), but has been reported to occur in some patients after multiple SLT treatments.[3]
- Corneal edema is also possible post-SLT, with several potential etiologies to consider:

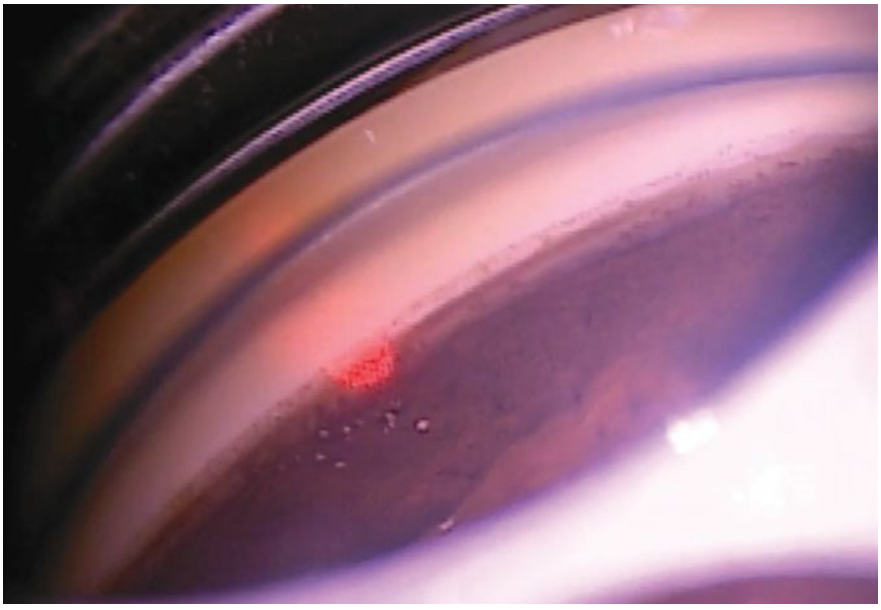


Photo: Nate Lighthizer, OD, and Komal Patel, OD

360° SLT is largely the standard for POAG, ocular hypertension and low-tension glaucoma.

– Excessive digital pressure applied to the cornea from the gonio lens used in the procedure.

– HSV reactivation. While rare, the proinflammatory cascade following SLT may reactivate the virus in some patients, in which case treatment is with the usual topical and/or oral antiviral medications.[4]

Hyphema is an exceedingly rare finding with SLT but, if noted, treatment protocols are consistent with other hyphema etiologies, including topical medications and keeping the head elevated until the blood resolves from within the anterior chamber.

Post-op and Follow-up Care

The IOP should be checked approximately 30 to 60 minutes post-procedure to monitor for an IOP spike, and if present, ocular hypotensive medications may be prescribed. The patient is then examined again in two to six weeks.[5] Depending on the IOP response, the fellow eye may be scheduled for SLT and/or normal glaucoma follow up protocols can then be resumed.

Coming soon in the US is direct SLT (Alcon). This device uses eye-tracking technology to ensure an accurate, automated treatment delivery through the limbus—eliminating the need for a gonio lens or manual aiming.[6]

LPI

This surgical procedure creates a small, full-thickness opening through the iris and is usually performed superiorly, between 11 o'clock and one o'clock, allowing for the upper lid to cover the opening in order to potentially reduce visual dysphotopsias, which may occur. Some studies have advocated for a three o'clock or nine o'clock LPI location to minimize dysphotopsias created by the tear prism at the superior lid margin, but there is no clear consensus on the best location to perform LPI. The purpose of the procedure is to allow aqueous from the posterior chamber to flow through the LPI opening into the anterior chamber and then into the trabecular meshwork in an unrestricted fashion to reduce the risk of angle closure. LPI may be performed with a YAG laser and/or an argon laser.

Indications

LPI is most commonly used in patients who have anatomically narrow angles, narrow angle glaucoma or in cases of pupillary block.[7] In rare cases, LPI may be performed prior to surgical insertion of an implantable contact lens for refractive correction. In the scenarios listed above, the end goal is to help maintain normal IOP for the patient.

Contraindications

As with any surgical procedure, caution should always be taken when making the decision to perform an LPI. Active intraocular inflammation should be treated prior to performing any laser procedure; if the inflammation cannot be controlled or resolved, the LPI should not be performed. In patients with phacomorphic narrowing of the angle, a strong consideration should be given to cataract extraction instead of LPI.

What glaucoma specialists would like us to know about LPI

• Careful and thorough discussion with the patient regarding the procedure should always occur as a condition of informed consent. The patient should demonstrate understanding of the purpose of LPI, alternative options (including the aforementioned cataract extraction in phacomorphic cases or monitoring) and potential risks. It's imperative to provide specific written postoperative instructions, including medication administration regimens, directions for contacting the provider in the event of a complication and when scheduled follow-up should occur.

• Here are some potential postoperative complications to be aware of:

– *IOP spike*. There may be a temporary increase in IOP, in which case an ocular hypotensive medication should be prescribed pending post-op follow-up in a few weeks. In the absence of indications to the contrary, a topical alpha-2 agonist is the medication of choice to reduce IOP due to the mild miosis it induces while also reducing aqueous production and enhancing aqueous outflow. This medication may be used immediately prior to and after surgery to blunt any potential IOP spike, then may be prescribed twice a day afterwards if needed.

– *Iritis*. The laser energy used to create the LPI opening may cause the ocular tissues to become inflamed. To reduce this risk and minimize loss of patency, a topical corticosteroid is usually prescribed QID for one to two weeks post-LPI.

– *Hyphema*. If the YAG laser strikes an iris blood vessel, it will bleed and will require tamponade of the anterior chamber via the laser LPI lens to stanch the bleeding. Once hemostasis is achieved, a microhyphema or a larger hyphema may persist, in which case typical standard protocols for hyphema management are initiated, including limiting physical activities and sleeping with head elevated until the blood has resorbed.

– *Mild discomfort*. This is not uncommon after LPI, and can be treated with acetaminophen; nonsteroidal anti-inflammatories such as aspirin and ibuprofen are relatively contraindicated if hyphema is present due to their anticoagulant effects.

– *Photophobia/blurred vision*. A small number of patients may temporarily experience these symptoms secondary to the iris debris released when creating the LPI, and/or from the laser lens and coupling fluid used during the procedure. These symptoms may be treated with topical corticosteroids several times a day pending follow-up. The patient may also wear tinted lenses or sunglasses to enhance comfort.

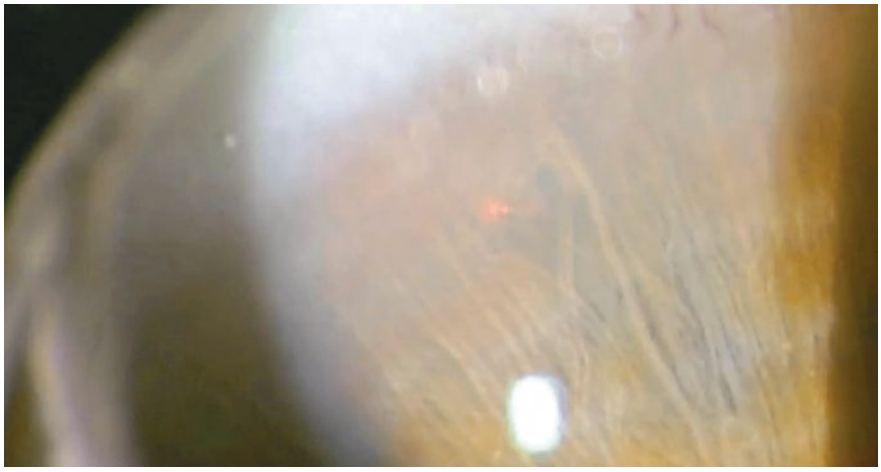


Photo: Joseph Shetler, OD, and Nate Lighthizer, OD

LPI may provide a solution for those at high risk of developing primary angle closure.

Postoperative and follow-up care

After the LPI is performed, it is recommended to check IOP within 30 to 60 minutes of surgery, then again at the post-op follow-up in one to two weeks.[8] Gonioscopy is another critical procedure to perform, allowing for a better visualization and to check for patency of the PI. If the entirety of the angle is deepened, the LPI remains patent and IOP is normal, then regular exam intervals may be resumed.

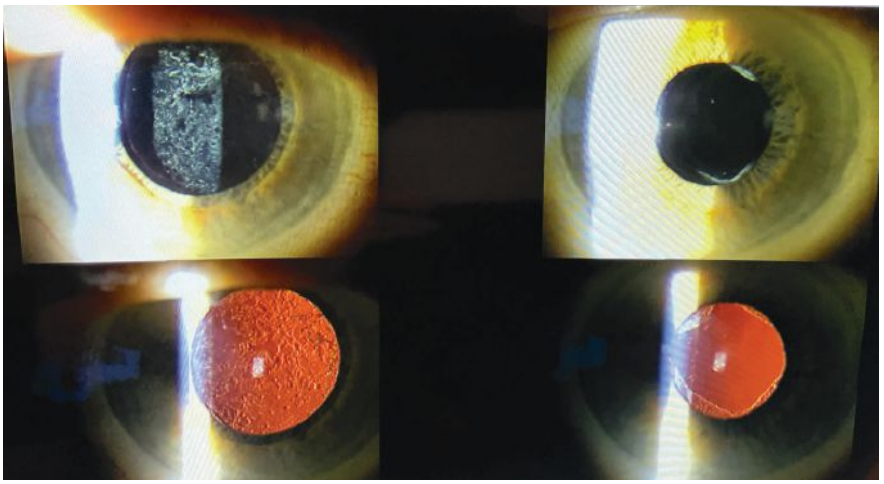
YAG Capsulotomy

This procedure uses a yttrium-aluminum-garnet (YAG) laser to treat posterior capsule opacification, a frequent complication that can occur following cataract surgery. Posterior capsular opacification, sometimes referred to as "secondary cataract," develops when the posterior part of the lens capsule becomes cloudy, leading to a gradual decline in visual acuity. YAG capsulotomy uses a laser to create an opening in the cloudy capsule, restoring clear vision without the need for invasive surgery. This procedure is typically safe and effective, with minimal downtime, and is a vital part of post-cataract care.

Indications

A capsulotomy is indicated "if they see it and you see it," meaning if the eyecare provider sees a cloudy posterior capsule and the patient has a visual complaint consistent with the level of posterior opacification present. Keep in mind the same requirements for medical necessity for cataract surgery also exist for YAG capsulotomy if the procedure is being billed to the patient's medical insurance. The patient's medical insurance guidelines for YAG capsulotomy should be reviewed, but in general there must be a documented

Photo: Nate Lighthizer, OD



The photos on the left show the pre-op appearance of a patient with grade 3 posterior capsule opacification. The right two photos reveal the post-op appearance after a YAG capsulotomy was performed by an optometrist, showing perfect clearing of the posterior capsule.

effect on daily living, a two-line reduction in best-corrected acuity attributable to the opacity and/or a brightness acuity test that demonstrates a two-line reduction in acuity from glare.

If patients are symptomatic but not eligible for surgery under their medical insurance, they can be given the option of paying your usual and customary fee out-of-pocket. If a patient reports their vision fluctuates throughout the day, ocular surface disease or something else is most likely the cause, as the cloudy capsule obviously does not fluctuate. If the patient does not have a visual complaint that matches the level of opacification and/or clinically significant opacification is not observed, a capsulotomy should not be performed.

It is not unusual for patients who see 20/20 to complain that their vision has deteriorated right after cataract surgery and who present with mild posterior capsular opacification. Then, after capsulotomy is performed—while the patient's acuity remains 20/20—they often report a marked subjective improvement in vision.

There are some unique situations where a capsulotomy may still be indicated even if the capsule itself is clear. One of these is when capsular contraction causes folds in the capsule, creating visual distortion and dysphotopsia. This may involve either the anterior or posterior capsule.

Anterior capsular phimosis results from fibrosis and contraction of the anterior capsule following cataract surgery capsulorhexis. If this contraction impinges on the visual axis and causes decreased acuity or other visual complaints, a capsulotomy may be indicated. In anterior capsular contraction syndrome, phimosis of the anterior capsule may cause the intraocular lens (IOL) to flex, in which case a capsulotomy is necessary to reduce the tension on the IOL.

With posterior capsular contraction syndrome, a Z formation of the IOL may sometimes occur. In this situation, one lens haptic is bent forward and the other is bent backwards. This is seen with plate haptic IOLs and accommodating IOLs (Crystalens, Bausch + Lomb), resulting in myopic and astigmatic shifts. It is standard practice now to perform a capsulotomy on Crystalens patients as soon as any lenticular astigmatism or fibrosis is observed. If the capsulotomy does not resolve the issues, alternative surgical correction may be necessary.

Occasionally, a YAG capsulotomy will be performed on a clear capsule in patients prior to corneal refractive surgery. This intervention is done as a prophylactic measure to reduce the risk of future lens flexure and refractive changes from capsular contraction syndromes.

Relative Contraindications

An open posterior capsule makes managing the vitreous more challenging if an IOL exchange is ever needed. If there is a possibility of an IOL exchange, the cataract surgeon should be consulted prior to performing a capsulotomy.

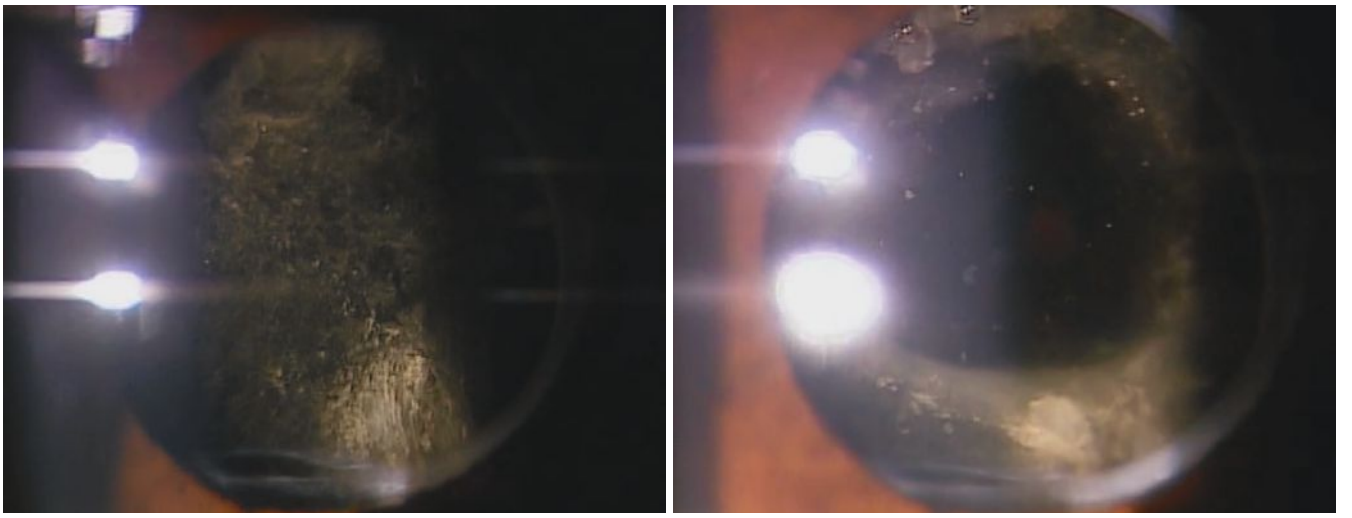
Caution is also advised any time visibility of the capsule is hindered due to corneal pathology. This visual obscuration could result from scars, epithelial basement membrane dystrophy (EBMD), radial keratotomy, Fuchs' dystrophy or edema. Visualization may be improved with the use of a contact capsulotomy laser lens, which also has the advantage of improved focusing, enhanced control of the eye and concentration of the laser beam. However, in cases of advanced EBMD there is a risk of corneal debridement/erosion if the laser lens adheres to the epithelium. A cornea that is not clear may also necessitate the use of a higher power setting, increasing the risk of complications such as IOP spike, cystoid macular edema (CME), inflammation and, in rare cases, retinal detachment.[9]

Stable fixation and head stability in the laser are also required to perform a capsulotomy. The use of a contact capsulotomy laser lens can aid in fixation, as it often suctions onto the eye with the coupling solution and may help temporarily reduce or eliminate blinking. Oral sedatives are sometimes used to reduce tremors and involuntary movements, and head straps may also aid with stability. Occasionally, despite the aforementioned aids, stability cannot be achieved. In these cases, surgical dissection under general anesthesia by a cataract or retina surgeon may be indicated.

The most germane complications associated with capsulotomy (as with most laser procedures) are inflammation, IOP spike and, in rare cases, retinal detachment. Therefore, any patient who has or is at increased risk for any of these conditions should be treated with caution.

Intraocular inflammation should be treated prior to a capsulotomy. This includes postoperative inflammation from the cataract surgery. It is generally advised to wait at least three months post-

Photo: Alla Cappellani, OD, and Sophia Leung, OD



Posterior capsular distension syndrome before and after Nd:YAG capsulotomy.

cataract surgery to perform a capsulotomy. This recommendation, while helping to ensure inflammation has completely resolved, is primarily to create a window to allow for IOL exchange if necessary. In addition to waiting a minimum of three months, there is some evidence that suggests that intraocular inflammation should be resolved for one month prior to performing the capsulotomy.[10]

Patients with new or worsening CME should not undergo YAG capsulotomy until the condition is resolved or, at a minimum, stabilized. For this reason, it is recommended that a macular OCT be obtained on all patients prior to a capsulotomy to screen for CME. Patients who have had a vitrectomy, are diabetic or who have an epiretinal membrane are at higher risk of developing CME and should also be treated with caution. One approach is to pre-treat these patients with a topical nonsteroidal anti-inflammatory one week prior to the procedure.[3]

Caution is also advised with patients who are at high risk of retinal detachment. These include patients whose axial length is greater than 24mm, who have coincident lattice degeneration or any other vitreoretinal pathology, have experienced intraoperative complications during cataract surgery or have a history of previous retinal detachment.[11] If YAG capsulotomy is performed, these patients should be monitored carefully during the postoperative period.

In all cases where patients are at higher risk of complications, it is advised to use lower total energy and to perform a smaller capsulotomy.

Absolute Contraindications

These are rare and involve older IOL materials that are infrequently seen in today's patients. Glass IOL implants are a contraindication due to the risk of lens fracture.[12] Older silicone and hydrogel lens materials may form calcification and crystalline deposits on the lens surface. This is typically not resolved with a capsulotomy, so an IOL exchange is required.[13,14]

Postoperative and Follow-up Care

After YAG capsulotomy is performed, patients are often prescribed a topical corticosteroid four times a day for one week, and are seen again in two to four weeks, at which time manifest refraction is performed along with slit lamp and dilated fundus examination. The latter may be postponed a few weeks until after the fellow eye is treated if both eyes require posterior capsulotomy.

Takeaways

Now that you have a broader picture of how these procedures help your patients care over the long-term course, as well as the potential risks and complications each one presents, it's time to take this knowledge and your lasers to the next level. ■

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LESSONS LEARNED FROM THE DRCR RETINA NETWORK

Here's how the expansive work of this group refined our understanding of diabetic macular edema, including a look at the implications for optometrists.

BY NICK FOGT, OD, PhD, AND ZACHARY COATES, OD, MS
COLUMBUS, OH

For nearly 40 years, the diagnosis, management and treatment of diabetic retinopathy (DR) and diabetic macular edema (DME) has been dominated by the landmark Early Treatment of Diabetic Retinopathy Study (ETDRS).[1] This famous trial was a randomized controlled study that enrolled 3,711 patients. The ETDRS originally sought to determine if and when laser photocoagulation is effective in both of these conditions. An example of an eye with DME is shown in *Figure 1*.

Amongst its many seminal contributions, the ETDRS developed the criteria for clinically significant and non–clinically significant diabetic retinopathy (*Table 1*). The study demonstrated that macular photocoagulation could decrease the risk of moderate visual loss from clinically significant macular edema (CSME). The ETDRS also resulted in a DR grading scale that linked retinal findings to the risk of developing proliferative diabetic retinopathy (PDR). While the ETDRS continues to be impactful in eye care, since its publication there have been significant newer developments in diagnostic technology (OCT and angiography) and treatments (*e.g.*, intravitreal anti-VEGF agents) that are now routinely applied to diabetic retinopathy. These technologies and treatments have necessitated the development of new assessment and management paradigms for DR and DME.

This article concludes a four-part series on the role of medical research in eye care with an in-depth look at the recent history of diabetic eye disease as advanced by one prominent network of researchers.

A Concerted Effort

In 2002 the Diabetic Retinopathy Clinical Research Network, now called the DRCR Retina Network (or DRCR for short), was formed with the goal of supporting multicenter clinical research initiatives in diabetes and other retinal disorders. To date, DRCR consists of over 160 research sites and is affiliated with over 500 physicians throughout the United States and Canada.[2] The DRCR Retina Network has published studies evaluating the outcomes of treatment of DR and DME with various modalities, including retinal laser photocoagulation, various intravitreal anti-VEGF agents, intravitreal steroids and nonsteroidal anti-inflammatory drugs.

With the additional imaging detail provided by OCT, new classifications and management protocols for DME have emerged from these studies. While the terms *clinically significant* and *non–clinically significant* are still broadly used, now macular edema is often described as either center-involved (CI) or non–center-involved (NCI) macular edema (*Table 1*).

DRCR has grouped its studies under various protocols, each of which focuses on a different clinical question.[2] In this article, we'll look at some of the results from protocols that we feel have been particularly impactful for eyecare practice. A list of the published articles derived from all of the DRCR protocols as well as ongoing studies can be found at https://public.jaeb.org/drcrnet/view/home_page.

While many of the protocols developed by the DRCR Retina Network have focused on the treatment of DME

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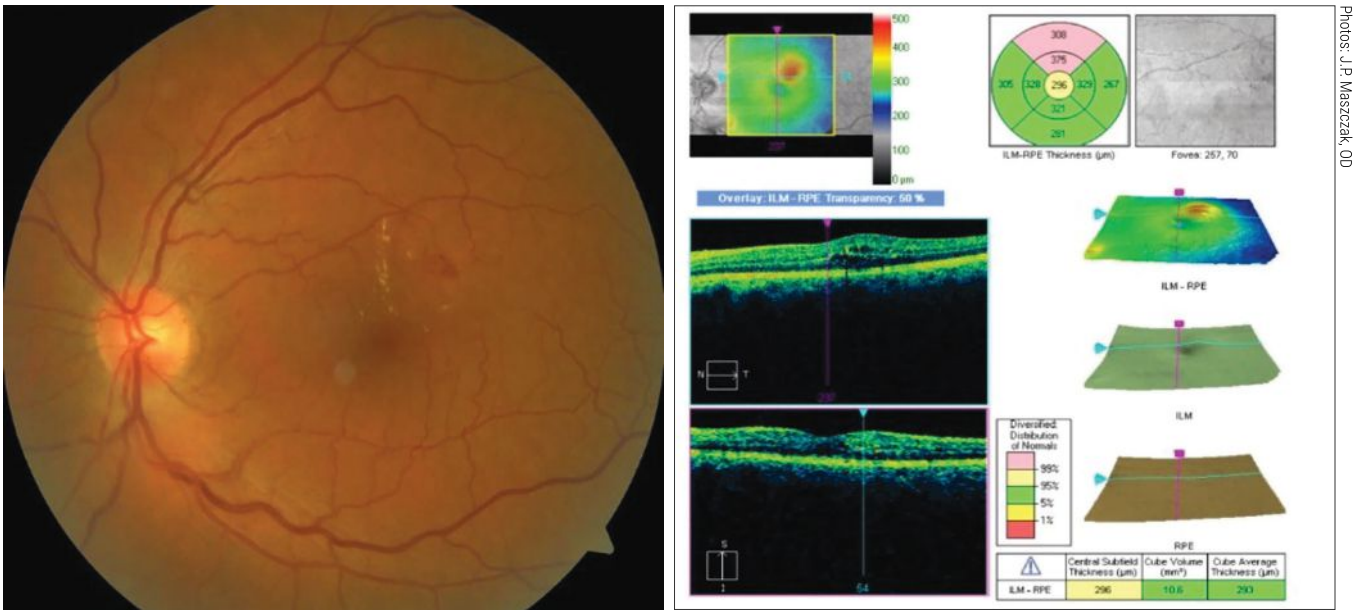


Photos: J.P. Maszczak, OD

Fig. 1. Example of a patient with diabetic macular edema. The OCT results (right) demonstrate an area of retinal thickening superior to the central subfield and corresponding to the area of hard exudates on the left.

and PDR, and thus are perhaps more applicable to our colleagues in ophthalmology, here we will emphasize protocols that can influence how optometrists manage our patients with DME. Of significant note is Protocol V, which concerns the management of patients with center-involving DME and good visual acuity. Special emphasis will be placed on this protocol. Interesting findings from some of the other protocols are shown in *Table 2*. Included in this table are the years in which these results were published.

Protocol V

As mentioned above, Protocol V (Treatment for CI-DME with Very Good VA Study) from the DRCR examined the eyes of patients with diabetes with DME and good visual acuity. The studies under this protocol were unique in that previous research on DME management had focused on patients with visual acuity worse than a particular threshold. For example, Protocols I and T of the DRCR enrolled patients with an upper threshold of 78 ETDRS letters or Snellen equivalent visual acuities of 20/32 or worse.[20]

In 2019, Baker and colleagues published a seminal paper associated with Protocol V.[21] Seven hundred and two adult individuals with type 1 or type 2 diabetes participated. Six hundred and twenty of these individuals completed the final two-year visit. Participants had been diagnosed with center-involved DME (thickening of the central macular subfield). Visual acuity in the eye under study had to demonstrate a Snellen equivalent visual acuity of 20/25 or better (at least 79 ETDRS letters). For the study eyes, mean baseline visual acuity letter score was 85.2 ±3.7 ETDRS letters. The mean hemoglobin A1c of the participants in all of the treatment groups was 7.6, more than 60% of the study eyes had moderate or better diabetic retinopathy, and the mean central subfield thickness was 311 ±57µm. Participants were initially randomized such that they received either aflibercept (2.0mg) injections (an injection at baseline and then "up to every four weeks as needed") or focal/grid laser photocoagulation (*Figure 2*); a control group was observed.

Injections were continued in those eyes that initially received aflibercept if visual acuity increased or decreased by five or more letters or central subfield thickness increased or decreased by ≥10% compared to either of the last two office visits. In the group initially treated with aflibercept injections, there were additional criteria (based on both the measured values and the stability of visual acuity and central subfield thickness) that were used to determine whether injections could be deferred, whether the follow-up period could be

TABLE 1. CLASSIFICATION CRITERIA FOR DIABETIC MACULAR EDEMA

Classification	Description
Clinically significant macular edema (CSME) from the ETDRS	· Thickening of the retina at or within 500µm of the fovea
	· Hard exudates at or within 500µm of the fovea if associated with thickening of adjacent retina
	· A zone, or zones, of retinal thickening one disc diameter or larger within one disc diameter of the fovea
Center-involved macular edema (CI-DME)	· Any intraretinal edema within the central subfield on OCT (the center subfield is defined as a 1mm diameter circle centered on the fovea)
Non–center-involved macular edema	· Intraretinal edema within the macula but outside of the central subfield

increased to eight and then 16 weeks, and whether laser photocoagulation was added. Eyes in the laser photocoagulation group received laser treatment at baseline and were retreated at 13 weeks if necessary. Eyes were re-examined at eight and 16 weeks in the photocoagulation and initial observation groups, and then every 16 weeks unless acuity declined or central subfield thickness increased. Eyes in the laser photocoagulation and observation groups received aflibercept injections if the visual acuity decreased from baseline by 10 or more letters at one visit, or by five to nine letters at two consecutive visits. In the two-year study period, 34% of eyes in the initial observation group and 25% of eyes in the laser photocoagulation group received "rescue" injections.

The primary outcome measure in the study was the number of eyes in which there was a decrease of at least five letters of visual acuity at two years, as this was considered to be a clinically meaningful loss of acuity. There was no significant difference at two years in the percentage of eyes with a five-letter acuity loss between the three treatment groups: aflibercept initially (16%), laser photocoagulation initially (17%) and observation initially (19%).

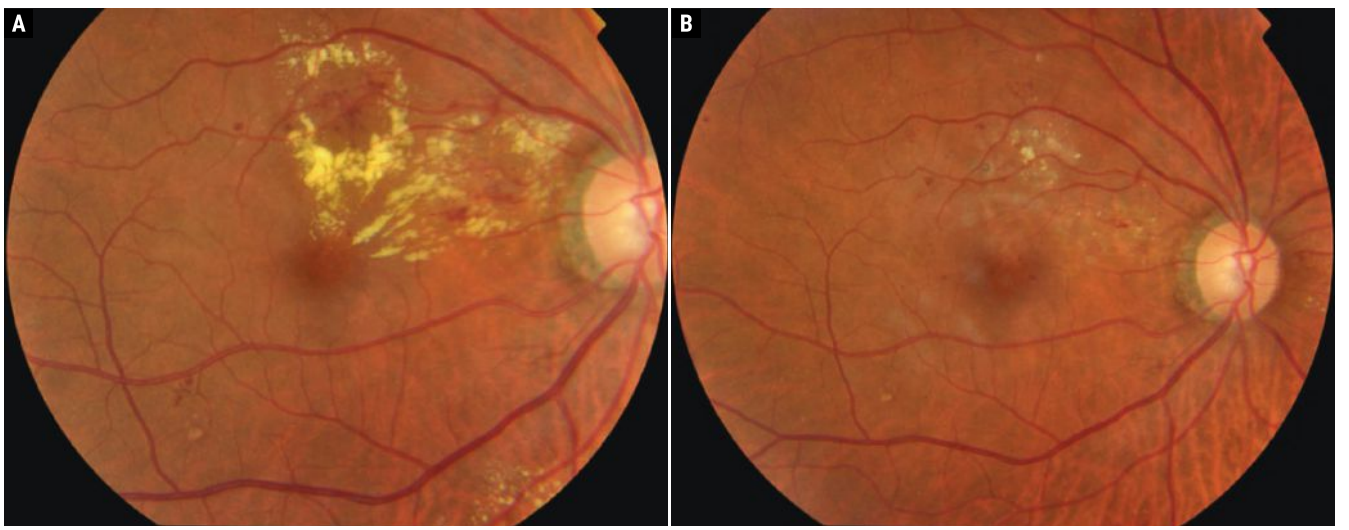
Additional analyses of these data in two other papers showed that there was no difference between the treatment groups in low-contrast visual acuity at two years and that there may be better cost savings on a "societal level" for patients with DME and good visual acuity if these patients are initially treated with laser photocoagulation or observation rather than aflibercept injections.[22,23] The results from the primary outcome measure in the study of Baker and colleagues suggest that, initially, close observation of patients with CI-DME could be reasonable. However, as with most studies, there are a number of factors that must be considered in applying these results to clinical patients.

First, Baker and colleagues reported secondary outcome measures that were found to be significantly different between the different treatment groups. For example, the percentage of eyes with visual acuity of 20/20 or better at two years was 77% in the aflibercept group, 71% in the laser photocoagulation group, and 66% in the initial observation group.[21] These percentages were compared and the difference between the aflibercept and the initial observation group was found to be statistically significant. This was the only significant difference for these visual acuity comparisons.

In another, prespecified analysis, the mean change in visual acuity letter score at two years was compared for the different treatment groups. These changes were +1.5 ±4.0 for the aflibercept group, 0.0 ±3.9 for the photocoagulation group and -0.4 ±4.2 for the observation group. Although these are relatively small differences, the value for visual acuity change for the aflibercept group was significantly different from the values for the other two groups. Clearly, the conclusion that the visual outcome was the same in all treatment groups requires some nuanced consideration.

In addition, each group in the study of Baker and colleagues had reasonably good HbA1c (median 7.6 in all three groups).[20,21] While the relationship between blood sugar control and vision in patients with CI-DME and good vision is not clear, a positive correlation between persistent CSME and hemoglobin A1c has been reported, as has increased risk of CSME in patients with HbA1c values ≥8%.[24,25] Further, the eyes in the study by Baker and colleagues had mean central subfield thicknesses (306 ±55µm in the aflibercept group, 314 ±52µm in the laser photocoagulation group and 314 ±64µm in the observation group) that, as pointed out by Wykoff, were much lower than the mean central subfield thickness of eyes in "most Phase III DME trials."[20] In these latter trials, central subfield thicknesses were in the 400s and 500s.

The significance of the central subfield thickness was examined in a



Photos: Srinivasan Sanjay, MD

Fig. 2. Clinically significant macular edema before (A) and after (B) focal laser photocoagulation. From the publication of ETDRS until the advent of anti-VEGF therapies, this approach was routinely undertaken.

(Images used under Creative Commons 4.0 license. Original citation: Mathew C, Yunirakasiwi A, Sanjay S. Updates in the management of diabetic macular edema. J Diab Res. April 23, 2015.)

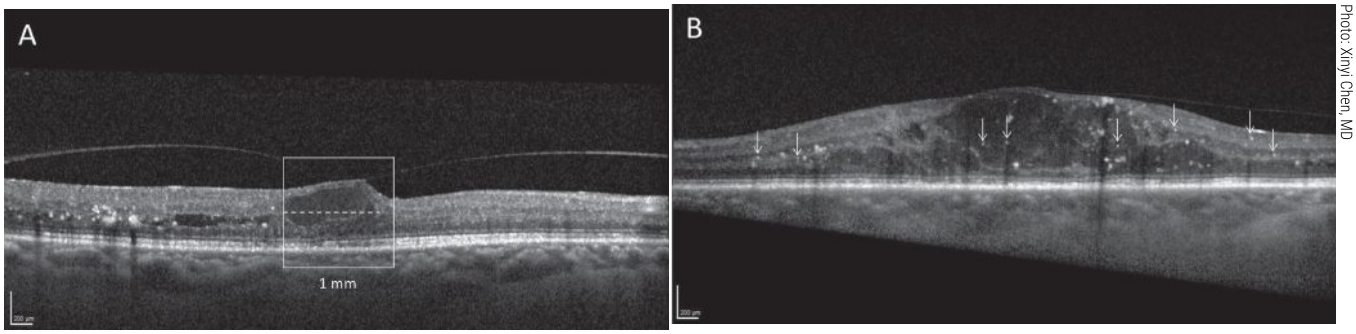


Photo: Xinyi Chen, MD

Fig. 3. Contemporary thinking on DME is such that "watchful waiting" may be appropriate in cases with good visual acuity. However, if inflammatory biomarkers such as (A) disorganization of retinal inner layers or (B) retinal hyperreflective foci are present, the patient may be suitable for referral to a retina specialist even in the absence of visual changes. *(Images used under Creative Commons 4.0 license. Original citation: Chen X, Yang W, Fong A, et al. Sex differences in inflammation-related biomarkers detected with optical coherence tomography in patients with diabetic macular edema. Ophthalmol Sci. July 18, 2024.)*

study by Glassman and colleagues.[26] In a secondary analysis of those data from the Baker study, Glassman et al. looked at factors correlated with the likelihood that eyes in the observation group required aflibercept injections. An eye was twice as likely to receive aflibercept injections if the central subfield thickness was at least 300µm or if the eye had moderately severe diabetic retinopathy (ETDRS Diabetic Retinopathy Severity Scale of 47 or higher), or if the non–study eye was treated for DME within four months of baseline.

Along with these aforementioned factors, there are other individual features that could influence the initial management of patients with CI-DME and visual acuity of 20/25 or better. Lane pointed out that issues around compliance with follow-up appointments could play a role in determining which treatment might be selected for a patient.[27] In Baker and colleagues' original study, the participants in the aflibercept group had a median number of 18 office visits over two years, while the median number of office visits was 11 for the laser photocoagulation group and 12 for the observation group. This suggests that some patients who may have difficulty making it to office visits might be best managed initially with laser photocoagulation or observation.

Cost might be a factor for individual patients as well. Hutton and colleagues demonstrated that there may be better cost savings if patients with CI-DME and good visual acuity are treated initially with laser photocoagulation rather than aflibercept.[23] However, it should be noted that in the original Baker study, the median number of injections was nine in the observation group, eight in the aflibercept group and seven for the laser photocoagulation group, so costs related to intravitreal injections may be less of a factor than expected.

Lastly, a retrospective study by Busch and colleagues demonstrated that in a group of patients with good vision (≤0.1 logMAR or ≥20/25 Snellen) and CI-DME who were initially untreated, these patients were more likely to demonstrate significant decreases in visual acuity over a 12-month period in the presence of baseline OCT markers, including hyperreflective foci (HRF), disorganization of inner retinal layers (DRIL) and ellipsoid zone (EZ) disruption.[28] See *Figure 3* for examples of DRIL and HRF.

Taken together, all of these findings suggest that the initial approach in managing patients with CI-DME and good visual acuity should be tailored to the individual. The patient's hemoglobin A1c level, central subfield thickness, level of diabetic retinopathy, history of treatment or lack thereof for DME in the fellow eye, OCT biomarkers (*e.g.*, the presence of HRF, DRIL and EZ disruption), challenges in making it to scheduled office visits and perhaps cost considerations should all be factored in to the decision regarding the initial management plan.

The results of other studies with similar aims to that of Baker et al. must also be considered in determining how to manage patients with diabetes who have CI-DME and good visual acuity. In a study separate from those of the DRCR, Busch and colleagues performed a retrospective record review that included 249 eyes of 210 patients.[29] Patients in the study were diabetes patients with CI-DME who had good visual acuity (≤0.1 logMAR or ≥20/25 Snellen). Some patients were treated at baseline while others were treated at some point over the 12-month period under study (various treatments were represented). Other patients were not treated.

At 12 months, most of the patients (58.1% in the treated group and 73.4% in the non-treated group) were found to have either gained visual acuity or to have lost less than five letters of acuity. However, if the visual acuity in the non-treated eyes decreased by five or more letters within six months, then the visual outcome for eyes was worse if no treatment was applied compared to cases where treatment occurred. The conclusion of this study was similar to that of Baker et al. in that close observation of patients with DME and good visual acuity is reasonable until the visual acuity drops by one line.

On the other hand, a non-DRCR study by Gabrielle and colleagues resulted in a slightly different conclusion from the work cited above.[30] In a retrospective study, these investigators looked at data from patients with what was termed clinically significant diabetic macular edema, defined as DME within 500µm of the foveal center or at least one disc diameter of swelling, any part of which

TABLE 2. SELECTED ADDITIONAL FINDINGS FROM THE DRCR RETINA NETWORK

Protocol	Title	Interesting Finding(s)
A	Laser Photocoagulation for Diabetic Macular Edema	· Only a modest relationship was found between central retinal thickness and visual acuity.[3,4] (2007, 2009)
AA	UWF Risk of DR Worsening Over Time	· About 70% of nonperfusion was found outside the posterior pole for patients with diabetic retinopathy.[5] (2022) · Greater baseline nonperfusion identified with ultra-widefield (UWF) fluorescein angiography and a greater number of predominately peripheral lesions at baseline were associated with a higher four-year risk of "disease worsening."[6] (2022)
AC	Aflibercept vs. Bevacizumab with Deferred Aflibercept for DME	· For the treatment of moderate vision loss due to CI-involved DME, there was no significant difference at two years in visual acuity or central subfield thickness when patients were treated with aflibercept monotherapy vs. bevacizumab first followed by aflibercept if needed.[7] (2022)
I	Laser-Ranibizumab-Triamcinolone for DME	· Patients with center-involved DME treated with ranibizumab with deferred laser showed better long-term improvements in vision compared to triamcinolone plus laser plus very deferred ranibizumab, or compared to laser plus very deferred ranibizumab.[8] (2016)
S	Prompt PRP vs. Ranibizumab + Deferred PRP for PDR Study	· At two years, treatment of PDR with ranibizumab "was not inferior" to panretinal PRP as assessed with visual acuity.[9] (2015). · Over two years, there was less worsening of PDR with ranibizumab treatment compared to PRP, "especially in eyes that did not require ranibizumab for center-involved DME."[10] (2017) · At five years, visual acuity was good for PDR patients treated with both PRP and those treated with ranibizumab. Severe visual loss and serious PDR complications were uncommon in both groups, but the ranibizumab group had a lower rate of vision-impairing DME and visual field loss.[11] (2018) · Factors to consider in treating PDR with anti-VEGF injections vs. PRP include cost (PRP cheaper), access (*e.g.*, transportation to receive multiple injections) and compliance (anti-VEGF injections require multiple/more office visits).[12] (2019) · Ranibizumab was superior compared to PRP for PDR for both visual acuity and development of vision impairing DME outcomes. The benefit of ranibizumab "seemed greater" for those with higher arterial pressure, those without prior history of focal/grid laser, those with neovascularization and those with more advanced PDR.[13] (2019) · Eyes with PDR were examined over five years. Those treated with PRP had substantial visual field loss at one year and this increased over time. Eyes treated with ranibizumab had loss of visual field sensitivity after two years if not treated with laser.[14] (2020)
T	Aflibercept, Bevacizumab and Ranibizumab Comparison for DME Study	· In treating CI-DME, aflibercept, bevacizumab and ranibizumab were equally effective in improving vision (focal/grid laser added when necessary). However, if visual acuity was initially ≤ 20/50, aflibercept was more effective at one year. At two years, aflibercept was superior only to bevacizumab.[15,16] (2015, 2016).
TX	Aflibercept, Bevacizumab and Ranibizumab Comparison for DME – Follow-up Extension Study	· After the initial two-year study (Protocol T), patients were treated at the discretion of the ophthalmologist. Two-thirds of the individuals from the original study were examined at five years. Mean retinal thickness was similar to that at two years, while mean visual acuity decreased by a line or two.[17] (2020)
W	Anti-VEGF for PDR/DME Prevention Study	· For moderate to severe NPDR with no CI-DME, the two-year rate of development of CI-DME with vision loss or PDR was 16.3% with aflibercept vs. 43.5% for sham treatment. The two-year change in visual acuity was almost the same between aflibercept and sham treatments. At four years, 33.9% of the aflibercept group developed CI-DME or PDR vs. 56.9% of the sham group. There were no significant differences in visual acuity.[18,19] (2021, 2023)

was within one disc diameter of the foveal center. Patients were required to have good visual acuity (≥79 letters read on a logMAR chart or 20/25 Snellen equivalent). Eyes were placed in the "initially treated" group if they received any type of treatment at baseline (*e.g.*, anti-VEGF injection, steroid implant, macular laser photocoagulation). Eyes were placed in the "initially untreated" group if they were observed for at least four months after the baseline visit. Eyes in the "initially untreated" group were in some cases treated (66% received at least one intravitreal injection, 20% received macular laser photocoagulation, and 13% received at least one intravitreal injection and macular laser).

The primary outcome measure was the proportion of eyes with visual acuity loss of five or more letters at 24 months. The number of eyes that lost five or more letters at 24 months was 65% in the initially untreated group and 42% in the initially treated group. While this difference was not statistically significant and was therefore consistent with the results of the study of Baker et al. from the DRCR, eyes in the initially untreated group had a greater likelihood of 10-letter and 15-letter visual acuity losses compared to the initially treated group. While there are myriad differences between this study and that of Baker and colleagues—including, for example, much less rigid management protocols and the inclusion of patients with CS-DME and not just CI-DME—this study could suggest that the results from Protocol V may not extend perfectly to everyday clinical practice.

Clinical Management of CI-DME Patients and Good Visual Acuity

The study from Baker and colleagues performed under Protocol V of the DRCR Retina Network was the first to

examine the management of CI-DME in patients with good visual acuity. Baker et al. concluded from the primary outcome measure that there was no difference in visual outcome at two years whether the study eyes were initially treated with aflibercept, initially treated with macular laser photocoagulation or initially observed.

This study has been foundational in determining how patients with CI-DME and good visual acuity are managed. However, as detailed above, combining the results of the study of Baker and colleagues with the results of other studies has made it clear that the decision as to how to manage a patient with CI-DME and good visual acuity must be based on a number of individual factors.

After a dilated fundus examination and an OCT scan, and after consideration of all of the patient-related factors, such as the patient's HbA1c and ability to comply with follow-up schedules, if the decision is made to monitor patients with CI-DME and good visual acuity (≥20/25 Snellen as measured while the patient views through the most up-to-date refraction in place), the follow-up period should be no longer than six weeks. In keeping with findings from the studies of Protocol V and from other studies, in patients who are initially observed, if the visual acuity at any follow-up decreases by five or more letters on an ETDRS chart or visual acuity is measured at ≤20/32 on a Snellen chart, or the central subfield thickness as assessed by OCT increases by ≥10% compared to the initial visit, then a referral to retinal ophthalmology within two to four weeks is warranted.[31]

A referral should also be strongly considered if, at follow-up visits, the dilated fundus examination suggests worsening retinopathy overall (especially if the diabetic retinopathy exceeds the moderate level at a study visit), or the patient reports an increase in their HbA1c to a value over 8% (assuming this value was under 8% initially), or the OCT scan shows significantly more HRF, DRIL and EZ disruption. Finally, if the patient can no longer return for regular follow-up visits, this could be the basis for an ophthalmological referral.

Summary

Studies on diabetic retinopathy from the DRCR Retina Network have contributed substantially to the evidence base upon which eyecare practitioners rely to determine how to best manage our diabetic patients with retinal complications. Each study answers some questions and raises others, so it is important for practitioners to keep up on new developments. Finally, there may be details in these studies beyond the conclusions of the primary analyses that can further guide or refine management protocols. ■

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BY JESSICA STEEN, OD

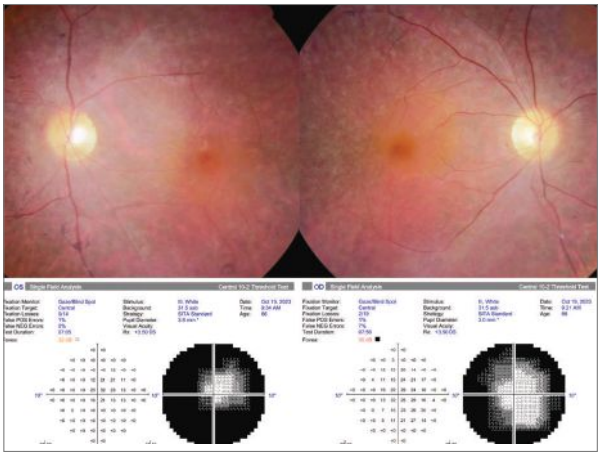
The Dorzolamide Diaries

Explore the use of CAIs as an off-label treatment or adjunct in the management of other conditions.

Cystoid macular edema (CME) is a known complication, which has central visual consequences in individuals with retinitis pigmentosa (RP). Reduction in central visual acuity (VA) in addition to the peripheral visual field constriction and night vision challenges that individuals with RP experience can have a significant impact on quality of life and independence. While treatment options for CME in RP vary, the use of topical ophthalmic carbonic anhydrase inhibitors (CAIs) may provide visual benefit as a noninvasive, off-label therapy.

A 67-year-old man presented for evaluation of reduced vision, particularly in the right eye. He had history of RP, and while he doesn't drive, he reported to begin to feel unsafe navigating due to constriction of his visual field in addition to the new change in central vision. He also had history of primary open-angle glaucoma in both eyes for which he used latanoprost 0.005% "a couple of times a week" in addition to generalized myasthenia gravis managed with pyridostigmine and oral prednisone, and hypercholesterolemia, managed with atorvastatin.

Best-corrected VA was 20/30- OD and OS and pupils were round and minimally reactive without afferent defect. Intraocular pressures (IOPs) were 12mm Hg in each eye, and he was pseudophakic bilaterally. Optic discs were sharp with 3+ diffuse pallor without notching of the neuroretinal rim. The macula appeared flat with epiretinal membrane bilaterally. There was attenuated retinal vasculature and diffuse 360° retinal pigmentary changes. Visual fields were severely constricted bilaterally and macular OCT demonstrated subtle cystoid macular edema along with parafoveal retinal pigment epithelium (RPE) and outer retinal atrophy with intact ellipsoid zone subfoveally and epiretinal membrane bilaterally.



Fundus photograph and automated 10-2 visual field of the right and left eye.

CME and RP

This condition in the context of RP occurs in up to 50% of individuals as a result of a range of proposed mechanisms, including breakdown of the blood-retinal barrier, RPE pump dysfunction and inflammation.[1,2] Treatment options range, in route of administration and treatment target, from oral or topical CAIs that target RPE pump function to intravitreal steroids aimed to reduce inflammatory markers and stabilize the outer blood-retinal barrier, as well as intravitreal anti-VEGF agents that decrease vascular permeability and restore compromised vascular endothelial function.[1,3] Carbonic anhydrase inhibition in the treatment of RP-associated CME has been subject to the most attention in the literature, with 14 studies centered on safety and efficacy of 32 total studies in the treatment of RP-associated CME in a recent meta-analysis and systematic review.[3]

The utility of carbonic anhydrase inhibition in RP-associated CME is not a new concept, with initial publication of a prospective study in 1988.[4] With the approval of topical ophthalmic dorzolamide 2% in 1994, considering the improved tolerability and safety profile vs. oral acetazolamide and similar response rate of approximately 40%, topical dorzolamide 2% three times daily is often positioned as a first-line off-label treatment in CME in the context of RP.[3,5]

Carbonic Anhydrase Inhibition

While we're very familiar with CAIs and their role in reduction of IOP due to suppression of aqueous production, their role as an off-label treatment or adjunct in the management of conditions resulting in intraretinal or subretinal fluid accumulation have been explored considering their impact on the outer blood-retinal barrier (BRB) and RPE pump function.

Breakdown of the BRB, with the inner blood retinal barrier maintained by tight junctions between endothelial cells of retinal vasculature and the outer blood retinal barrier maintained by tight junc-

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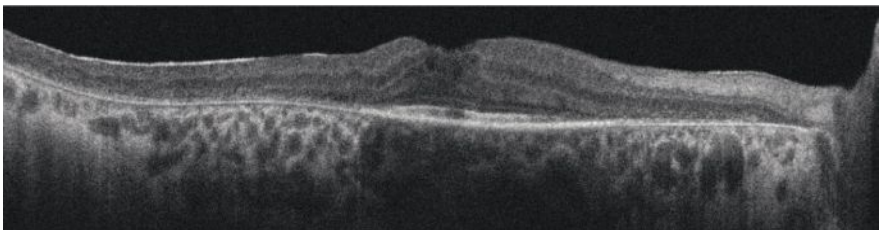
tions of RPE cells leads to cystoid macular edema.[6] Acetazolamide, whether orally or topically administered, inhibits carbonic anhydrase IV, present at both the apical and basal surface of RPE cells, increasing active transport through the outer BRB, increasing the net movement of fluid through the RPE towards the choroid and increasing RPE-retina adhesion.[7-9]

Potential risks related to topical CAI use should be evaluated prior to prescribing, including evaluation of presence of corneal endothelial dysfunction. Hypersensitivity to sulfonamide antibiotics is not an absolute contraindication to non-antibiotic sulfonamide use, including dorzolamide and acetazolamide. While the potential for cross-reactivity cannot be excluded, if an IgE-mediated allergy develops to a non-sulfonamide antibiotic such as dorzolamide in an individual with sulfonamide antibiotic allergy, it is most likely due to two separate allergies.[10]

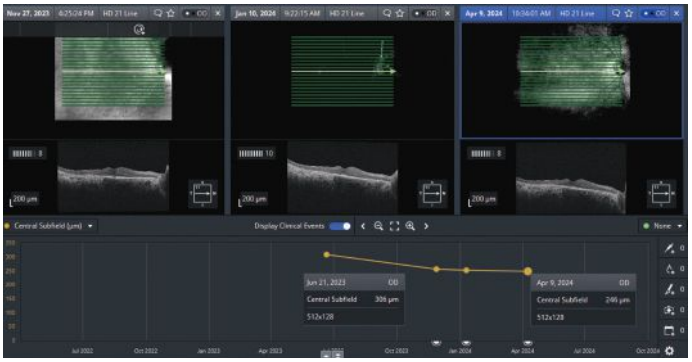
The most common and expected ocular adverse effects of topical ophthalmic CAIs are burning, stinging and ocular discomfort associated with instillation, which were demonstrated in approximately 33% of patients in pivotal trials of dorzolamide 2%.[5] Dorzolamide 2% has a pH of 5.6, while the pH of latanoprost 0.005% is 6.7, which impacts its overall tolerability upon instillation.[5,11] Despite a similar pH to dorzolamide 2%, the fixed-dose combination of dorzolamide-timolol has been reported to have an improved tolerability profile with 21.5% of patients reporting ocular burning or stinging.[12] While the fixed-dose combination of dorzolamide-timolol may improve tolerability vs. dorzolamide 2% alone, potential adverse effects of both dorzolamide and timolol should be carefully assessed prior to prescription. Topical dorzolamide is preferred to brinzolamide due to greater posterior segment tissue penetration as measured in animal models.[13]



SD-OCT of the right macula demonstrating cystoid macular edema, epiretinal membrane and parafoveal ellipsoid zone loss.

Case Approach

After a discussion of risks, benefits, off-label use and expected effects, the patient was prescribed dorzolamide 2% three times daily in each eye with follow up examination set for six weeks. Despite the potential for improved tolerability, dorzolamide-timolol fixed combination was not used, as topical ophthalmic timolol is contraindicated due to the patient's history of myasthenia gravis. He returned five months later with reported subjective improvement in VA in the right eye. Best-corrected VA was 20/25- OD and 20/30- OS, with a five-letter gain noted in the right eye. Central subfield thickness measured by OCT reduced from 306µm to 254µm in the right eye and has since remained stable, with a 23µm reduction in central subfield thickness observed in the left eye.



Reduction in central subfield thickness in the right eye following initiation of dorzolamide 2% three times daily.

The patient's optic disc appearance and visual field appearance were not consistent with glaucomatous optic neuropathy and latanoprost was discontinued without measurable change to central subfield thickness or IOP. Genetic testing was pursued at the patient's request in consideration of his children with a variant of uncertain significance identified. Further evaluation was advised with a genetic counselor for a more detailed investigation. The patient continues to opt to use topical dorzolamide 2% two to three times daily bilaterally and receives periodic retinal evaluation in addition to low vision services. ■

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BY RAMI ABOUMOURAD, OD

White Christmas

This proliferation of lymphocytes requires an aggressive approach.

A 76-year old European female patient presented for evaluation of chronic blurry vision OS for about 12 months. She carries a diagnosis of central retinal vein occlusion status post multiple intravitreal bevacizumab injections. There was previous concern for giant cell arteritis, and she underwent subsequent temporal artery biopsy, which was negative. She previously underwent uncomplicated cataract surgery OU. Systemic history included stage I diffuse large B-cell lymphoma diagnosed two years prior that was treated with chemotherapy and radiation, and the patient has been in remission since completing treatment.

Her presenting visual acuity (VA) was 20/30 OD and 20/200 OS, with no improvement with pinhole OU. Intraocular pressures were 16mm Hg OD and 20mm Hg OS, extraocular motilities were full and symmetric OU and there was a relative afferent pupillary defect OS. Slit lamp exam showed well-positioned posterior chamber intraocular lenses OU and 3+ vitreous cells present in sheets OS.

Take the Retina Quiz:

1. What is the most likely diagnosis?
a. Birdshot chorioretinitis.
b. Metastatic uveal lymphoma.
c. Primary uveal lymphoma.
d. Primary vitreoretinal lymphoma.

2. All of the following are typical features of this disease, except:
a. Leopard spotted appearance on fundus auto fluorescence (FAF).
b. Multifocal yellow-white sub-RPE lesions.
c. Posterior synechiae.
d. Vitreous cells.

3. What is the most appropriate next step?
a. Diagnostic pars plana vitrectomy.
b. Enucleation.
c. Observation.
d. Oral prednisone.

4. Which of the following may be suggestive, or confirmatory, of this patient's disease?
a. *CD20*-positive B-cells.
b. Elevated interleukin-10 in the aqueous.
c. *MYD88* gene mutation.
d. All of the above.

5. Which of the following is true regarding prognosis for this disease?
a. Diagnosis is challenging and may be delayed due to misdiagnosis.
b. Ophthalmic intervention does not impact systemic prognosis.
c. Prognosis is poor with high rates of morbidity and mortality.
d. All of the above.

For answers to the quiz, see page 66.

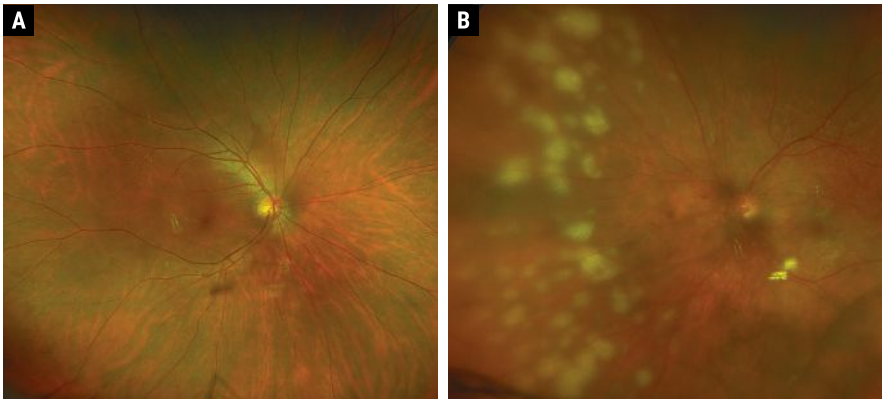

Fig. 1. Widefield optos fundus photograph of right and left eyes.

Diagnosis

Fundus exam OD showed a posterior vitreous detachment and few intraretinal hemorrhages along the inferotemporal arcade (*Figure 1*). Fundus examination OS disclosed sheets of vitreous cells, peripapillary intraretinal hemorrhages, peripapillary and macular exudates and numerous round, creamy-white retinal infiltrates dispersed throughout the nasal equatorial fundus (*Figure 1*). Fluorescein angiography showed early hypofluorescence and late hyperfluorescence of the lesions (*Figure 2*). The patient underwent a diagnostic pars plana vitrectomy and fine needle aspiration biopsy of the lesions. Immunohistochemistry showed atypical *CD20* positive lymphoid cells, and cytogenetics showed that the *MYD88* gene contained an L265P point mutation, consistent with a diagnosis of primary vitreoretinal lymphoma.

Discussion

Primary vitreoretinal lymphoma (PVRL) is a rare malignancy that represents the most common manifestation of intraocular lymphoma, followed by uveal lymphoma.[1,2] PVRL is primarily a high-grade lymphoma and a subset of primary central nervous system lymphoma (PCNSL) that occurs when the retina and vitreous are the primary site of involvement (about 20% of patients).[1,2] Importantly, up to 25% of patients presenting with PCNSL will

About Dr. Aboumourad

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also show symptoms of PVRL or go on to development it, and up to 90% of patients with PVRL are expected to have central nervous system (CNS) disease or to progress to CNS involvement within 29 months, which is the typical etiology for associated disease mortality.[1,2]

Epidemiology

Most patients present later in life, typically in the fifth and sixth decades, with no definitive gender predilection.[1,3] Given its rarity, exact incidence of PVRL is unknown, but estimated to be between 50 and 380 annual cases in the United States, and PCNSL is estimated to be about 1,900 annual cases in the US.[2,4] Presenting VA can range from 20/20 to hand motions and median overall survival time is approximately 58 months, neither of which are dependent upon local interventional approach.[1,2] The only identified risk factors for development of PVRL seem to be immunodeficiency (*e.g.*, human immunodeficiency virus; HIV) and Epstein-Barr virus infection.[3]

Pathophysiology

Our understanding of PVRL supports that clonal proliferation of malignant lymphocytes likely occurs outside the CNS, within the systemic circulation.[1] Subsequently, these malignant lymphocytes infiltrate the eye and brain, presumably reaching the eye via retinal endothelial receptors; immunocompromise and reduced local immunosurveillance may permit or facilitate cellular infiltration.[1]

In PVRL, the vitreous humor, neurosensory retina, RPE and optic nerve may be infiltrated, with Bruch's membrane serving as a barrier for further dissemination into the choroid/uveal tract, which is notably not involved in this disease.[1,4] In contrast, metastatic systemic lymphoma to the eye involves the uveal tract, most commonly via the rich choroidal circulation.[1] Additionally, primary uveal lymphoma, also referred to as benign reactive lymphoid hyperplasia, is felt to be a low-grade B-cell lymphoma with little/no metastatic potential, though can still cause local organ morbidity.[1]

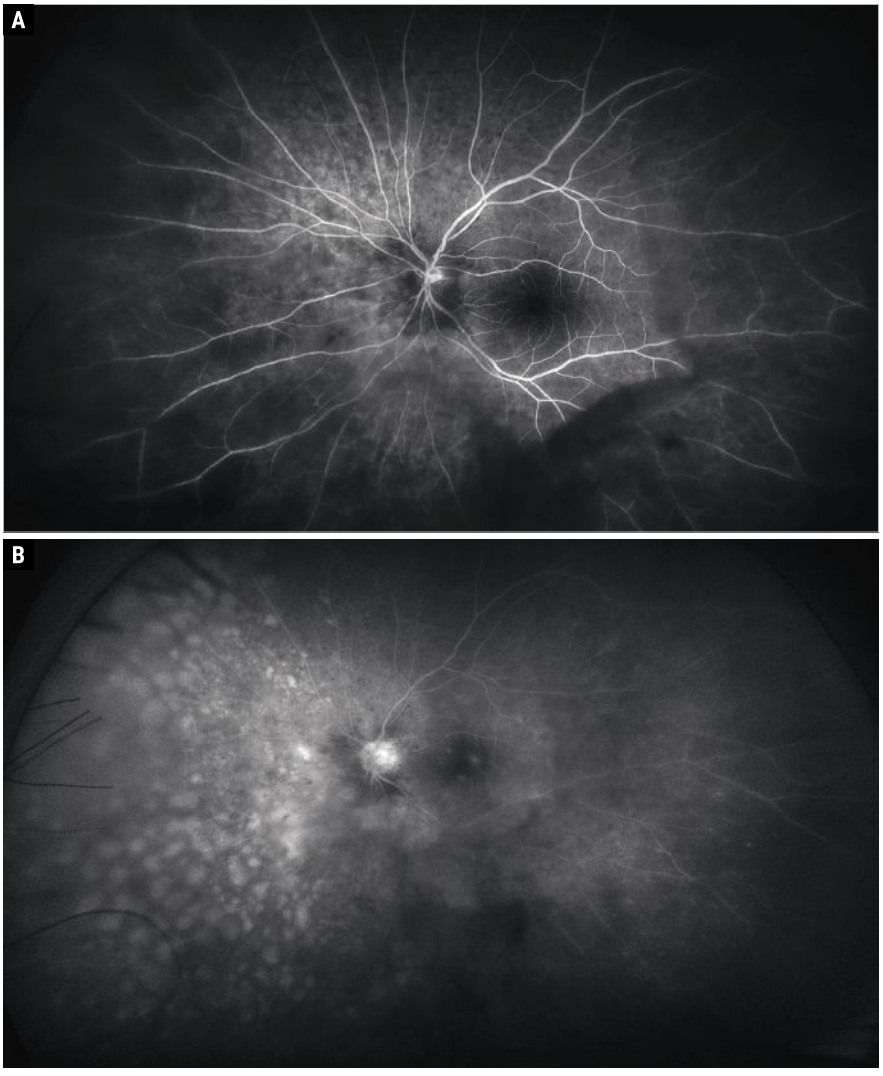

Fig. 2. Widefield Optos fluorescein angiogram early and late phase of the left eye.

Differential Diagnosis

All the intraocular lymphomas are uveitis masquerade syndromes. First used in 1967 to describe a chronic conjunctivitis secondary to carcinoma, the term "masquerade syndrome" has since been adapted to refer to any disease in which there is cellular infiltration mimicking the appearance of intraocular inflammation in the absence of a truly immune-mediated or infectious process.[5]

Differential diagnoses for primary vitreoretinal lymphoma primarily include different infectious and inflammatory etiologies of intermediate and posterior uveitis such as syphilis, tuberculosis, toxoplasmosis, viral retinitis, sarcoidosis, birdshot chorioretinitis and infectious endophthalmitis.

Clinical and Multimodal Imaging Features

Typical clinical features of PVRL include a moderate, non-clumped cellular reaction in the vitreous cavity, with cells often arranged in sheets, and white/yellow/orange retinal infiltration.[1,2] Malignant lymphoid cells often begin along Bruch's membrane and proliferate in the sub-RPE space, with subsequent RPE alterations and migratory clumping overlying the infiltrate; this may produce the typical leopard-spotted appearance.[2,6] Presence of symptomatic iritis (*i.e.,* redness, pain, photophobia) and posterior synechiae should prompt reconsideration of diagnosis.

FAF imaging may show normal, hypo- or hyperAF based on depth and extent

of lesions present, as well as overlying lipofuscin and RPE changes.[1,2,6] Fluorescein angiography (FA) generally shows hypofluorescence of the lesions in the early and late phases of the angiogram but can also be hyperfluorescent as well.[2,4] Rarely, there may be retinal venous leakage, periarteriolar staining and cystoid macular edema.[1,2] OCT demonstrates hyperreflective nodular deposits at the level of the RPE, and there may be confluence and elevation in the subretinal or sub-RPE space over time.[2,6] While FAF may be normal, a "granular" pattern on FAF is highly predictive of PVRL, the hyperAF lesions correlate with hypofluorescence on FA in about half of the cases and hyperreflective nodularity of the RPE on OCT in about one third of cases.[6]

Diagnosis

Making the diagnosis first requires a high degree of clinical suspicion to initiate the proper workup. Patients with chronic noninfectious posterior or panuveitis not responding to anti-inflammatory therapy should raise suspicion for a masquerade syndrome, *e.g.*, PVRL.

Anterior chamber paracentesis testing of aqueous humor for elevated levels of interleukin (IL)-10, as well as elevated ratio of IL-10 to IL-6, have been proposed as a screening modality as it is indicative of possible PVRL.[1,2,4] IL-10 serves as a scaffold for B-cell lymphocyte proliferation and is also anti-inflammatory, resulting in the typical "white and quiet" appearing eye without an overt inflammatory reaction in response to uncontrolled cellular proliferation.[1] Immune-mediated uveitis generally has elevated IL-6, which is associated with breakdown of the vitreous humor structure, and there may be subsequent stranding and aggregations of vitreous opacities.[1]

Definitive diagnosis requires identification of malignant intraocular lymphocytes in vitreous humor specimen obtained either via direct vitreous aspiration or pars plana vitrectomy.[1,3] Since lymphoid cells are fragile, the cytology sample must be analyzed promptly to avoid necrosis and false negative studies.[3] Typical immunohistochemistry stains employed to detect most B-cell lymphomas include CD20 and kappa/lambda light chain markers, though these are limited in detecting rarer, more aggressive, T-cell lymphomas.[1] Cytogenetics have identified mutations in *MYD88* and *CD79B* as the two most prevalent mutations, present in 88% and 35% of patients with PVRL, respectively.[3,4]

Management and Prognosis

When presenting as isolated PVRL without CNS involvement, local therapy is recommended and options include local radiation and intravitreal chemotherapy with methotrexate or rituximab.[1,2] When presenting with concomitant ophthalmic and CNS disease, high-dose systemic methotrexate with or without rituximab is combined with local therapy.[2,3]

The prognosis is generally poor, with mortality rates ranging from 9% to 81% and a five-year overall survival rate of less than 25%.[3] Treatment is effective at local tumor control but does not alter CNS disease or overall survival.[3] Vision is generally preserved until there is direct cellular infiltration of the central macula. The alterations to the retina and RPE, once damaged, are irreversible even once necessary therapy has been initiated.[6]

Our patient received 10 intravitreal injections of methotrexate OS administered approximately every 10 days. Vision improved one line to 20/100, though she eventually developed vitreous cells OD for which she also received 10 injections of methotrexate. She has been followed off treatment for six months OD and 18 months OS without intraocular recurrence OU or CNS disease development on serial neuroimaging surveillance. ■

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Responsibilities: Candidates are expected to be highly knowledgeable in the field of Pediatrics and can develop and teach courses and/or laboratories in the subject area. The candidate must also be able to provide direct patient care and clinical instruction to professional students as well as residents, and be involved in interdisciplinary practice with other educational professionals.

Candidates must be willing to actively participate in curricular assessment, professional development, student counseling and service activities within the college, university and the scientific community. Successful candidates are also expected to be involved in research and scholarly activities, and have a sincere commitment to optometric education, community service and patient care. Primary duties include, but are not limited to:

a) **Teaching**
- Developing and delivering lectures and/or laboratories for the area of specialty and related areas as assigned;
- Embracing and enhancing the didactic philosophies in the O.D. program;
- Maintaining and expanding the high quality clinical practice environment for optometry students on rotation;
- Precepting students on clinical rotation at the Midwestern University Eye Institute;

b) Service
- Helping to maintain and grow the state of the art optometry program with a strong interdisciplinary focus that meets the needs of patients in the surrounding community; is efficient, patient friendly, and cost-effective;
- Working closely together with all optometry and ophthalmology faculty to provide a complete range of eye and vision care services;
- Participating in leadership roles in state, regional, and national optometry organizations;
- Participating on College and University committees, as assigned;
- Participating in College and University service activities

c) Scholarly activity
- Engaging in research and scholarly activity, including presentations at scientific meetings, research, and publication in peer reviewed journals sufficient to qualify for academic advancement in a non-tenure track position.

Qualifications: Candidates must possess a Doctor of Optometry degree from an ACOE-accredited institution, must have completed an ACOE-accredited residency, and must be eligible for an optometric state license in the state in which the college is located. Primary eye care clinical expertise is also required.

Contact information: Interested applicants should click on the link to apply at https://www.midwestern.edu/employment-mwu and include curriculum vitae and letter of interest specifying the position and college that he/she wishes to be considered for. Inquiries may be directed to Dr. Samantha Rice, Associate Dean; Midwestern University: srice@midwestern.edu.

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BY ANDREW S. GURWOOD, OD

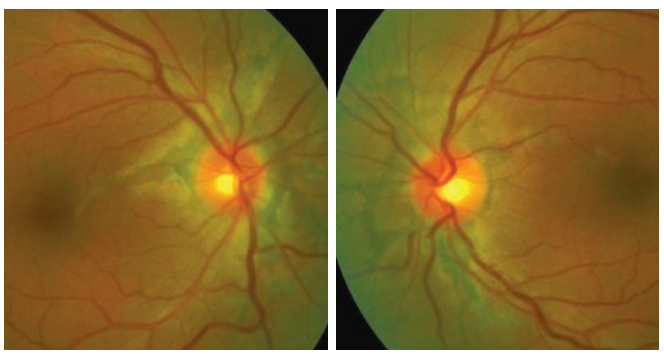
DIAGNOSTIC QUIZ

Losing Streak

These fundus findings can be cause for concern. What should you anticipate in such cases?

A 57-year-old Black man presented to the office with a chief complaint of blurry vision OU of one month's duration. He was interested in a new spectacle prescription. He had no prior history of trauma or pain. His systemic and ocular histories were unremarkable. He denied allergies of any kind.

His best-corrected acuities were 20/20 OD and 20/20 OS at distance and near. External exam was normal and there was no afferent pupil defect. Refraction was negligibly different with an excellent visual response. His anterior segment structures were normal with Goldmann tonometry measuring 17mm Hg OU. Cup/disc ratios were 0.2 OD and 0.25 OS. The dilated fundus findings were normal peripherally, with the pertinent findings surrounding both nerves demonstrated in the photographs.



Fundus appearance of the patient's right and left eyes.

Additional studies might include color photography of both nerves, automated perimetry to rule out functional loss and five-line raster of the area about both nerves to rule out choroidal neovascularization. Additional history might be requested to rule out collagen vascular disease such as pseudoxanthoma elasticum and Ehlers-Danlos syndrome, Paget's disease and sickle cell anemia. Lab work and correspondence with the GP was completed.

What would be your diagnosis based on the findings presented? What's the likely prognosis? To find out, read the online version of this article at www.reviewofoptometry.com. ■

About Dr. Gurwood

Dr. Gurwood is a professor of clinical sciences at The Eye Institute of the Pennsylvania College of Optometry at Salus University. He is a co-chief of Primary Care Suite 3. He is attending medical staff in the department of ophthalmology at Albert Einstein Medical Center, Philadelphia. He has no financial interests to disclose.

Retina Quiz Answers—Q1: d, Q2: c, Q3: a, Q4: d, Q5: d

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44% and 55% of patients taking XDEMVY in SATURN-1 (N=209) and SATURN-2 (N=193), respectively, achieved a significant improvement in their eyelids (reduction of collarettes to no more than 2 collarettes per upper lid) at Day 43 vs 7% (N=204) and 12% (N=200) of patients taking vehicle ($P<0.01$ in each trial).*

INDICATIONS AND USAGE

XDEMVY (lotilaner ophthalmic solution) 0.25% is indicated for the treatment of *Demodex* blepharitis.

IMPORTANT SAFETY INFORMATION:

WARNINGS AND PRECAUTIONS

Risk of Contamination: Do not allow the tip of the dispensing container to contact the eye, surrounding structures, fingers, or any other surface in order to minimize contamination of the solution. Serious damage to the eye and subsequent loss of vision may result from using contaminated solutions.

Use with Contact Lenses: XDEMVY contains potassium sorbate, which may discolor soft contact lenses. Contact lenses should be removed prior to instillation of XDEMVY and may be reinserted 15 minutes following its administration.

ADVERSE REACTIONS: The most common adverse reaction with XDEMVY was instillation site stinging and burning which was reported in 10% of patients. Other ocular adverse reactions reported in less than 2% of patients were chalazion/hordeolum and punctate keratitis.

Please see next page for a Brief Summary of the full Prescribing Information.

*The safety and efficacy of XDEMVY for the treatment of DB were evaluated in a total of 833 patients (415 of whom received XDEMVY) in two 6-week, randomized, multicenter, double-masked, vehicle-controlled studies (SATURN-1 and SATURN-2). Patients were randomized to either XDEMVY or vehicle at a 1:1 ratio, dosed twice daily in each eye for 6 weeks. All patients enrolled were diagnosed with DB. The primary efficacy endpoint was defined as the proportion of patients with collarette reduction to no more than 2 collarettes per upper eyelid at Day 43.

Reference: XDEMVY [prescribing information]. Tarsus Pharmaceuticals, Inc; 2023.

tarsus