REVIEW® of Ophthalmology

December 2020

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IMPROVING THE PATIENT EXPERIENCE

Experts share their advice on keeping patients happy, both in-office (P.30) and online (P. 40).

ALSO INSIDE:

- How to Handle Pseudoexfoliation During Cataract Surgery P. 46

DEXYCU®
(dexamethasone intraocular suspension) 9%

The first and only FDA-approved, single-dose, sustained-release, intracameral steroid for the treatment of postoperative inflammation[1-3]

With a single injection at the end of cataract surgery, anti-inflammatory efficacy begins as early as day 1 and continues through day 30[1]*

- The percentage of patients who received **DEXYCU®** (dexamethasone intraocular suspension) 9% (517 mcg) who had anterior chamber cell clearing on day 8 was 60% (n=94/156) vs 20% (n=16/80) in the placebo group[1]
- The cumulative percentage of subjects receiving rescue medication of ocular steroid or nonsteroidal anti-inflammatory drug (NSAID) by day 30 was significantly lower in the **DEXYCU** (517 mcg) treatment group (20%; n=31/156) compared to placebo (54%; n=43/80)[1]

*DEXYCU was studied in a randomized, double-masked, placebo-controlled trial. Patients received either DEXYCU or a vehicle administered by a physician at the end of the surgical procedure. The primary endpoint was the proportion of patients with anterior chamber cell clearing (cell score=0) on postoperative day 8.

INDICATION AND USAGE

DEXYCU® (dexamethasone intraocular suspension) 9% is indicated for the treatment of postoperative inflammation.

IMPORTANT SAFETY INFORMATION

CONTRAINDICATIONS

None.

WARNINGS AND PRECAUTIONS

Increase in Intraocular Pressure
- Prolonged use of corticosteroids, including DEXYCU, may result in glaucoma with damage to the optic nerve, defects in visual acuity and fields of vision
- Steroids should be used with caution in the presence of glaucoma

Delayed Healing
- The use of steroids after cataract surgery may delay healing and increase the incidence of bleb formation
- In those diseases causing thinning of the cornea or sclera, perforations have been known to occur with the use of corticosteroids

Exacerbation of Infection
- The use of DEXYCU, as with other ophthalmic corticosteroids, is not recommended in the presence of most active viral diseases of the cornea and conjunctiva including epithelial herpes simplex keratitis (dendritic keratitis), vaccinia, and varicella, and also in mycobacterial infection of the eye and fungal disease of ocular structures
- Use of a corticosteroid in the treatment of patients with a history of herpes simplex requires caution and may prolong the course and may exacerbate the severity of many viral infections
- Fungal infections of the cornea are particularly prone to coincidentally develop with long-term local steroid application and must be considered in any persistent corneal ulceration where a steroid has been used or is in use. Fungal culture should be taken when appropriate
- Prolonged use of corticosteroids may suppress the host response and thus increase the hazard of secondary ocular infections. In acute purulent conditions, steroids may mask infection or enhance existing infection

Cataract Progression
- The use of corticosteroids in phakic individuals may promote the development of posterior subcapsular cataracts

ADVERSE REACTIONS

- The most commonly reported adverse reactions occurred in 5-15% of subjects and included increases in intraocular pressure, corneal edema and iritis

Please see brief summary of full Prescribing Information on adjacent page.

References: 1. DEXYCU® (dexamethasone intraocular suspension) 9% full U.S. Prescribing Information. EyePoint Pharmaceuticals, Inc. June 2020. **2.** Donnenfeld E, Holland E. Dexamethasone intracameral drug-delivery suspension for inflammation associated with cataract surgery: a randomized, placebo-controlled, phase III trial. *Ophthalmology.* 2018;125(6):799-806. **3.** Data on file. EyePoint Pharmaceuticals, Inc.

EyePoint® PHARMACEUTICALS

06/2020
US-DEX-2000094

DEXYCU (dexamethasone intraocular suspension) 9%,
for intraocular administration
Initial U.S. Approval: 1958

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

1 INDICATIONS AND USAGE

DEXYCU (dexamethasone intraocular suspension) 9% is indicated for the treatment of postoperative inflammation.

4 CONTRAINDICATIONS

None.

5 WARNINGS AND PRECAUTIONS

5.1 Increase in Intraocular Pressure

Prolonged use of corticosteroids including DEXYCU may result in glaucoma with damage to the optic nerve, defects in visual acuity and fields of vision. Steroids should be used with caution in the presence of glaucoma.

5.2 Delayed Healing

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

5.3 Exacerbation of Infection

The use of DEXYCU, as with other ophthalmic corticosteroids, is not recommended in the presence of most active viral diseases of the cornea and conjunctiva including epithelial herpes simplex keratitis (dendritic keratitis), vaccinia, and varicella, and also in mycobacterial infection of the eye and fungal disease of ocular structures.

Employment of a corticosteroid medication in the treatment of patients with a history of herpes simplex requires caution. Use of ocular steroids may prolong the course and may exacerbate the severity of many viral infections of the eye (including herpes simplex). Fungal infections of the cornea are particularly prone to develop coincidentally with long-term local steroid application. Fungus invasion must be considered in any persistent corneal ulceration where a steroid has been used or is in use. Fungal culture should be taken when appropriate.

Prolonged use of corticosteroids may suppress the host response and thus increase the hazard of secondary ocular infections. In acute purulent conditions, steroids may mask infection or enhance existing infection.

5.4 Cataract Progression

The use of corticosteroids in phakic individuals may promote the development of posterior subcapsular cataracts.

6 ADVERSE REACTIONS

The following adverse reactions are described elsewhere in the labeling:

- Increase in Intraocular Pressure *[see Warnings and Precautions (5.1)]*
- Delayed Healing *[see Warnings and Precautions (5.2)]*
- Infection Exacerbation *[see Warnings and Precautions (5.3)]*
- Cataract Progression *[see Warnings and Precautions (5.4)]*

6.1 Clinical Trials Experience

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

The following adverse events rates are derived from three clinical trials in which 339 patients received the 517 microgram dose of DEXYCU. The most commonly reported adverse reactions occurred in 5-15% of subjects and included increases in intraocular pressure, corneal edema and iritis. Other ocular adverse reactions occurring in 1-5% of subjects included, corneal endothelial cell loss, blepharitis, eye pain, cystoid macular edema, dry eye, ocular inflammation, posterior capsule opacification, blurred vision, reduced visual acuity, vitreous floaters, foreign body sensation, photophobia, and vitreous detachment.

8 USE IN SPECIFIC POPULATIONS

8.1 Pregnancy

Risk Summary

There are no adequate and well-controlled studies of DEXYCU (dexamethasone intraocular suspension) in pregnant women. Topical ocular administration of dexamethasone in mice and rabbits during the period of organogenesis produced cleft palate and embryofetal death in mice and malformations of abdominal wall/intestines and kidneys in rabbits at doses 7 and 5 times higher than the injected recommended human ophthalmic dose (RHOD) of DEXYCU (517 micrograms dexamethasone), respectively *[see Data in the full prescribing information].*

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.

8.2 Lactation

Risk Summary

Systemically administered corticosteroids are present in human milk and can suppress growth, interfere with endogenous corticosteroid production, or cause other unwanted effects. There is no information regarding the presence of injected DEXYCU in human milk, the effects on breastfed infants, or the effects on milk production to inform risk of DEXYCU to an infant during lactation. The developmental and health benefits of breastfeeding should be considered, along with the mother's clinical need for DEXYCU and any potential adverse effects on the breastfed child from DEXYCU.

8.4 Pediatric Use

Safety and effectiveness of DEXYCU in pediatric patients have not been established.

8.5 Geriatric Use

No overall differences in safety or effectiveness have been observed between older and younger patients.

Manufactured for: EyePoint Pharmaceuticals US, Inc. Watertown, MA 02472

01/2020
US-DEX-2000014

REVIEW NEWS
Volume XXVII • No. 12 • December 2020

Academy Spearheads First Global Myopia Task Force

By 2050, it's projected that nearly half of the global population will be affected by myopia, particularly in East and Southeast Asia, where 80 to 90 percent of children and young adults are already myopic. Furthermore, high myopia is expected to affect around 10 percent of the global population, or approximately 925 million people, by 2050, according to estimates by the Brien Holden Vision Institute in Sydney, Australia.

Richard L. Abbott, MD, co-chair of the Academy's Task Force on Myopia, says that developing high myopia isn't merely a matter of an increased need for thick glasses. "The risk of developing vision-threatening eye conditions is clearly linked to high myopia," he says. "There's an estimated six-times increased risk of retinal detachment for patients with high myopia, an approximately 50-percent increased risk of developing glaucoma, a 20-percent increase in need for cataract surgery and a significant risk of myopia maculopathy."

The Academy's task force aims to reduce the age of myopia onset and slow worldwide myopia progression by

- educating the health-care community, public policy makers and the public about the public health burden of myopia;
- promoting myopia as a global public health concern; and
- working with pediatric and family organizations to encourage outdoor time and early diagnosis of children.

The task force will collaborate with recognized experts in myopia prevention and treatment, public health experts, the American Academy of Optometry, the American Academy of Pediatrics and representatives from the American Academy of Family Physicians.

Members of the panel discussed the optical strategies currently available for myopia control: contact lenses and spectacles. "Spectacle lenses include bifocals—either progressive addition lenses or executive bifocals—and customized single-vision lenses," says Susan Cotter, OD, MS, FAAO, a professor of optometry at Marshal B. Ketchum University in Fullerton, California, and incoming president of the American Academy of Optometry. "In the COMET and COMET 2 studies, PALs were able to slow myopia progression over three years more effectively than SVLs, but only by about a quarter-diopter (treatment differences: 0.2 D and 0.28 D, respectively). These differences were statistically, but not clinically, significant.[1]

"A randomized clinical trial comparing SVLs to executive bifocals +1.5 D, with and without 3Δ base-in prism, found a mean three-year progression of -2.06 D (SVL), -1.25 D (BIF) and -1.01 D (BIF/Δ)," she adds.[2]

Customized lenses are also in development now. Dr. Cotter says that Defocus Incorporated Multiple Segments have a clear optical zone with multiple 1-mm +3.5-D segments in the periphery that create a "blurring effect."[3]

"The two-year data from the clinical trial comparing DIMS lenses to SVLs found a difference of almost half a diopter of myopia (DIMS -0.41D, SVL -0.85 D; mean difference: 0.44 D)," she says. "In 21.5 percent of the DIMs group and 7.4 percent of the SVL


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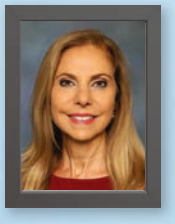
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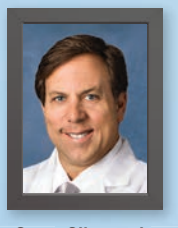
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INDICATIONS AND USAGE

OMIDRIA® (phenylephrine and ketorolac intraocular solution) 1% / 0.3% is added to ophthalmic irrigating solution used during cataract surgery or intraocular lens replacement and is indicated for maintaining pupil size by preventing intraoperative miosis and reducing postoperative ocular pain.

IMPORTANT SAFETY INFORMATION

OMIDRIA must be added to irrigating solution prior to intraocular use.

OMIDRIA is contraindicated in patients with a known hypersensitivity to any of its ingredients.

Systemic exposure of phenylephrine may cause elevations in blood pressure.

Use OMIDRIA with caution in individuals who have previously exhibited sensitivities to acetylsalicylic acid, phenylacetic acid derivatives, and other nonsteroidal anti-inflammatory drugs (NSAIDs), or have a past medical history of asthma.

The most commonly reported adverse reactions at ≥ 2% are eye irritation, posterior capsule opacification, increased intraocular pressure, and anterior chamber inflammation.

Please see the Full Prescribing Information for OMIDRIA at www.omidria.com/prescribinginformation.

You are encouraged to report Suspected Adverse Reactions to the FDA. Visit www.fda.gov/medwatch, or call 1-800-FDA-1088.

References: 1. Omeros survey data on file. **2.** OMIDRIA [package insert]. Seattle, WA: Omeros Corporation; 2017. **3.** Al-Hashimi S, Donaldson K, Davidson R, et al; for ASCRS Refractive Cataract Surgery Subcommittee. Medical and surgical management of the small pupil during cataract surgery. *J Cataract Refract Surg*. 2018;44:1032-1041.

The healthcare professionals portrayed in this advertisement are consultants of Omeros Corporation.

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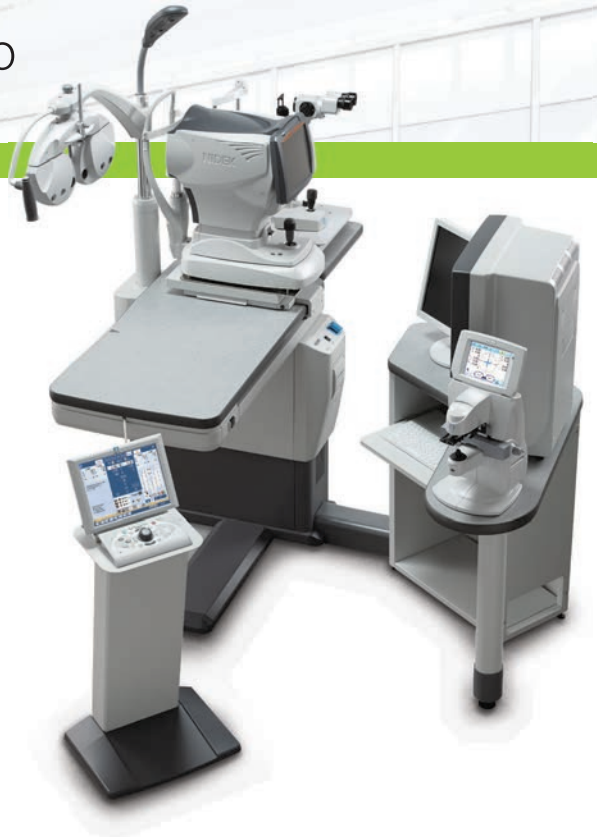

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group, there was no myopia progression."[4] She adds that there are several other lenses in the pipeline.

As for contact lenses, the current options include multifocals and keratology lenses. "A recent meta-analysis of ortho-K lenses showed a two-year slowing of axial elongation, which was clinically significant at 0.28 mm," Dr. Cotter says.[5] "Soft multifocal contact lenses, such as MiSight for daily wear, demonstrated results similar to those of the three-year randomized bifocal studies compared to SVLs.[6] Soft multifocal contact lenses yielded about a two-thirds-diopter difference in myopia progression and also slowed axial elongation.

"The BLINK trial randomized children to three groups: a high add power; a medium add power; and a single-vision lens control group," she continues. "The high add power contact lens demonstrated greater slowing of myopia progression than the medium-power contact lens and much greater slowing than the SVL."[7]

Dr. Cotter says that combination strategies are currently under evaluation. One meta-analysis of four studies found that a combination of atropine 0.01% and ortho-K was more effective in slowing axial elongation than ortho-K monotherapy.[8]

The future of myopia prevention and intervention almost certainly points to a combination of treatments, says Michael X. Repka, the AAO's medical director for governmental affairs. "Much of what we know about outdoor time and atropine is based on data from East Asia," he says. "We think the mechanism is likely related to dopamine levels in the retina, which slow axial elongation. One study found a 9.1 percent reduced rate of myopia onset with an added 40-minue period outdoors,[9] and a meta-analysis of outdoor activities identified a reduced myopic shift of 0.3 D compared to a control group after three years.[10] This effect is small in an individual patient, but cumulatively these effects could greatly limit the public health damage caused by myopia. I must caution, however, that significant questions remain on the amount of outdoor time and the quality and intensity of light needed. We don't know the quantitative impact in the West.

"A daily dose of one drop of atropine 0.01% to 0.05% has been shown to slow progression by 30 to 50 percent in normal, school-aged children while on treatment," he continues. "This doesn't seem to stop progression, so much as reduce the amount it progresses. It's incumbent on us that both prescribing doctors and parents understand this.

"The treatment and management of myopia includes everyone," Dr. Repka adds. "Tackling myopia will require a lot of advocacy for therapy, care and reviewing research. The Academy supports strengthening regulatory science for the evaluation of drugs and devices for myopia control. It's also promoting patient access to safe and effective therapies, appropriate reimbursement and awareness among physicians, educators and policy makers." REVIEW

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BRIEF SUMMARY OF PRESCRIBING INFORMATION

This Brief Summary does not include all the information needed to use LOTEMAX® SM safely and effectively. See full prescribing information for LOTEMAX® SM.

LOTEMAX® SM (loteprednol etabonate ophthalmic gel) 0.38%

For topical ophthalmic use
Initial U.S. Approval: 1998

INDICATIONS AND USAGE

LOTEMAX® SM is a corticosteroid indicated for the treatment of post-operative inflammation and pain following ocular surgery.

DOSAGE AND ADMINISTRATION

Invert closed bottle and shake once to fill tip before instilling drops. Apply one drop of LOTEMAX® SM into the conjunctival sac of the affected eye three times daily beginning the day after surgery and continuing throughout the first 2 weeks of the post-operative period.

CONTRAINDICATIONS

LOTEMAX® SM, as with other ophthalmic corticosteroids, is contraindicated in most viral diseases of the cornea and conjunctiva including epithelial herpes simplex keratitis (dendritic keratitis), vaccinia, and varicella, in mycobacterial infection of the eye and fungal diseases of ocular structures.

WARNINGS AND PRECAUTIONS

Intraocular Pressure (IOP) Increase: Prolonged use of corticosteroids may result in glaucoma with damage to the optic nerve, defects in visual acuity and fields of vision. Steroids should be used with caution in the presence of glaucoma. If this product is used for 10 days or longer, intraocular pressure should be monitored.

Cataracts: Use of corticosteroids may result in posterior subcapsular cataract formation.

Delayed Healing: The use of steroids after cataract surgery may delay healing and increase the incidence of bleb formation. In those diseases causing thinning of the cornea or sclera, perforations have been known to occur with the use of topical steroids. The initial prescription and renewal of the medication order should be made by a physician only after examination of the patient with the aid of magnification such as slit lamp biomicroscopy and, where appropriate, fluorescein staining.

Bacterial Infections: Prolonged use of corticosteroids may suppress the host response and thus increase the hazard of secondary ocular infections. In acute purulent conditions of the eye, steroids may mask infection or enhance existing infection.

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

Fungal Infections: Fungal infections of the cornea are particularly prone to develop coincidentally with long-term local steroid application. Fungus invasion must be considered in any persistent corneal ulceration where a steroid has been used or is in use. Fungal cultures should be taken when appropriate.

Contact Lens Wear: Contact lenses should not be worn when the eyes are inflamed.

ADVERSE REACTIONS

Because clinical trials are conducted under widely varying conditions, adverse reaction rates observed in the clinical trials of a drug cannot be directly compared to rates in the clinical trials of another drug and may not reflect the rates observed in practice. Adverse reactions associated with ophthalmic steroids include elevated intraocular pressure, which may be associated with infrequent optic nerve damage, visual acuity and field defects, posterior subcapsular cataract formation, delayed wound healing and secondary ocular infection from pathogens including herpes simplex, and perforation of the globe where there is thinning of the cornea or sclera. There were no treatment-emergent adverse drug reactions that occurred in more than 1% of subjects in the three times daily group compared to vehicle.

USE IN SPECIAL POPULATIONS

Pregnancy: Risk Summary: There are no adequate and well controlled studies with loteprednol etabonate in pregnant women. Loteprednol etabonate produced teratogenicity at clinically relevant doses in the rabbit and rat when administered orally during pregnancy. Loteprednol etabonate produced malformations when administered orally to pregnant rabbits at doses 4.2 times the recommended human ophthalmic dose (RHOD) and to pregnant rats at doses 106 times the RHOD. In pregnant rats receiving oral doses of loteprednol etabonate during the period equivalent to the last trimester of pregnancy through lactation in humans, survival of offspring was reduced at doses 10.6 times the RHOD. Maternal toxicity was observed in rats at doses 1066 times the RHOD, and a maternal no observed adverse effect level (NOAEL) was established at 106 times the RHOD. The background risk of major birth defects and miscarriage for the indicated population is unknown. However, the background risk in the U.S. general population of major birth defects is 2 to 4%, and of miscarriage is 15 to 20%, of clinically recognized pregnancies. Data: *Animal Data.* Embryofetal studies were conducted in pregnant rabbits administered loteprednol etabonate by oral gavage on gestation days 6 to 18, to target the period of organogenesis. Loteprednol etabonate produced fetal malformations at 0.1 mg/kg (4.2 times the recommended human ophthalmic dose (RHOD) based on body surface area, assuming 100% absorption). Spina bifida (including meningocele) was observed at 0.1 mg/kg, and exencephaly and craniofacial malformations were observed at 0.4 mg/kg (17 times the RHOD). At 3 mg/kg (128 times the RHOD), loteprednol etabonate was associated with increased incidences of abnormal left common carotid artery, limb flexures, umbilical hernia, scoliosis, and delayed ossification. Abortion and embryofetal lethality (resorption) occurred at 6 mg/kg (256 times the RHOD). A NOAEL for developmental toxicity was not established in this study. The NOAEL for maternal toxicity in rabbits was 3 mg/kg/day. Embryofetal studies were conducted in pregnant rats administered loteprednol etabonate by oral gavage on gestation days 6 to 15, to target the period of organogenesis. Loteprednol etabonate produced fetal malformations, including absent innominate artery at 5 mg/kg (106 times the RHOD); and cleft palate, agnathia, cardiovascular defects, umbilical hernia, decreased fetal body weight and decreased skeletal ossification at 50 mg/kg (1066 times the RHOD). Embryofetal lethality (resorption) was observed at 100 mg/kg (2133 times the RHOD). The NOAEL for developmental toxicity in rats was 0.5 mg/kg (10.6 times the RHOD). Loteprednol etabonate was maternally toxic (reduced body weight gain) at 50 mg/kg/day. The NOAEL for maternal toxicity was 5 mg/kg. A peri-/postnatal study was conducted in rats administered loteprednol etabonate by oral gavage from gestation day 15 (start of fetal period) to postnatal day 21 (the end of lactation period). At 0.5 mg/kg (10.6 times the clinical dose), reduced survival was observed in live-born offspring. Doses ≥ 5 mg/kg (106 times the RHOD) caused umbilical hernia/incomplete gastrointestinal tract. Doses ≥ 50 mg/kg (1066 times the RHOD) produced maternal toxicity (reduced body weight gain, death), decreased number of live-born offspring, decreased birth weight, and delays in postnatal development. A developmental NOAEL was not established in this study. The NOAEL for maternal toxicity was 5 mg/kg.

Lactation: There are no data on the presence of loteprednol etabonate in human milk, the effects on the breastfed infant, or the effects on milk production. The developmental and health benefits of breastfeeding should be considered, along with the mother's clinical need for LOTEMAX® SM and any potential adverse effects on the breastfed infant from LOTEMAX® SM.

Pediatric Use: Safety and effectiveness of LOTEMAX® SM in pediatric patients have not been established.

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

NONCLINICAL TOXICOLOGY

Carcinogenesis, Mutagenesis, Impairment of Fertility: Long-term animal studies have not been conducted to evaluate the carcinogenic potential of loteprednol etabonate. Loteprednol etabonate was not genotoxic *in vitro* in the Ames test, the mouse lymphoma tk assay, or in the chromosomal aberration test in human lymphocytes, or *in vivo* in the mouse micronucleus assay. Treatment of male and female rats with 25 mg/kg/day of loteprednol etabonate (533 times the RHOD based on body surface area, assuming 100% absorption) prior to and during mating caused preimplantation loss and decreased the number of live fetuses/live births. The NOAEL for fertility in rats was 5 mg/kg/day (106 times the RHOD).

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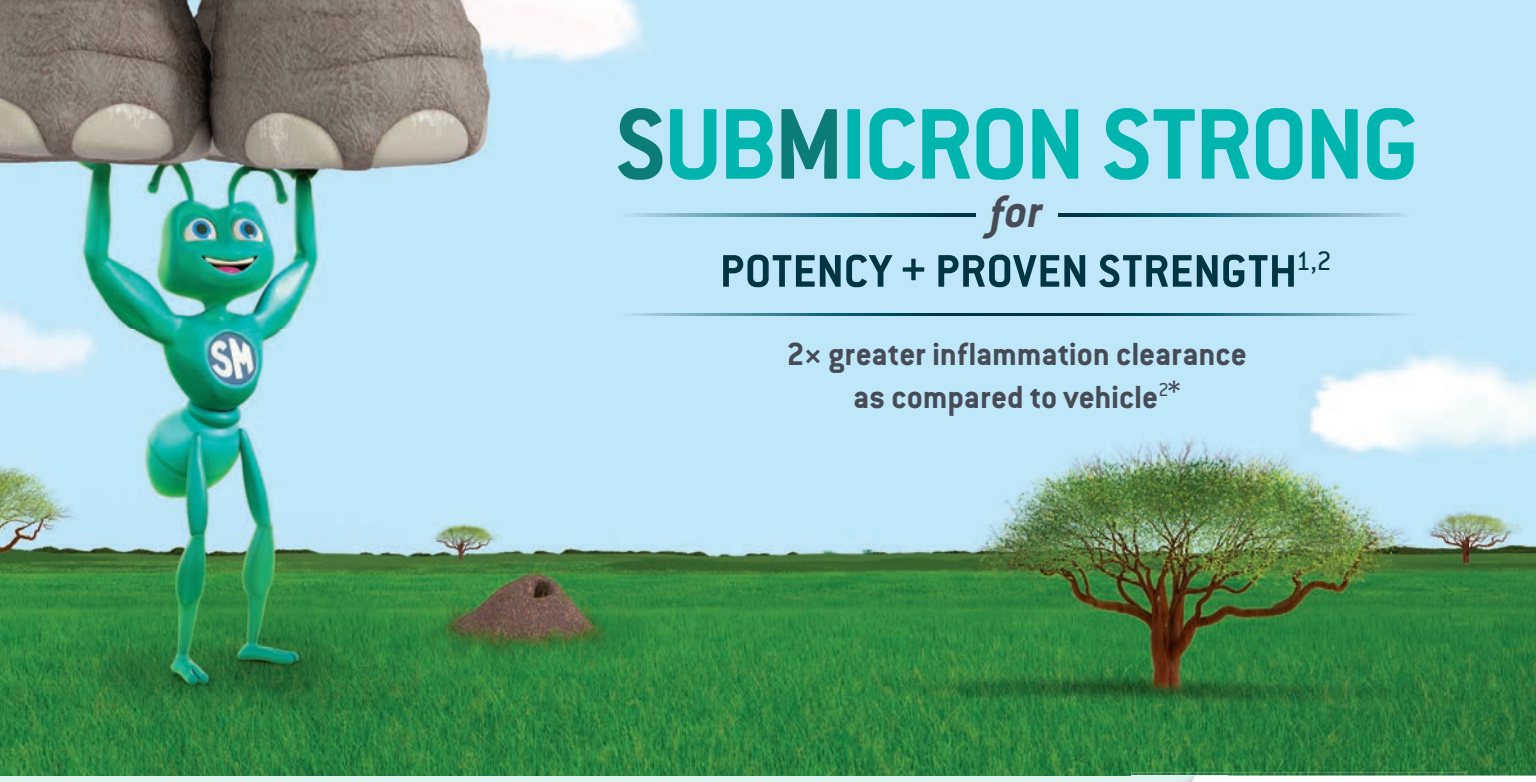

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Clinical significance of these preclinical data has not been established.

LOTEMAX® SM
(loteprednol etabonate ophthalmic gel) 0.38%

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*PROVEN STRENGTH

- **30% of LOTEMAX® SM patients had complete ACC resolution** vs vehicle (15%) at Day 8 (N=371, *P*<0.0001)[1,2†]
- **74% of LOTEMAX® SM patients were completely pain-free** vs vehicle (49%) at Day 8 (N=371, *P*<0.0001)[1,2‡]

†Pooled analysis of Phase 3 clinical studies. **Study 1:** 29% LOTEMAX® SM (N=171) vs 9% vehicle (N=172). **Study 2:** 31% LOTEMAX® SM (N=200) vs 20% vehicle (N=199); *P*<0.05 for all.

‡Pooled analysis of Phase 3 clinical studies. **Study 1:** 73% LOTEMAX® SM (N=171) vs 48% vehicle (N=172). **Study 2:** 76% LOTEMAX® SM (N=200) vs 50% vehicle (N=199); *P*<0.05 for all.

Indication

LOTEMAX® SM (loteprednol etabonate ophthalmic gel) 0.38% is a corticosteroid indicated for the treatment of post-operative inflammation and pain following ocular surgery.

Important Safety Information

- LOTEMAX® SM, as with other ophthalmic corticosteroids, is contraindicated in most viral diseases of the cornea and conjunctiva including epithelial herpes simplex keratitis (dendritic keratitis), vaccinia, and varicella, and also in mycobacterial infection of the eye and fungal diseases of ocular structures.
- Prolonged use of corticosteroids may result in glaucoma with damage to the optic nerve, defects in visual acuity and fields of vision. Steroids should be used with caution in the presence of glaucoma. If LOTEMAX® SM is used for 10 days or longer, IOP should be monitored.
- Use of corticosteroids may result in posterior subcapsular cataract formation.

Important Safety Information (cont.)

- The use of steroids after cataract surgery may delay healing and increase the incidence of bleb formation. In those with diseases causing thinning of the cornea or sclera, perforations have been known to occur with the use of topical steroids. The initial prescription and renewal of the medication order should be made by a physician only after examination of the patient with the aid of magnification such as slit lamp biomicroscopy and, where appropriate, fluorescein staining.
- Prolonged use of corticosteroids may suppress the host response and thus increase the hazard of secondary ocular infections. In acute purulent conditions, steroids may mask infection or enhance existing infections.
- Employment of a corticosteroid medication in the treatment of patients with a history of herpes simplex requires great caution. Use of ocular steroids may prolong the course and may exacerbate the severity of many viral infections of the eye (including herpes simplex).
- Fungal infections of the cornea are particularly prone to develop coincidentally with long-term local steroid application. Fungus invasion must be considered in any persistent corneal ulceration where a steroid has been used or is in use. Fungal cultures should be taken when appropriate.
- Contact lenses should not be worn when the eyes are inflamed.
- There were no treatment-emergent adverse drug reactions that occurred in more than 1% of subjects in the three times daily group compared to vehicle.

You are encouraged to report negative side effects of prescription drugs to the FDA. Visit **www.fda.gov/medwatch** or call **1-800-FDA-1088**.

Please see brief summary of Prescribing Information on adjacent page.

References: 1. LOTEMAX SM Prescribing Information. Bausch & Lomb Incorporated. **2.** Data on file. Bausch & Lomb Incorporated. **3.** Cavet ME, Glogowski S, Lowe ER, Phillips E. Rheological properties, dissolution kinetics, and ocular pharmacokinetics of loteprednol etabonate (submicron) ophthalmic gel 0.38%. *J Ocul Pharmacol Ther.* 2019. doi: 10.1089/jop.2019;35(5):291-300.

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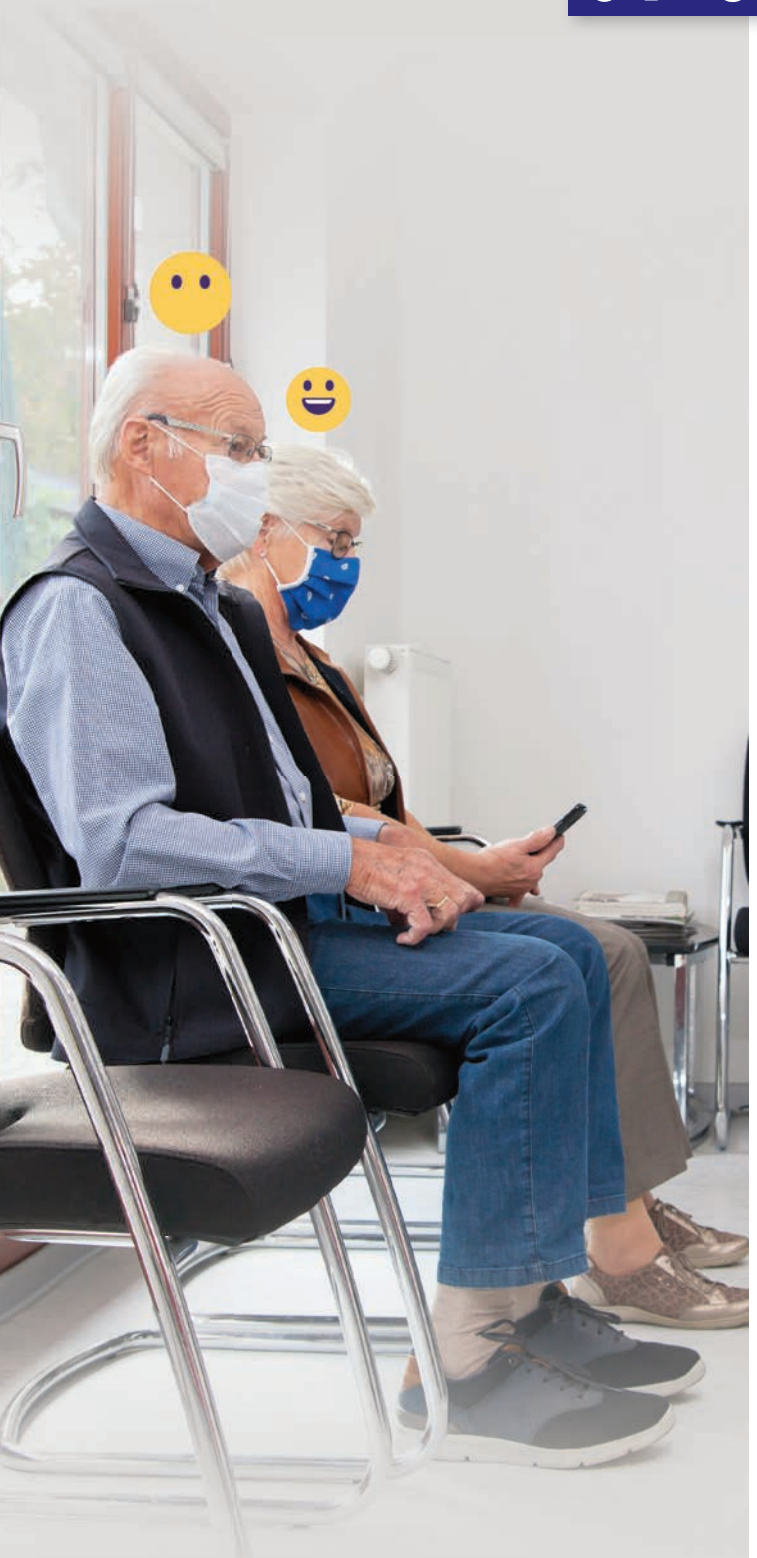

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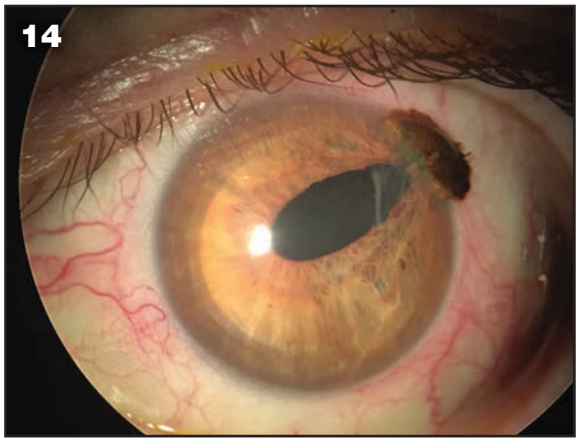

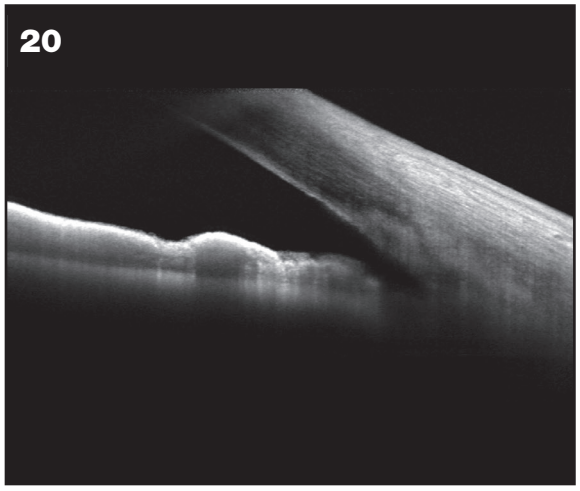

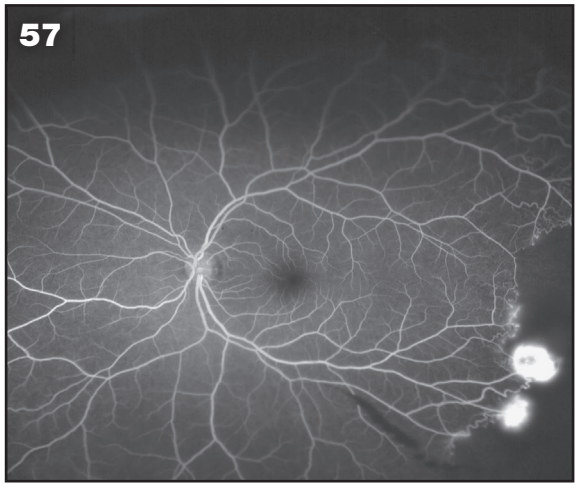

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How to Manage Iris Prolapse

How to anticipate and recognize unwanted trouble, and then respond proactively during surgery.

Sean McKinney, Senior Editor

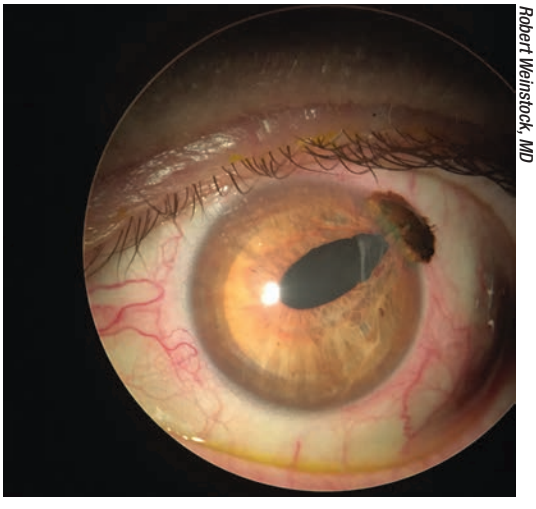
How many times have you been confronted by an iris that either prolapses or threatens to prolapse during cataract surgery? As any surgeon will tell you, once is too often. So: Are there reliable strategies you can use to stop it from recurring? The answer is yes—but not always. Think about the many risk factors you need to consider while managing the intense complexity of a 10-to-20-minute operation on eyes that vary widely anatomically and in terms of intraoperative responses.

"Just being aware of all the risk factors is the most significant precaution you can take preoperatively for patients who are predisposed to iris prolapse," says Audrey R. Talley-Rostov, MD, a partner at Northwest Eye Surgeons in Seattle. "Beyond that, there's not a lot that you can do, per se, until you begin the surgery. We need to be prepared to respond to a lot of possible challenges, some much bigger than others."

In this report, surgeons with a track record of decades of experience in understanding and controlling this common complication will explain how they identify and manage risk factors, implement time-proven preventive measures and effectively respond to acute episodes in the management of iris prolapse.

Game Planning Wisely

Most surgeons group risk factors of iris prolapse into two categories—pre-existing and intraoperative. The most common pre-existing factor is a patient's history of taking alpha-1 adrenergic receptor antagonists (so called alpha-blockers), which can cause intraoperative floppy iris, as first described in a 2005 study by John R. Campbell, MD, and David F. Chang, MD.[1]



Robert Weinstock, MD

Figure 1. Surgeons note that an iris prolapse and an irregularly-shaped pupil appearing at the outset of surgery may require you to halt the procedure and plan an alternative surgical approach.

The major uses of alpha-blockers are for treatment of hypertension and symptomatic benign prostatic hypertrophy, although the primary agent prescribed for men with BPH—tamsulosin (Flomax, Boehringer Ingelheim)—can also help women experiencing difficulty passing urine, as well as female and male patients struggling to pass large kidney stones. Other alpha-blockers used for BPH therapy include terazosin (Hytrin), doxazosin (Cardura), alfluzosin HCL (Uroxatral) and silodosin (Rapaflo).

These agents bind to and inhibit type 1 alpha-adrenergic receptors and thus inhibit smooth muscle con-

traction, compromising the dilator muscle in the patient. The result can be a floppy, billowing iris accompanied by progressive miosis during cataract surgery, with the iris threatening to prolapse through the tunnel and side-port incisions.

Even years after a patient stops taking one of these medications, surgeons note, the patient remains at risk for developing the manifestations of intraoperative floppy iris syndrome.[2]

Up to 90 percent of men develop BPH by their 70s or 80s,[3] a fact that should significantly increase your concern when screening patients.

"Knowing if your patient has any history of taking these medications is very important, obviously, but confirming this history can sometimes be very challenging, as we all know," says Kavitha R. Sivaraman, MD, a partner at the Cincinnati Eye Institute and a clinical assistant professor of ophthalmology at the University of Cincinnati. "If they're poor dilators preoperatively, I will ask them if they have ever taken Flomax or any of these other medications. A lot of times, they don't remember. A look at their current medications to see if any of them are for the treatment of prostate issues can clue you in to a potential risk factor. Or you can ask patients if they have had past prostate issues, which they should remember, and that will help you identify them."

Besides sleuthing for evidence of past alpha-blocker usage, Dr. Talley-Rostov looks for a history of trauma, pseudoexfoliation and, like her colleagues, a pupil that doesn't dilate well, even absent any reported alpha-blocker usage. "We should also be vigilant in patients who've undergone previous ocular surgery, specifically any procedure creating iris transillumination defects," she says. "In addition, remain alert for a previous infection with herpes-zoster disease, a history of uveitis or previous inflammatory disease. All are risk factors."

Robert Weinstock, MD, director of cataract and refractive surgery at the Eye Institute of West Florida, in Largo, looks for a patient with a shallow anterior chamber, as might be found in highly hyperopic patients. "I also check for a history of peripheral laser iridotomy, which tends to damage the iris. Patients with lightly colored eyes also suggest the possibility of anatomical muscular weakness of the iris."

Samuel Masket, MD, in practice in Los Angeles, carefully evaluates patients with a crowded anterior segment. "You can see lenses that are particularly thick and a small corneal diameter," he notes. He urges you to also be aware of the increased risk associated with distinct types of crowded anterior segments, typically present in small hyperopic eyes, as follows:

- microphthalmos, characterized by a small corneal diameter and small anterior and posterior dimensions;
- relative anterior microphthalmos, which involves (even in some myopic patients) an eye of normal anatomic length but a small anterior segment; and
- nanophthalmos, a rare condition, often confused with microphthalmos, characterized by a thickened sclera, a normal-sized anterior segment and a very foreshortened back of the eye.

He also pays attention preoperatively to external forces that may put pressure on the eye. This increase in pressure could be caused by a lid speculum; a thick neck; and elevated episcleral venous pressure in the upper part of the body. The latter factors are often associated with congestive heart failure and chronic obstructive pulmonary disease.

Retrobulbar anesthesia is another risk factor, potentially leading to a hemorrhage in the orbit, which induces posterior pressure that pushes on the eye, increasing the risk of iris

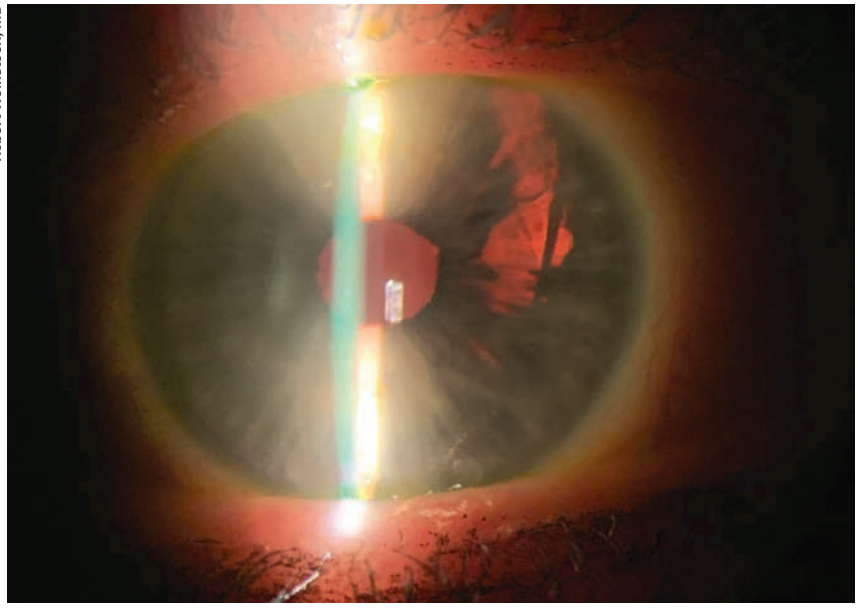

Robert Weinstock, MD

Figure 2. An iris that prolapses early into cataract surgery can lead to additional prolapses if you try to "muscle" through the procedure, according to Robert Weinstock, MD. He notes that the trauma caused by the multiple prolapses brushes off the pigment layer on the back side of the iris, leading to transillumination defects and transparent areas of the iris that light can penetrate, causing visual phenomenon for the patient after the procedure.

prolapse, says Dr. Masket.

Intraoperative Risk Factors

Intraoperative risk factors may or may not be associated with IFIS or other pre-existing risk factors. Once you begin surgery, Dr. Weinstock cautions against making a wound that's too posterior or steep, with a short tunnel into the anterior chamber, particularly in a patient with a pre-existing risk factor.

"A wound that's too large or wide is also ill-advised, potentially allowing leakage and room for the iris to prolapse in the presence of a phaco needle with a lot of play in the wound," he says.

Dr. Sivaraman agrees. "I always pay special attention to wound architecture," she says. "I want to create a true triplanar incision of the appropriate length. A very short wound will also predispose to iris prolapse." In addition, inadvertently contacting the iris with the phaco needle can complicate surgery, damaging the iris and making it more likely to prolapse from the mechanical trauma that occurs, according to Dr. Weinstock. Such a mishap is more of a risk in the smaller anterior segments that Dr. Masket mentions.

Aside from avoiding problems created by poorly structured wounds and a stray phaco needle, you should do certain things if you think you have a patient who's prone to iris prolapse, Dr. Weinstock continues. "Pupil size management is very important," he says. "In a patient who's been exposed to tamsulosin, I recommend that you use a Malyugin Ring to minimize intraoperative miosis. Or you could use three, four, five or even six iris hooks to pull the iris back and out of the way, where you can hold it still so it won't make contact with your phaco needle."

Dr. Talley-Rostov routinely performs small incision bi-manual cataract surgery, which, besides serving as her preferred technique, minimizes the risk of iris prolapse. "I do everything through two 1.3-millimeter incisions," she says. "And then I expand the incision for the IOL insertion. By working with two very small incisions, I can usually maintain fluidics that reduce the incidence of iris prolapse. If necessary, I can also lower the flow, which is important."

All things considered, Dr. Wein-

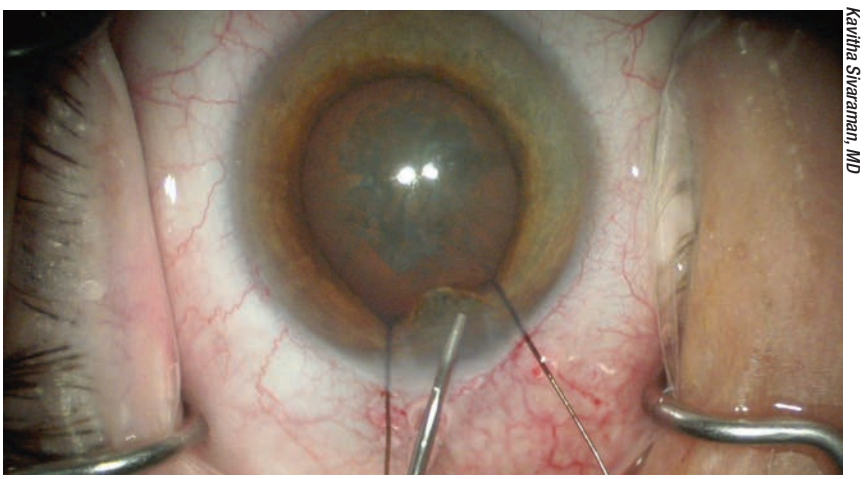

Kavitha Sivaraman, MD

Figure 3. If an iris prolapses at the main incision, Kavitha Sivaraman, MD, notes that you still may be able to safely continue with surgery, placing either one subincisional iris hook or two hooks on either side of the main incision, as shown. Either approach will keep the iris away from the internal opening of the incision. A small amount of dispersive viscoelastic can be used to gently push the iris posteriorly before you enter the eye with another instrument.

stock notes that even the best surgeons can make a bad surgical wound. "If right out of the gate this happens during your surgery, you can suture that inappropriately-sized wound shut and make a fresh wound," he points out. "Or, if the wound is just too wide, you can put a suture through the edge of the wound that tightens it up just in that region. That creates a more controlled wound for your phaco needle to go through without all of that play on the side, which could allow the iris to get out."

Right Solutions

Dr. Weinstock notes that phenylephrine and ketorolac intraocular solution (Omidria, Omeros) helps manage at-risk patients if you put it in the BSS bottle before starting the case. The solution provides a constant stream of dilating and anti-inflammatory agents throughout the case, limiting pupillary constriction and intraoperative floppy iris problems, he notes.

Because some payers don't cover the cost of this prophylactic treatment, some surgeons use alternative solutions. "I rely on intracameral Shugarcaine solution (epinephrine 0.025% and lidocaine 0.75%) in a fortified balanced salt solution," says Dr. Sivaraman. "I tend to use it even for a tamsulosin patient who doesn't have dilation problems. I've never regretted using it."

The Shugarcaine solution, introduced by the late Joel K. Shugar, MD, MSEE, features one part sulfite-free, preservative-free epinephrine mixed with three parts Shugarcaine (unpreserved lidocaine diluted 1:3 with balanced salt solution), designed to spare endothelial cells damage because the pH of the mixture measures 6.90, well above the minimum safe threshold of 6.50.[4]

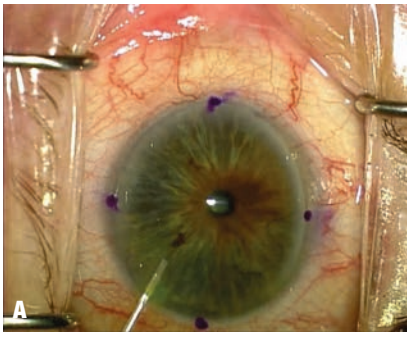
Another solution used for this purpose is cyclopentolate 0.1%, phenylephrine 1.5% and lidocaine 1% (intracameral Lundberg and Behndig's dilation solution). In her experience, however, Dr. Talley-Rostov says the use of sufficiently diluted simple intraocular preservative-free epinephrine can be very helpful.

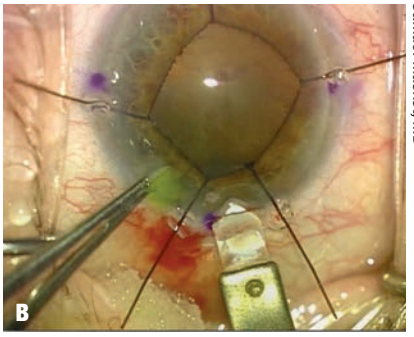
"A lot of surgeons use these mixtures as an adjunct to Omidria, or as a substitute for Omidria," says Dr. Weinstock. "Surgeons will use them when they begin hydrodissection or right when they enter the eye, if the pupil is small. The solutions provide another form of pharmacotherapy that can be used intraoperatively to control the patient's pupil."

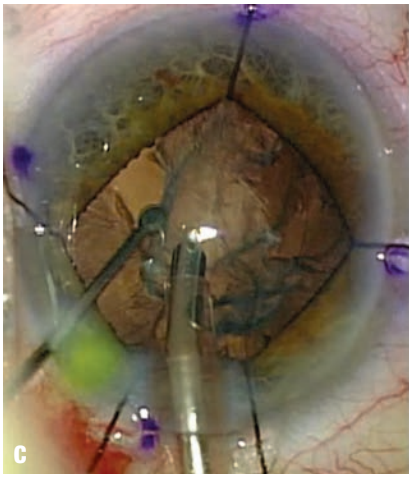
For any patient with an established history of intraoperative floppy iris syndrome, Dr. Masket also administers atropine 1%, t.i.d. for two days before surgery, enhancing the effect of intraoperative intracameral epinephrine, as validated in a 2007 study he led.[5] "Although this preoperative treatment is very effective, you have to keep two important issues in mind," he says. "Number one, the logistics of beginning the therapy two days before surgery, when ophthalmologists typically don't see the patient, has to be coordinated," he says. "The second important point is patients often think they should stop taking tamsulosin in advance of surgery. Doing this can create a low but serious risk of acute urinary retention, which obviously needs to be avoided. I emphasize in the strongest terms to my patients that they need to continue taking their tamsulosin while taking preoperative atropine."

All About Pressure

"Safeguarding the iris is also all about controlling pressure," says Dr. Sivaraman. "If the pressure in the eye is high, the iris is going to come out. The iris is going to follow the pressure gradient. This typically happens a lot during hydrodissection. So after







Samuel Masket, MD

Figures 4. This patient presents with an intumescent cataract with a pupil that won't dilate properly (A). Five Iris hooks are used to expand the pupil (B), allowing for the use of phacoemulsification to remove the nucleus (C) and for eventual placement of an IOL.

I make my capsulorhexis, I burp out quite a bit of that viscoelastic. When I do cortical-cleaving hydrodissection, I use small bursts and decompress the lens—meaning I push the lens down and let the fluid come out around it. The pressure building up in the eye is a very common cause of this problem. Decompress the pressure inside of the eye until it equals the atmospheric pressure outside of the eye."

Dr. Weinstock agrees. "Any time you raise eye pressure, it's going to be pushing out because the fluid has to escape somewhere," he says. "A floppy iris is also going to be forced out of the eye, as it would be after any other trauma. Also, at the end of the surgery, when you're hydrating the wound and sealing the eye, you can overinflate it and then have a sudden burp under heavy pressure. The iris can pop out of the eye."

In eyes with overcrowded anterior segments, Dr. Masket says he prepares for the need to reduce the volume of the vitreous when posterior pressure increases. "I recommend the use of mannitol, 0.5 to 1 gram per kilogram of body weight, or if necessary, prophylactic removal of a small amount of vitreous via pars plana vitrectomy," he says. "First and foremost, however, I strongly recommend my dosing level of mannitol, which I think ophthalmologists often use in doses that are too low and inadequate."

Besides increased vitreous pressure as a cause of rising IOP, Dr. Talley-Rostov considers all other potential causes. "The pressure could be increasing because the patient has to go to the bathroom, or is holding his or her breath and experiencing a Valsava-like effect. We also look for high blood pressure and see if the patient's in pain. We can administer IV lidocaine or pain medication, if we have established IV access preoperatively. Verbal assurance can help reduce pressure in anxious patients. If I find the problem is truly increased IOP and I see the start of an iris prolapse, I'm thinking the patient is at risk for a choroidal hemorrhage. I can use mannitol, of course, but I find the quickest way to reduce IOP acutely in the OR is to provide IV lidocaine, which lowers high IOP very quickly."

The Role of Viscoelastics

Dr. Weinstock uses viscoelastics, such as Viscoat (Alcon), Healon5 (Johnson & Johnson Vision) and OcuCoat (Bausch + Lomb) to help manage the intraoperative risk of iris prolapse. The cohesive and dispersive properties of these OVDs create an effective adjunct to surgery, he says. "A mechanical agent is effective at pushing the iris down and away from the wounds," he says. "It provides space in the eye, which I find helpful. These are great tools for when you're about to operate on an at-risk patient or when you get into trouble during surgery."

However, the dispersive component stays in the eye longer, he cautions. "The biggest risk is that it stays in the eye and then causes postop pressure spikes," he notes. "So you have to make sure you evacuate all of the OVD solution with irrigation and aspiration."

Dr. Masket, however, only uses a cohesive viscoelastic when operating on a patient at high risk for iris prolapse. "The dispersive agents tend not to maintain space well and are very tissue-protective," he says. "The problem is that in certain situations, as the agent comes out of the eye, it tends to bring that tissue with it. So in the case of a crowded anterior segment, positive pressure in the eye or IFIS, I don't recommend the use of dispersive agents. I recommend the use of cohesive agents. That's a very important point and most ophthalmologists aren't aware of it. But I learned it the hard way over a long career."

Dr. Talley-Rostov acknowledges that some surgeons find OVDs such as Healon5 helpful for managing iris prolapse, but she's not one of them. "I tried this a while ago and found

that, in my hands, it was not exceedingly helpful," she says. "I instead prefer to use a Malyugin ring and iris hooks, while using OVD as a cohesive or viscoadaptive agent, as needed. But I find Healon5 is hard to get out of the eye and can contribute to a risk of increased IOP postop. You have to make sure you irrigate it out. Otherwise, you can see a temperature increase, risking a wound burn."

Responding to a Prolapse

Dr. Masket watches for the globe getting firm right before an iris prolapse. "A common mistake is for the surgeon to try to add more OVD through the main incision, pushing on the iris," he says. "That will only tend to make holes in the iris."

If the iris prolapses, he recommends that you remove some of the fluid pressure from the paracentesis, using bimanual I/A or single-port aspiration, allowing you to reduce the internal pressure in the eye and bring the iris back in through the port. "Sometimes you can do it externally," adds Dr. Masket. "But do not—I repeat—do not push the iris through the main incision. The best approach is to soften the eye and then, if the iris doesn't go back in, it might be caught on the lip of the wound. You can massage over the external aspect of the incision, not the iris itself. If that doesn't bring the iris in, then sweep it in through another sideport." Even in this situation, Dr. Masket again warns against pushing on the iris, since doing so could create holes in it rather than settling it back into the eye.

To be as gentle as possible on a prolapsed iris, Dr. Weinstock recommends that you go through a secondary wound and *completely* shallow the chamber.

Unlike many of his colleagues, Dr. Weinstock will gently push on the iris at times. "Depending on where the iris is, you may be able to use a Kuglen hook, phaco needle, I/A tip or viscoelastic to gently push on it and—again, only if the eye is soft—the iris will go back into the eye," he says.

An alternative approach is to make sure only a small amount of fluid remains in the eye, then approach the iris with a side paracentesis and sweep it back into the eye, according to Dr. Weinstock. "It would be very difficult to go into a secondary wound with an instrument if the chamber is completely shallowed," he notes. "So if you're going to go sweep the iris back into the eye, you need to have some chamber depth."

An iris prolapse early in the procedure raises the greatest risks. "After you've drawn a prolapsed iris back into the eye, the risk of recurrent prolapses increases," notes Dr. Weinstock. "Every time it prolapses as you continue with surgery, the trauma of the prolapse brushes off the epithelial pigment layer on the back side of the iris, some of its most fragile tissue," says Dr. Weinstock. "Then you get transillumination defects and transparent areas of the iris that light can penetrate because of the loss of pigment. Patients affected by these issues can notice visual phenomenon after surgery."

An even worse development can occur if the trauma of repeated prolapses damages the sphincter muscle of the iris.

"With this problem, your patient will be left with an irregular pupil, and that can affect the optics and vision and can also be a cosmetic issue," Dr. Weinstock says. "That's probably one of the most severe and worrisome aspects of iris prolapse during surgery. Remember that if you leave the iris prolapse and continue to phaco, the phaco needle—with the iris prolapsed around or under it—is continually rubbing the iris and damaging the tissue because this tissue is so fragile. You have to be careful to avoid a permanent trauma to the iris sphincter or the loss of iris tissue."

Another important consideration is that the fibers that make up the iris surface can be very filamentous. "If you touch or damage the iris, those little strands want to come out of the wound, and it can be hard to get them to stay back in the eye," says Dr. Weinstock. "This is also more of a problem in light-colored eyes." He notes that acetylcholine chloride (Miochol–E) or carbachol (Miostat) can help in these cases by shrinking the pupil and pulling the iris away from the wound.

All Things Considered

Surgeons say there seemingly is no end to the considerations to keep in mind to avoid and manage iris prolapses, which is why no surgeon has ever been able to prevent them entirely. "Quite simply, iris prolapse occurs when you have a discontinuity in pressures between the outside of the eye and the inside of the eye," says Dr. Masket. "So many things can potentiate this discontinuity that it will always be a concern during surgery." REVIEW

Dr. Talley-Rostov is a consultant for Alcon and Bausch + Lomb. Dr. Weinstock is a speaker for Bausch + Lomb. Drs. Sivaraman and Masket have no financial interests in any of the products or companies mentioned in this article.

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Anterior Segment OCT: Still Evolving

Although this hasn't yet become the standard-of-care, more surgeons are finding it very helpful—and the best may lie ahead.

Christopher Kent, Senior Editor

Ever since it first appeared, optical coherence tomography has been evolving. In particular, the scanning speed of commercially available OCT units has steadily increased, allowing the technology to be used for an ever-longer list of clinical tasks. (Faster scanning rates means more sampliing and denser data per volume scanned.)

Anterior segment OCT has been feasible for a number of years, but it's been slow to achieve widespread use in the United States. Here, surgeons discuss its advantages, how it compares to other technologies used for this purpose, and why they believe it's taking a while to become popular. In addition, they offer some pearls for surgeons who are adding this to their list of clinical tools.

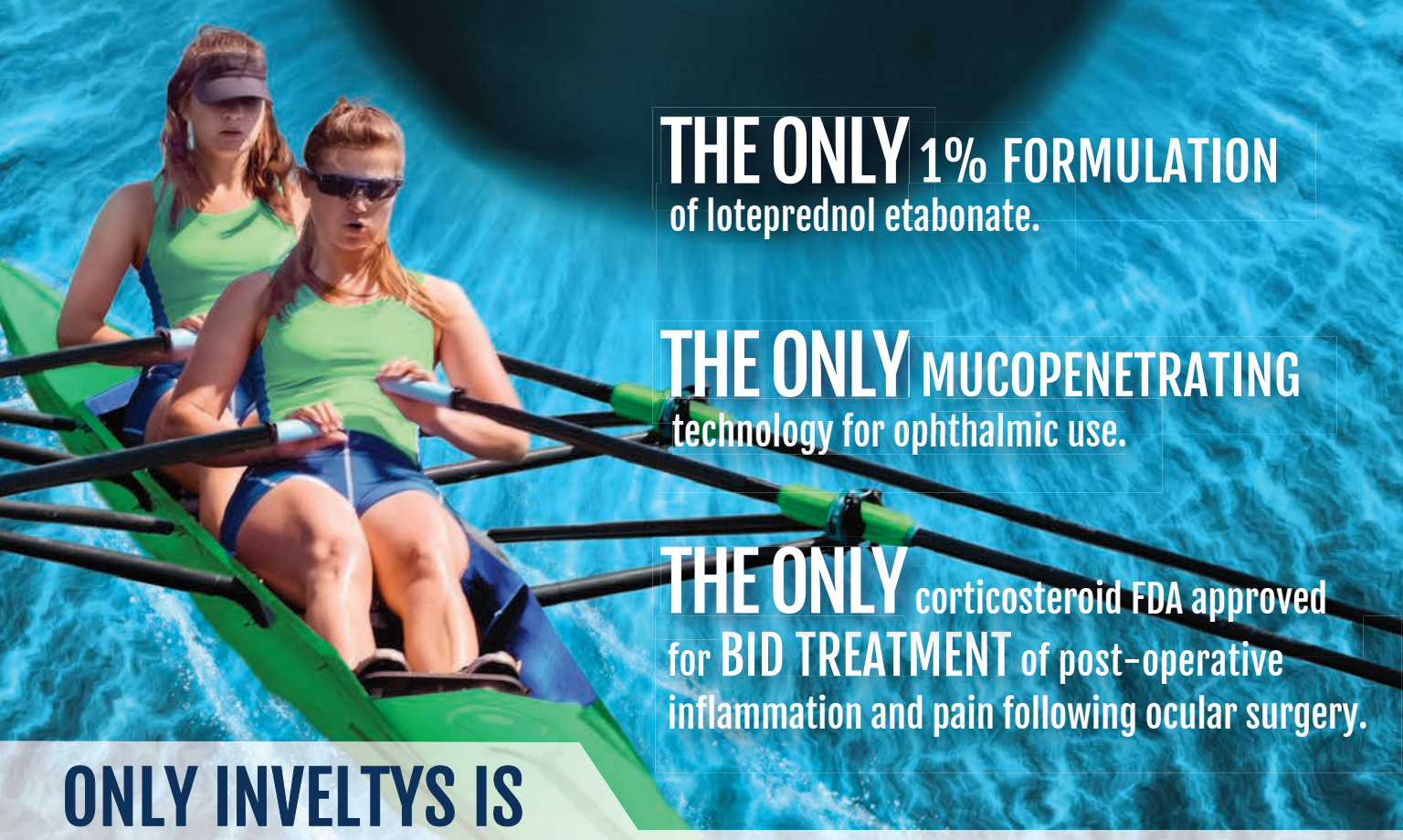
The Advantages of AS-OCT

"Anterior segment OCT can measure almost anything in the front part of the eye," says Joel S. Schuman, MD, FACS, Elaine Langone Professor and vice chairman for research in the department of ophthalmology, and professor of neuroscience and physiology, at NYU Langone Health, NYU Grossman School of Medicine, in New York City. "Depending on the wavelength, you may or may not be able to see deep into the angle or behind the iris, but you can see the various corneal layers in high detail, and there are ways of looking at the cornea's anterior and posterior curvature. For that reason, this technology should have great value for an anterior segment surgeon, especially in cases of corneal pathology, or as a pre- or postoperative tool when performing various types of corneal surgery that involve the endothelium or Descemet's membrane.

"Some OCT instruments [outside the United States] are able to get a 360-degree view of the anterior segment, and some can give you essentially a video of the angle, as if you're sitting inside the eye looking at it," he continues. "If you're interested in looking at the palisades of Vogt, you can see that with anterior segment-OCT; in fact, our group recently received a patent for using anterior segment OCT to evaluate the stem cell niche. (We think that area will be important going forward, in terms of making clinical decisions regarding a patient's stem cell capacity, which will have implications for corneal transplants and other procedures.) When managing keratoconus you can look at the tissue thickness and confirm the corneal structure, especially in the area of the cone. And of course, one of the great powers of OCT is measuring the axial length."

David Huang, MD, PhD, the Peterson Professor of Ophthalmology, and a professor of biomedical engineering at Oregon Health & Science University in Portland, notes that an important advantage of OCT is that it has excellent resolution compared to ultrasound or Scheimpflug imaging. "For example, it can measure the thickness of the epithelium—in some systems also the endothelium—which would be beyond the capability of other technologies," he says. "It also has a wide field of view; some systems can scan a 20-mm area. Confocal microscopy, in comparison, has a very narrow view and requires contact with the eye. I think it's in a sweet spot in terms of resolution and field of view."

Vikas Chopra, MD, medical director of the Doheny Eye Centers Pasa-



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Prolonged use of corticosteroids may suppress the host response and thus increase the hazard of secondary ocular infections. In acute purulent conditions, steroids may mask infection or enhance existing infection.

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

Fungal infections of the cornea are particularly prone to develop coincidentally with long-term local steroid application. Fungus invasion must be considered in any persistent corneal ulceration where a steroid has been used or is in use.

In clinical trials, the most common adverse drug reactions were eye pain (1%) and posterior capsular opacification (1%). These reactions may have been the consequence of the surgical procedure.

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

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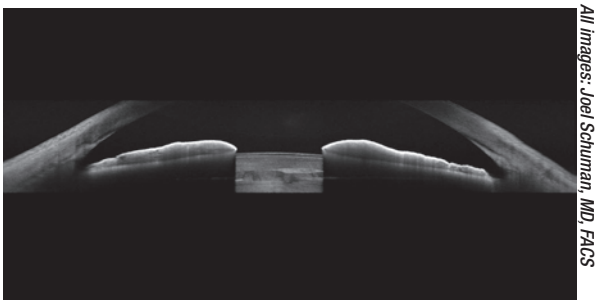
dena, and an associate professor of ophthalmology at the David Geffen School of Medicine at UCLA, notes other advantages. "Anterior segment OCT is non-contact, which is even more important now due to the COVID-19 crisis limiting contact with the patient," he explains. "It can be done with standardized lighting conditions, including complete darkness, and it provides precise measurements that have been shown to have excellent reproducibility and repeatability. In contrast, a procedure like gonioscopy requires contact with the patient's eye, hands-on-training to learn—and sometimes years of practice to master—and it provides subjective measurements. It also requires some light to visualize the angle."



All images: Joel Schuman, MD, FACS

Anterior segment OCT can image the complete anterior chamber, providing an overall view of the anterior chamber angles. (Image captured by Topcon's Triton OCT.)

Drs. Chopra and Huang note the pros and cons of AS-OCT compared to ultrasound biomicroscopy. "UBM is harder to use because it requires eye contact, it's messy and it's not as good at measuring shape," Dr. Huang points out. "I think UBM should be limited to situations where you really need penetration, such as when you want to look through a uveal or iris tumor or evaluate a ciliary body problem. Some biometry measurements, like sulcus-to-sulcus width, need that kind of penetration. But I think OCT will be used a lot more because it's non-contact and it's versatile. There's more justification for buying one."

"UBM allows visualization of the ciliary body and structures posterior to the iris, which anterior segment OCT typically hasn't been able to image well," notes Dr. Chopra. "However, this is now changing. The Heidelberg Anterion can provide stunning 360-degree anterior segment images, along with good imaging of the ciliary body." Dr. Chopra says that he and his colleagues presented a poster at the recent virtual AAO meeting showing how this technology can visualize ciliary muscles and how they behave during active accommodation.

Of course, AS-OCT has other noteworthy limitations. "Anterior chamber OCT scans spot-by-spot, so until you have a very fast system, or a parallel system, it doesn't cover as much area as quickly as some of the other technologies," says Dr. Huang.

Practical Uses in the Clinic

Surgeons are now using anterior segment OCT for several purposes:

• ***When performing LASIK.*** "AS-OCT is helpful for determining the quality of the corneal surface, and can clearly delineate an existing LASIK flap," notes Dr. Chopra.

Dr. Huang points out that it's a highly sensitive way to detect forme fruste keratoconus when evaluating a potential LASIK patient. "I also use it before any retreatment to look at the flap thickness and rule out ectasia," he says.

• ***When performing cataract surgery.*** "AS-OCT can help measure the anterior chamber angle area, which can help determine better approaches for cataract surgery," says Dr. Chopra. "It also measures the anterior lens vault, which can help determine the level of phacomorphic cataract and the expected improvement."

• ***When managing keratoconus.*** "When you combine anterior topography, posterior topography, the epithelial map and the pachymetry map, corneal OCT provides comprehensive information about the cornea, and it can pick up very subtle changes," says Dr. Huang. "The problem is that the topography capability hasn't been FDA-approved and people aren't familiar with the other maps, so there's an educational process that needs to take place for clinicians to be comfortable using this relatively new technology. I use it a lot for this purpose, and I teach it, but it hasn't taken off yet."

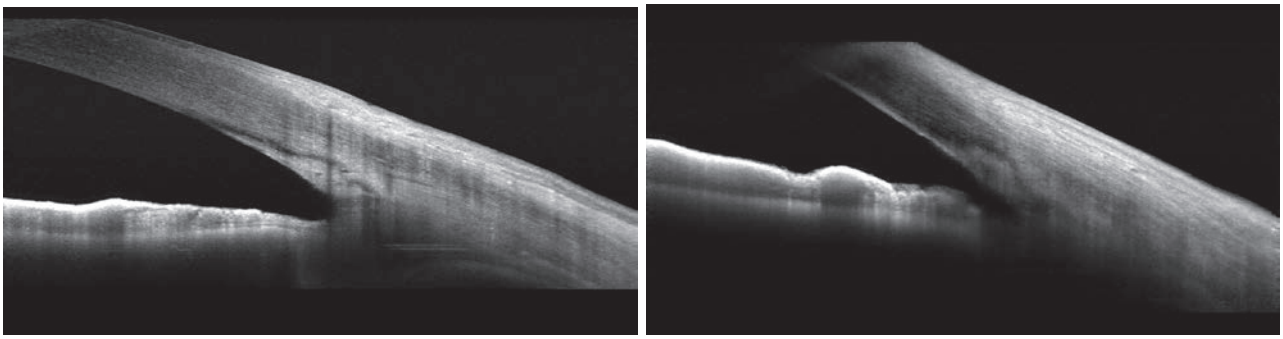
Dr. Chopra says he also uses AS-OCT to monitor corneal thinning in keratoconus patients. "Its detailed corneal pachymetry measurements are very good for this purpose," he notes.

"I also use corneal OCT before performing crosslinking on keratoconus patients, to make sure the cornea is thick enough," Dr. Huang adds.

• ***When treating corneal opacities or irregularities with PTK.*** "In my practice I do transepithelial PTK and topography-guided PTK," says Dr. Huang. "Much of the treatment planning is based on OCT scans, looking at the epithelial thickness map and opacity depth measurement to see how deep the ablation needs to go to get the benefit of epithelial masking."

• ***When calculating IOL power.*** "This is very helpful for eyes that have previously had LASIK," says Dr. Huang. "Many regression-based formulas are specialized for that, and they work pretty well. But I also use the OCT corneal power measurement that includes the posterior surface refractive power. If the two IOL calculations disagree, often the best result comes from averaging them."

Dr. Chopra agrees. "AS-OCT can reveal the differences between anterior corneal curvature and posterior corneal curvature," he says. "That can be useful for IOL measurements



One advantage of anterior segment OCT is that scans can be done in the dark, allowing clinicians to see how closed the angle becomes under these conditions. Above: An angle scanned in light conditions (left) narrows further in the dark (right), but doesn't close. This angle isn't likely to be occludable, and the patient doesn't require laser iridectomy.

when the patient has had refractive surgery."

• ***When performing laser procedures on the iris.*** "Angles can be assessed before and after laser procedures such as iridotomy and iridoplasty, and [the technology can] even confirm the patency of a laser PI," notes Dr. Chopra.

• ***Measuring astigmatism for toric IOLs.*** "The speed of current OCT systems is fast enough to be able to use the corneal map scans to measure topography, astigmatism and aberrations," explains Dr. Huang. "This has been approved outside the United States for several years, but it's more of a research application in the United States right now. We have an NEI grant to study the measurement of astigmatism and topography with corneal OCT, and we're finding it's more accurate than other technologies."

Angle Evaluation in Glaucoma

Anterior segment OCT has multiple potential uses relating to managing glaucoma:

• ***Evaluating potential angle closure.*** "Anterior segment OCT can be very helpful if you want to know whether an angle is going to close in the dark," Dr. Schuman points out. "This is one of the real advantages of AS-OCT technology. You can do an anterior segment-OCT with the lights off, if your environment will permit that, and determine how much the angle closes. Imaging it in dark conditions is probably the best way to determine whether it's occludable."

Dr. Chopra says he uses AS-OCT to examine patients suspicious for narrow angles or angle closure. "We regularly use AS-OCT in our clinic on the first visit, along with assessing the RNFL and performing macular ganglion cell analysis," he explains.

Dr. Chopra points out that AS-OCT and gonioscopy can be quite comparable when analyzing the angle. "However, anterior segment OCT typically finds angles to be narrower than gonioscopy," he says. "That's probably because some pupillary constriction occurs during gonioscopy, since light is used to look at the angle, while an AS-OCT scan can be done in complete darkness. However, surgeons can't use AS-OCT to perform indentation to try to open narrow angles to assess for peripheral anterior synechiae. Nevertheless, AS-OCT can usually distinguish between narrow angles and PAS if an expert evaluator examines the images."

Dr. Schuman believes the tide may be shifting regarding whether gonioscopy or anterior segment imaging is the more reliable tool for evaluating the angle. "Tin Aung, MD, PhD, spoke at the September 2020 FDA Collaborative Communities on Ophthalmic Imaging conference," he says. "One of the things he suggested was that gonioscopy—currently the gold standard for judging things like how open or closed the angle is—probably shouldn't be the gold standard. Imaging should be. It's hard to argue with that, because gonioscopy involves a subjective judgment made by the observer. The observer may or may not be expert, and even expert observers make mistakes."

• ***When performing MIGS procedures.*** Dr. Chopra says he routinely uses AS-OCT when patients are undergoing angle-based minimally invasive glaucoma surgery. "I use it both before and after surgery," he explains. "It's especially useful for teaching residents and Fellows. It lets them see if their targeted procedures have achieved the desired surgical outcomes, in terms of targeting the correct anatomy."

• ***For patient education.*** "The images are incredibly useful for teaching patients about their iridocorneal angle anatomy, especially if they're asymptomatic," says Dr. Chopra. "In my opinion, this greater understanding allows a much-more-informed consent for proceeding with laser iridotomy, laser iridoplasty or cataract extraction to treat angle closure."

• ***When evaluating the condition of the angle.*** While this technology offers some advantages for this purpose, it also has notable limitations. Dr. Schuman says that one potential problem when trying to visualize the

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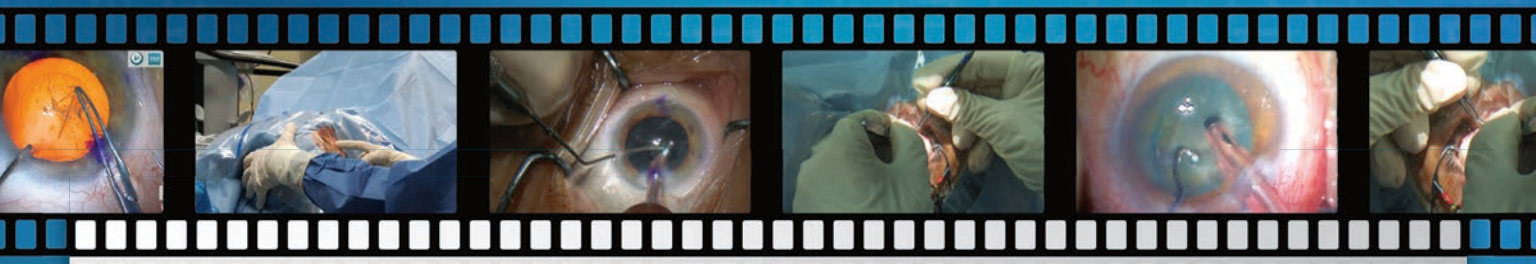

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Episode 60:
"Combined Cataract and Trabecular Microstent Implantation"

Surgical Video by:
Richard J. Mackool, MD

Video Overview:
A patient with glaucoma and previous LASIK undergoes implantation of recently modified trabecular microstents after cataract extraction with IOL implantation. Stent implantation technique, post-refractive surgery IOL calculation methods, and persistent leakage from the clear corneal incision caused by the "flipped lip syndrome" are demonstrated and discussed.

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angle with OCT is that you can have shadowing from the scleral structures of the angle itself. "Sometimes you can see almost the whole angle, but you lose the most posterior portion that's really of interest," he explains. "How much shadowing you see depends on how the images are acquired and the wavelength of the light; the longer the wavelength, the deeper into the angle you'll be able to see. If you're using swept-source OCT with wavelength around 1 µm, then you'll see deeper than with a standard near-infrared OCT.

"I think this has limited the applicability of anterior segment-OCT for viewing the angle, although you can still get a pretty good idea of what's going on," he continues. "If you really want to see the angle structure, the ciliary processes and the relationship of the ciliary process to the iris, UBM is a better technology in most cases. The drawback with UBM is that it requires contact. In many cases anterior segment OCT will provide you with sufficient information to be able to make a clinical decision, so it's worth trying. With it, I can spare the patient some time, and also the contact procedure. However, there may be cases where you won't be able to get an adequate view using AS-OCT."

Dr. Schuman adds that when it comes to visualizing the angle, gonioscopy has some capabilities that anterior segment imaging doesn't. "Those capabilities have to do with what you can see, rather than the openness or closedness of the angle," he explains. "You can see if there are vessels; you can see pigmentation; you can see the color and character of the tissue. But what most people are looking at when they're evaluating the angle is whether the angle is open or closed. Are there synechiae? Is it just appositional when it's closed? Those questions, for the most part, can be answered with imaging. A lot of the value of gonioscopy at this point lies in revealing things that imaging can't reveal.

"The other advantage of gonioscopy is that you can visualize the angle 360 degrees," he adds. "It's awkward and tedious to try to capture 360 degrees with most conventional OCTs that we have in this country. Of course, that's just a matter of engineering. Obviously it can be done, since it's already possible using instruments available outside the United States."

What About Angiography?

Dr. Huang notes that anterior segment OCT angiography is still embryonic, with only a few publications relating to it. "Using this technology you can see corneal, conjunctival and episcleral blood vessels with much higher contrast than you see at the slit lamp," he points out. "You'll be surprised by how many vessels there are! It can also evaluate iris vessels to some extent, unless the eye is heavily pigmented. We're currently looking at iris melanoma and other tumors with longer-wavelength swept-source OCT angiography, which penetrates the tumor better. Tumor vasculature is very sensitive to radiation treatment, making OCT angiography a useful measure of treatment effectiveness."

"The added benefit of using OCTA in the anterior segment is still being investigated," says Dr. Schuman. "In most cases, if an eye has enough neovascularization to be considered abnormal, you'll be able to see it. But OCTA could be useful in some situations, and there are a number of areas to be explored, including cases of neo-

Posterior OCT With Adapter? Or Dedicated Anterior OCT?

Rather than being intended specifically for scanning the anterior segment, many devices are designed to scan the posterior segment and come with a lens that allows anterior scanning. What are the pros and cons of each approach?

"The wavelength is really the big issue in terms of being able to penetrate the scleral tissue that shadows the angle," notes Joel S. Schuman, MD, FACS, Elaine Langone Professor and vice chairman for research in the department of ophthalmology, and professor of neuroscience and physiology, at NYU Langone Health, NYU Grossman School of Medicine, in New York City. "The Visante instrument was specifically designed for the anterior segment. It's a time-domain-based instrument with a wavelength of 1.3 µm. It provides an excellent view of the angle, because a longer wavelength means less tissue shadow.

"However, one problem with an instrument like the Visante that's dedicated to the anterior segment is that people have to buy the machine just for that purpose," he notes. "A second problem is that because the Visante is time-domain, it's much slower. You can't really get an accurate sense of tissue curvature; there could be some distortion because of the time it takes to scan the image. Tomey's CASIA SS-1000 OCT [not available in the United States] is designed just for the anterior segment, and it uses swept-source OCT. It provides a 360-degree video of the angle."

David Huang, MD, PhD, the Peterson Professor of Ophthalmology, and a professor of biomedical engineering at Oregon Health & Science University in Portland, notes that the newer dedicated anterior segment systems generally use swept-source technology with a 1,050-µm or 1,310-µm wavelength. "That wavelength can penetrate deeper and provide a wider scan than a shorter wavelength such as 830 µm," he says. "These instruments capture more of the anterior eye surface—not just the cornea, but also the scleral surface, anterior chamber and the crystalline lens. However, the longer wavelengths have less resolution, so it's more difficult to do things like look at the epithelial thickness or evaluate the endothelium. That requires higher resolution.

"There is a novel full-range spectral-domain OCT technique that can be used to scan the whole anterior segment using the shorter 840-µm wavelengths," he adds. "Using that technique will give you the high-resolution advantage."

—CK

vascularization or tumors."

Dr. Chopra agrees that it's not clear yet how useful anterior segment OCT angiography will be. "Currently, the images tend to be filled with artifacts because the vasculature is in so many planes," he says. "Of course, the software provided by various manufacturers hasn't been optimized for this purpose. That being said, we're currently using AS-OCT angiography in our research setting."

"Anterior segment OCT angiography may be developing more slowly because the diseases it would help to manage are less common than retinal diseases like macular degeneration," Dr. Huang adds. "Companies aren't competing to provide software to perform this kind of imaging or provide automated analysis and measurements. But I think eventually these useful applications will be developed. It will just take a little longer to catch on."

Pearls for Clinical Use

Surgeons offer these tips for those just beginning to use AS-OCT:

• ***Take advantage of the software provided with your instrument.*** "Many devices have software that can help you analyze anterior segment images," Dr. Schuman points out. "That can provide a lot of useful information you couldn't pick up without it."

• ***When measuring depth, measure perpendicularly.*** "I see a lot of people measuring depths such as opacity depth on OCT cross-sections incorrectly," notes Dr. Huang. "If you section the cornea at an oblique angle, you can't measure the depth accurately. You have to have a perpendicular section. The easiest way to do that is to have your technician get a cross-section that goes through the center of the cornea, defined by either the vertex or pupil center, or limbal centering. Then you need a caliper that measures depth perpendicular to the anterior surface."

• ***When looking at the angle, be as perpendicular to the tissue as possible.*** Dr. Schuman makes a related point. "Most surgeons just scan right across the eye, with the eye looking straight ahead," he says. "However, that will give you a distorted view of the angle. When looking at the angle, you want to be as perpendicular to the tissue as you can be. Try different positions, so you can get the best possible image."

• ***Remember to apply the dewarping software correction to depth measurements.*** "This gets rid of the distortion due to the index transition at the air-cornea interface," Dr. Huang explains. "If you do a corneal map scan, the measurements are automatically corrected for those distortions. But if you take a cross-section by doing a line scan, perhaps to measure the depth of a corneal lesion, it will measure it as being much deeper than it really is unless you use the dewarping correction."

• ***Start by working with healthy eyes.*** "Practice makes perfect," notes Dr. Chopra. "Those doing imaging with this technology should start by imaging healthy patients with open angles. That will help the surgeon perfect the techniques that can then be used easily and reliably in more challenging patients with angle narrowing or other angle abnormalities."

• ***Expect a learning curve.*** "Using anterior segment OCT correctly is a learning process," Dr. Huang observes. "You have to learn what to look for in order to evaluate different things. For example, if you want to diagnose forme fruste keratoconus with the existing corneal mapping software that's available in the United States, you'll be looking for epithelial and pachymetric thinning patterns that are different from the patterns you see on topography. So you'll have to take a course or read up on it to learn to do that."

What Lies Ahead?

Given the advantages of AS-OCT, it's worth asking why it's catching on so slowly. "Anterior segment OCT isn't turnkey or routine in most offices at this point, unlike posterior segment OCT imaging," Dr. Schuman points out. "Ophthalmologists are very busy, and any time you do something outside of your routine it takes longer to do it and to interpret it. Also, the number of people who will benefit from this use of OCT will be smaller than the number who benefit from posterior segment OCT imaging, at least initially.

"So, it's not that anterior segment OCT isn't useful—it is," he says. "You can get beautiful images and extract a lot of useful information with it. It's just that the utility of this technology hasn't yet been fully exploited. I do think there will eventually be a paradigm shift. However, it may take doctors a long time to accept machine classification of angle status."

"I think many glaucoma specialists believe that gonioscopy is easy and simple to perform," Dr. Chopra says. "That may be why they haven't incorporated anterior segment OCT into their clinic flow."

"Given the unique advantages of anterior segment OCT," Dr. Huang notes, "it has a lot of room to grow, in terms of being more widely used. That's especially true now that there are high-speed systems available that can do topography and widefield scanning of the entire cornea and beyond. I think it will rapidly progress as a technology." REVIEW

Drs. Schuman and Chopra report no financial ties to any product discussed. Dr. Huang reports that Opto-Vue provides research support to his laboratory and licenses some of the algorithms and technology developed by his research group. He has stock ownership in the company.

Ang-2=angiopoietin-2; Ang-Tie=angiopoietin/Tie; DME=diabetic macular edema; nAMD=neovascular age-related macular degeneration; VEGF=vascular endothelial growth factor.

References: 1. Saharinen P, et al. *Nat Rev Drug Discov.* 2017;16:635-661. **2.** Fiedler U, et al. *Nat Med.* 2006;12:235-239.


PREDATOR
Focus on the threat that's lurking in nAMD and DME – Ang-2, and its ability to inhibit the Ang-Tie pathway[1,2]
Is there another driver of disease hiding just beyond the VEGF pathway? Take a closer look at the crucial role angiopoietins play in vascular instability.[1]
See the potential of Ang-2 at thehiddenpredator.com
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THE WINDOW TO CHANGE
Genentech
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When Your Patients Aren't Happy

Sean McKinney, Senior Editor

How to improve their experience at your practice. (And why it's more critical than ever.)

Like your peers, you always strive to excel as a diagnostician, clinician and surgeon. But what if your patients are healthy yet your practice isn't? What if it's suffering from a bad case of ill will caused by disgruntled patients and the typically related issue of unhappy staff? How do you recognize the symptoms, correct underlying problems and ensure that the improvements you make stay in place?

In this article, surgeons and practice management experts offer advice that you can use to unmask these problems and make needed changes, which, they argue, can help you nip reputation-damaging episodes in the bud.

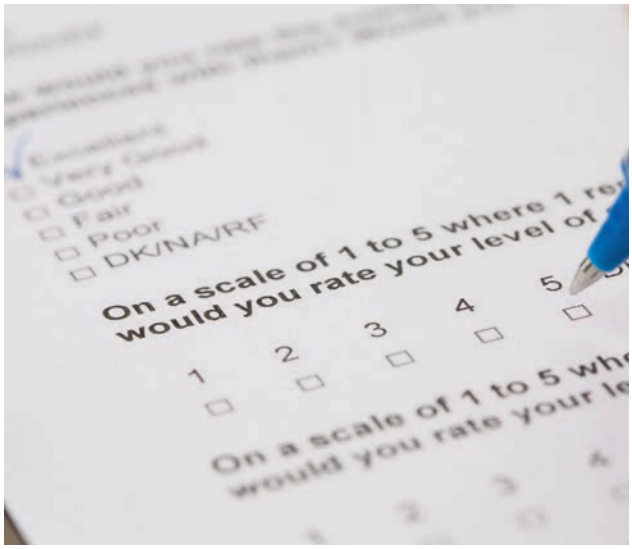
Remembering to Ask

"The best way to find out if you have any of these problems is to ask," says Mark Packer, MD, president of Packer Research Associates in Boulder, Colorado. "The problem is that people won't tell you the truth directly because they feel vulnerable, whether they're patients depending on you to perform good surgery or members of your staff who want to keep working for you."

Besides his background in private practice and his current role as a monitor for FDA trials, Dr. Packer works on practice improvement programs on behalf of drug and equipment makers, helping practices to optimize the patient experience—or, in the parlance of practice management experts, the "journey." He notes that "using an anonymous survey of your patients can help a lot. At the end of the visit, hand the patient an envelope containing the anonymous survey and say, 'I'd really appreciate it if you'd fill this out truthfully. I'll never know what you say personally. I'll just see percentages of survey respondents who answer questions different ways. There

are 20 items on there, so it shouldn't take you long to fill it out."

Dr. Packer recommends asking questions that will help you find out if your patients feel you listen to them and provide clear explanations. Then you can ask about your waiting room: "Was it comfortable? Were the front office staff and receptionist friendly? Did they take care of your questions? If you had an insurance issue, did the staff offer you help with that?"



Regular patient surveys such as this one are critical to obtaining objective evaluations of doctors, staff, waiting times and other aspects of your practice that may need to be changed. Blinded surveys are essential, encouraging patients to candidly express their views.

The top complaint Dr. Packer's practice received on the surveys every year—echoed by other doctors and experts interviewed for this article—focused on long waiting times. "We established a never-attainable goal of zero waiting time and were able to get it down from more than 20 minutes to five minutes," says Dr. Packer. "We worked with each technician to streamline the performance of about 10 tasks, such as pressure checks and manifest refractions, done before the patient was seen by the doctor. Then we manipulated the schedule so a technician would do, on average, one new patient and three returning patients each hour. That's what we could comfortably do. Of course, you always had emergencies and add-ons, but we tried not to let them disrupt our flow, once we implemented these changes. It made a big difference."

Kendall E. Donaldson, MD, MS, a professor and medical director at the Bascom Palmer Eye Institute in Plantation, Florida, likewise recommends you rush to reduce waiting times.

"Patients can love us and they can have perfect vision after surgery, but if we make them wait too long, that is not tolerated," she says. "In our surveys, wait time has the been the biggest source of dissatisfaction."

Dr. Donaldson notes that her practice has benefited from training by the renowned Disney Institute, which helps develop high-performing staff, grounded in superior customer service, competence and confidence. "From the very highest level of administration down to the technicians and front-desk people and support staff, I believe it's very important for everybody to remain on the same page so that patients get the same message from the time they enter your practice until they leave," she says.

South Florida surgeon Alan Aker, MD, says he learned to treat all patients the same early in his career when he performed cataract surgery on one of the leading cataract surgeons in history. "He said, 'Alan, you have to treat me like any other patient,'" recalls Dr. Aker, who owns and operates the Aker Kasten Eye Center with his wife, Ann Kasten, MD, in Boca Raton. (Dr. Aker asks that the prominent surgeon, now deceased, not be named.) "I can still hear him saying it. And he was exactly right. He realized that I was changing the way I did things because it was him. So now we don't change anything for any patient. We treat every patient the way we would treat a governor or a princess—and we've treated both. Whether patients are our mission cases, for which we seek no compensation, or international royalty, we treat them all in a way that we hope will make their heads turn."

Alternative Insights

Daniel Fernandez, chief experience officer at the Symphony Agency, Tampa Bay, Florida, consults with ophthalmologists to optimize their patients' journey from initial appointment to continuity of care. The goals are to increase patient satisfaction scores, throughput, profits and retention of patients and staff, as well as to decrease errors. "The most common mistake a practice can make is to focus solely on patient feedback," he says. "The best-performing practices understand that exceptional care is delivered when the patients, caregivers and leadership teams' expectations are all in alignment."

When trying to help a practice bolster its patient satisfaction scores, he administers what he calls a rapid reputation audit, which includes the following:

1. experience surveys, gathering input from patients, caregivers and the practice's leadership team;

2. assessment and aggregation of all online reviews of the practice;

3. assessment of social media presence, including how well the practice is engaging with patients and poten-

FIRST AND ONLY
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IT'S TIME FOR A BREAKTHROUGH
IT'S TIME FOR TEPEZZA

INDICATION

TEPEZZA is indicated for the treatment of Thyroid Eye Disease.

IMPORTANT SAFETY INFORMATION

Warnings and Precautions

Infusion Reactions: TEPEZZA may cause infusion reactions. Infusion reactions have been reported in approximately 4% of patients treated with TEPEZZA. Reported infusion reactions have usually been mild or moderate in severity. Signs and symptoms may include transient increases in blood pressure, feeling hot, tachycardia, dyspnea, headache, and muscular pain. Infusion reactions may occur during an infusion or within 1.5 hours after an infusion. In patients who experience an infusion reaction, consideration should be given to premedicating with an antihistamine, antipyretic, or corticosteroid and/or administering all subsequent infusions at a slower infusion rate.

Preexisting Inflammatory Bowel Disease: TEPEZZA may cause an exacerbation of preexisting inflammatory bowel disease (IBD). Monitor patients with IBD for flare of disease. If IBD exacerbation is suspected, consider discontinuation of TEPEZZA.

EXPLORE THE VIRTUAL BOOTH AT
TEPEZZAexperience.com

Visit the interactive virtual booth to test your knowledge of Thyroid Eye Disease (TED), see the breakthrough data for TEPEZZA, and experience TED through a patient's eyes.

Hyperglycemia: Increased blood glucose or hyperglycemia may occur in patients treated with TEPEZZA. In clinical trials, 10% of patients (two-thirds of whom had preexisting diabetes or impaired glucose tolerance) experienced hyperglycemia. Hyperglycemic events should be managed with medications for glycemic control, if necessary. Monitor patients for elevated blood glucose and symptoms of hyperglycemia while on treatment with TEPEZZA. Patients with preexisting diabetes should be under appropriate glycemic control before receiving TEPEZZA.

Adverse Reactions

The most common adverse reactions (incidence ≥5% and greater than placebo) are muscle spasm, nausea, alopecia, diarrhea, fatigue, hyperglycemia, hearing impairment, dysgeusia, headache, and dry skin.

Please see Brief Summary of Prescribing Information on following page.

HORIZON

TEPEZZA®
teprotumumab-trbw

TEPEZZA™
teprotumumab-trbw

For injection, for intravenous use

Brief Summary - Please see the TEPEZZA package insert for full prescribing information.

INDICATIONS AND USAGE

TEPEZZA is indicated for the treatment of Thyroid Eye Disease.

WARNINGS AND PRECAUTIONS

Infusion Reactions

TEPEZZA may cause infusion reactions. Infusion reactions have been reported in approximately 4% of patients treated with TEPEZZA. Signs and symptoms of infusion-related reactions include transient increases in blood pressure, feeling hot, tachycardia, dyspnea, headache and muscular pain. Infusion reactions may occur during any of the infusions or within 1.5 hours after an infusion. Reported infusion reactions are usually mild or moderate in severity and can usually be successfully managed with corticosteroids and antihistamines. In patients who experience an infusion reaction, consideration should be given to pre-medicating with an antihistamine, antipyretic, corticosteroid and/or administering all subsequent infusions at a slower infusion rate.

Exacerbation of Preexisting Inflammatory Bowel Disease

TEPEZZA may cause an exacerbation of preexisting inflammatory bowel disease (IBD). Monitor patients with IBD for flare of disease. If IBD exacerbation is suspected, consider discontinuation of TEPEZZA.

Hyperglycemia

Hyperglycemia or increased blood glucose may occur in patients treated with TEPEZZA. In clinical trials, 10% of patients (two-thirds of whom had preexisting diabetes or impaired glucose tolerance) experienced hyperglycemia. Hyperglycemic events should be controlled with medications for glycemic control, if necessary.

Monitor patients for elevated blood glucose and symptoms of hyperglycemia while on treatment with TEPEZZA. Patients with preexisting diabetes should be under appropriate glycemic control before receiving TEPEZZA.

ADVERSE REACTIONS

The following clinically significant adverse reactions are described elsewhere in the labeling:

- Infusion Reactions [see Warnings and Precautions]
- Exacerbation of Inflammatory Bowel Disease [see Warnings and Precautions]
- Hyperglycemia [see Warnings and Precautions]

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 TEPEZZA was evaluated in two randomized, double-masked, placebo-controlled clinical studies (Study 1 [NCT:01868997] and Study 2 [NCT:03298867]) consisting of 170 patients with Thyroid Eye Disease (84 received TEPEZZA and 86 received placebo). Patients were treated with TEPEZZA (10 mg/kg for first infusion and 20 mg/kg for the remaining 7 infusions) or placebo given as an intravenous infusion every 3 weeks for a total of 8 infusions. The majority of patients completed 8 infusions (89% of TEPEZZA patients and 93% of placebo patients).

The most common adverse reactions (≥5%) that occurred at greater incidence in the TEPEZZA group than in the control group during the treatment period of Studies 1 and 2 are summarized in Table 1.

Table 1. Adverse Reactions Occurring in 5% or More of Patients Treated with TEPEZZA and Greater Incidence than Placebo

Adverse Reactions	TEPEZZA N=84 N (%)	Placebo N=86 N (%)
Muscle spasms	21 (25%)	6 (7%)
Nausea	14 (17%)	8 (9%)
Alopecia	11 (13%)	7 (8%)
Diarrhea	10 (12%)	7 (8%)
Fatigue[a]	10 (12%)	6 (7%)
Hyperglycemia[b]	8 (10%)	1 (1%)
Hearing impairment[c]	8 (10%)	0
Dysgeusia	7 (8%)	0
Headache	7 (8%)	6 (7%)
Dry skin	7 (8%)	0

a - Fatigue includes asthenia
b - Hyperglycemia includes blood glucose increase
c - Hearing impairment (includes deafness, eustachian tube dysfunction, hyperacusis, hypoacusis and autophony)

Immunogenicity

As with all therapeutic proteins, there is potential for immunogenicity. The detection of antibody formation is highly dependent on the sensitivity and specificity of the assay.

In a placebo-controlled study with TEPEZZA, 1 of 42 patients treated with placebo had detectable levels of antidrug antibodies in serum. In the same study, none of the 41 patients treated with TEPEZZA had detectable levels of antidrug antibodies in serum.

USE IN SPECIFIC POPULATIONS

Pregnancy

Risk Summary

Based on findings in animals and its mechanism of action inhibiting insulin-like growth factor-1 receptor (IGF-1R), TEPEZZA may cause fetal harm when administered to a pregnant woman. Adequate and well-controlled studies with TEPEZZA have not been conducted in pregnant women. There is insufficient data with TEPEZZA use in pregnant women to inform any drug associated risks for adverse developmental outcomes. In utero teprotumumab exposure in cynomolgus monkeys dosed once weekly with teprotumumab throughout pregnancy resulted in external and skeletal abnormalities. Teprotumumab exposure may lead to an increase in fetal loss [see Data]. Therefore, TEPEZZA should not be used in pregnancy, and appropriate forms of contraception should be implemented prior to initiation, during treatment and for 6 months following the last dose of TEPEZZA.

If the patient becomes pregnant during treatment, TEPEZZA should be discontinued and the patient advised of the potential risk to the fetus.

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

Data

Animal Data

In an abridged pilot embryofetal development study, seven pregnant cynomolgus monkeys were dosed intravenously at one dose level of teprotumumab, 75 mg/kg (2.8-fold the maximum recommended human dose [MRHD] based on AUC) once weekly from gestation day 20 through the end of gestation. The incidence of abortion was higher for the teprotumumab treated group compared to the control group. Teprotumumab caused decreased fetal growth during pregnancy, decreased fetal size and weight at caesarean section, decreased placental weight and size, and decreased amniotic fluid volume. Multiple external and skeletal abnormalities were observed in each exposed fetus, including: misshapen cranium, closely set eyes, micrognathia, pointing and narrowing of the nose, and ossification abnormalities of skull bones, sternebrae, carpals, tarsals and teeth. The test dose, 75 mg/kg of teprotumumab, was the maternal no observed adverse effect level (NOAEL).

Based on mechanism of action inhibiting IGF-1R, postnatal exposure to teprotumumab may cause harm.

Lactation

Risk Summary

There is no information regarding the presence of TEPEZZA in human milk, the effects on the breastfed infant or the effects on milk production.

Females and Males of Reproductive Potential

Contraception

Females

Based on its mechanism of action inhibiting IGF-1R, TEPEZZA may cause fetal harm when administered to a pregnant woman (see Use in Specific Populations). Advise females of reproductive potential to use effective contraception prior to initiation, during treatment with TEPEZZA and for 6 months after the last dose of TEPEZZA.

Pediatric Use

Safety and effectiveness have not been established in pediatric patients.

Geriatric Use

Of the 171 patients in the two randomized trials, 15% were 65 years of age or older; the number of patients 65 years or older was similar between treatment groups. No overall differences in efficacy or safety were observed between patients 65 years or older and younger patients (less than 65 years of age).

OVERDOSAGE

No information is available for patients who have received an overdosage.

PATIENT COUNSELING INFORMATION

Embryo-Fetal Toxicity

Advise females of reproductive potential that TEPEZZA can cause harm to a fetus and to inform their healthcare provider of a known or suspected pregnancy.

Educate and counsel females of reproductive potential about the need to use effective contraception prior to initiation, during treatment with TEPEZZA and for 6 months after the last dose of TEPEZZA.

Infusion-Related Reactions

Advise patients that TEPEZZA may cause infusion reactions that can occur at any time. Instruct patients to recognize the signs and symptoms of infusion reaction and to contact their healthcare provider immediately for signs or symptoms of potential infusion-related reactions.

Exacerbation of Inflammatory Bowel Disease

Advise patients on the risk of inflammatory bowel disease (IBD) and to seek medical advice immediately if they experience diarrhea, with or without blood or rectal bleeding, associated with abdominal pain or cramping/colic, urgency, tenesmus or incontinence.

Hyperglycemia

Advise patients on the risk of hyperglycemia and, if diabetic, discuss with healthcare provider to adjust glycemic control medications as appropriate. Encourage compliance with glycemic control.

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HORIZON

Martha C Tello, BGS, COMT, OSC

What would you tell a forgetful patient who erupts in your chair because you haven't delivered sharp near, intermediate and distance vision that wasn't possible in her case?

tial patients;

4. a competitive analysis; and

5. a review of the good and bad information about the practice and its doctors that might surface during a Google search.

Thomas P. Jeffrey, president of the SullivanLuallin Group, a consulting firm in San Diego that uses a variety of tools to help ophthalmologists improve the patient experience, says practices need to faithfully follow "service protocols" as rigidly as they follow clinical protocols.

"I would say that it doesn't really matter if people in the office are having a bad day," he notes. "It comes down to whether you're following your protocols. That includes smiling, warmly greeting patients and calling them by their names. We recommend putting a clear model in place for your practice to follow. Your team members must know what you expect of them and they must know how to meet your expectations."

After many years of doing patient surveys and working with practices, Mr. Jeffrey says his company has found that employees typically respond positively to supportive feedback more than to compensation. Patients, in turn, mirror this response because they tend to judge you by how you treat your employees.

"We talk about praise in public and counsel in private," he adds. "A warm hand-off of the patient between the staff and the physician—those types of things."

Your direct personal approach to the patient is also critical, according to Andrew Golden, MD, a family practice physician and medical director at SullivanLuallin. He urges you to follow the time-tested advice of Sir William Osler, who helped establish the field of internal medicine, co-founded Johns Hopkins University School of Medicine in 1893 and helped develop the system of clinical medical education used to this day.

"Osler said, 'The good physician treats the disease; the great physician treats the patient who has the disease,'" Dr. Golden recalls. "Being an excellent diagnostician, clinician and surgeon is not enough anymore, if it ever was, considering Osler said that it wasn't enough more than a century ago. You really have to provide individualized care to make a difference to the patient."

Martha C. Tello, BGS, COMT, OSC

Kendall E. Donaldson, MD, MS, listens thoroughly and repeats her documented preop instructions, typically calming the patient. Above all, she says, she treats the unhappy patient "like a VIP."

Are You the Problem?

Your demeanor can significantly affect how your patients rate your practice. Just ask Dr. Packer. "One of my partners was impossibly taciturn and impatient with people, acting as if they should just take his advice with-

The Patient's Always Right

Mark Packer, MD, president of Packer Research Associates in Boulder, Colorado, says he learned early in his career to never tell patients they're wrong. A high-profile public official asked him to perform minor oculoplasty on her slightly droopy upper eyelids, in a subtle manner that would not suggest to people that she had undergone cosmetic surgery. She returned postoperatively six weeks later, complaining that no one had noticed the surgery, he recalls.

"At first I said, 'you told me you didn't want anyone to notice.' Oh, was that a bad way to go with her," recalls Dr. Packer with a chuckle. "She told me she didn't appreciate what I said. So I had to back myself out of that hole. I promised her a touch-up at no charge, and that made her happy. Boy was I grateful. This public official was not going to be out there telling people I didn't provide her with what she wanted. After that, I'd always listen to any issue at hand and not take it personally. The most important thing is not to get into this type of disagreement and instead to solve the problem, whatever that problem is. Should I fix the problem for free? My answer is: always, always, always. You can't calculate the damage an unhappy patient can do to you out there in the community. It's too much and it's just not worth it."

If the cost of offering free enhancements or make-up procedures is a concern, Dr. Packer urges you to build the cost into the price you charge. "Bill whatever you think is fair. That's the beauty of these procedures. If you find your enhancement costs are 5 to 10 percent, on average, build that extra cost into your price."

—SM

out asking any questions," he recalls.

On the practice surveys, the partner consistently received zeroes and ones on a scale of one to five for most questions. "It was incontrovertible evidence that patients didn't like his approach," says Dr. Packer. "I knew it first-hand because many patients switched to me, telling me that doctor X never took enough time with them."

Like Dr. Packer, Dr. Donaldson recommends carefully evaluating objective data about how patients respond to you. "You think you're doing great in this area until you start looking at the numbers," she says. "Analyzing aspects of the care you provide in detail is very important, whether it be the patient experience or the surgical outcomes."

As a provider in the University of Miami Health System, Dr. Donaldson receives the results of monthly surveys that present her with a percentage-based overall rating, plus a finding that shows what percent of survey respondents would recommend her practice to a potential patient.

More specifically, the scores show whether a doctor:

- provides instructions that are easy for the patient to understand;
- knows important aspects of the patient's medical history;
- respects what patients say;
- spends enough time with the patients.

"I get a report on my staff and me, so I can see how we're doing," she says. "This objective information is very helpful to us in making positive changes."

The objective insights that most helped Drs. Aker and Kasten came from a pricey consulting company that parked at their practice for more than a year, 35 years ago. "At first, I thought they were too expensive," admits Dr. Aker. "But they were more than worth it." The consultant recommended elimination of the eye center's pyramid management structure, suggesting the creation of five self-managing teams that allowed the husband-and-wife surgeons to focus almost exclusively on providing quality care. With accountability spread throughout the center, Dr. Aker says their practice self-downsized from 72 to 56 employees who now provide more efficient care that better meets the needs of patients.

"We'd been operating under the Peter Principle," he reflects with a laugh. "Instead of getting rid of employees who weren't working out in particular positions, we were pushing them to the side and giving them other jobs, then hiring other people to replace them. Now, we let our staff take care of managing what needs to be managed in their respective areas and, as a result, the patient experience has never been better. We used to look for people with good experience and skills and try to train them to be nice. What you want to do is look for nice people and train them to be good at what they do. If a new employee has a smiling face and the right attitude, they can learn fast. Our practice is now 40 years old and we've never had a lawsuit."

Mr. Fernandez says ophthalmologists often fail to appreciate deficiencies in their management or personal style that could affect patient satisfaction. "When your physician reviews speak to your ability to deliver exceptional outcomes but mention nothing about personal demeanor, this is usually a good indicator that things need to change," he says. "While patients may respect your expertise, what they're looking for these days are doctors and support people they can relate to. I suggest looking for simple ways to connect."

When doing observational work in practices, Dr. Golden asks ophthalmologists to rate the importance of patient satisfaction on a scale of one to 10. "That question is critical,"

he says. "I find that physicians who aren't very good at satisfying patients rate patient satisfaction as a lower priority. Cognitively, they have to change that priority or they're never going to improve."

Changing Things Up

Sometimes increasing patient satisfaction can boil down to revamping your office layout, patient flow and other aspects of your physical practice. Ophthalmologists and consultants weigh in on what modifications can produce the best results.

"In our case we were stuck with what we had—one waiting room and no dilation room—because of space limitations," says Dr. Packer. "We gave patients something to do while they were dilating, such as iPads with questionnaires that would help them understand more about what might have been affecting them, such as dry eye, cataracts and other conditions. Once patients were seen by technicians and they were waiting for a doctor, if they were doing something that was tailored to them personally, it kept them busy and made the time go by faster."

When modifying her practice, Dr. Donaldson responded to an analysis of waiting and processing times. "We now have all the technicians clustered in one area and all of the physicians together in another area," she says. "We used to have a technician stay with the physician and patient."

The practice also now clusters similar types of patients. "For example, ocular surface disease patients [cluster together], allowing us to concentrate a certain period of time on those patients," she continues. "We put the postoperative patients together so their visits can be better expedited. We schedule certain half-days for refractive patients. By grouping these patients by half-days or by other time frames needed to ensure efficient, high-quality care, you can expedite their flow through the office."

She also recommends that her colleagues visit other practices to see how the practices handle schedules and patient management. "It gives you another perspective on what you're doing," she notes. "You tend to get boxed in on what you're doing and continue to make the same mistakes, doing things the same way, just because you haven't been exposed to another way of doing it."

"Efficiency should be measured and improved. Seconds add up to minutes, saving time that increases productivity and time spent with patients."

Time management and efficiency should be constantly measured and improved. "Seconds add up to minutes, saving time that increases productivity and time spent with patients," says Mr. Jeffrey of the SullivanLualin Group. "The physician shouldn't be walking longer distances than necessary to reach patients. One effective approach is setting up access to the EHR in the hallway. The doctor can more efficiently gather needed information before entering a room to see the next patient."

Constantly setting and meeting patient expectations is also important. "For example, you might need to tell a patient that the doctor has had to do emergency surgery and will be 45 minutes late," says Mr. Jeffrey. "Offer the patient the opportunity to leave the office and receive a text message when the doctor's ready. Or, reschedule the visit. Most patients will say they'll just wait until the doctor is ready. Allowing the patient to participate in the decision-making process can make a positive difference, fostering more satisfaction. The physician should also apologize for making the patient wait. There's a tendency when things aren't going smoothly to shy away from this type of simple communication. But this is when you want to be more outgoing with patients. Also, make sure the right hand knows what the left hand is doing. If a delay results in a patient not getting a test, for example, that's really going to affect quality of care. All these little things go a long way toward achieving success."

Managing Disgruntled Patients

Many patients don't remember—or at least don't appreciate—that you told them preop about the risks and less-than-perfect results that were possible. How do you avoid these communication failures and resulting patient complaints?

"The main thing here is setting expectations beforehand and emphasizing if the patient has an extra risk factor, such as pseudoexfoliation syndrome, a history of Flomax treatment in a patient who has a non-dilating pupil, or macular degeneration in a patient that makes implantation of a premium IOL inappropriate for him," says Dr. Donaldson. "You really have to spend extra time emphasizing these points and documenting in the chart what you've communicated to the patient. I'm also careful to repeat the same general message about cataract surgery and premium IOLs. And then I say, 'In your case, this is what I recommend and this is the special risk factor for you.' I know exactly what I've said to the patient because I've scripted it."

When one of Dr. Aker's patients

reports dissatisfaction to him, he focuses intently on the patient. "I look the patient right in the eye and I say, 'The first thing I want to get across to you is that I am on your side. I want to hear everything you have to say. I'm going to do everything in my power to make this right and make you happy.' We've given patients back money paid for premium IOLs when they've got what on paper looks like a perfect result—good distance, intermediate and near vision."

Dr. Aker says he goes to any length to meet a patient's needs, including giving every postop patient his mobile phone number so the patient can call with questions. "I call every patient the night of surgery to make sure he or she is doing okay," he adds.

Martha C Tello, BGS, COMT, OSC

Without the close connection to your patients so easily maintained before COVID-19, as shown here, you can still use good communication strategies to keep them on your side.

Despite Best Efforts

The issue of troubled patients will always persist, surgeons and consultants say. It's best to have a coordinated strategy for handling them.

"When you recognize that a patient who has undergone surgery or medical treatment is unhappy, you have to rise to another level of care and treat that patient like a VIP," says Dr. Donaldson. "I have a staff member who is very patient- and customer-service oriented. I assign her to patients who need this extra care. She makes sure the patient doesn't wait, spends extra time talking to the patient and then she comes directly to me. I like to get a feel for how the patient is coming along. I want to make sure the patient is getting the right level of customer service."

Dr. Packer followed the same approach when he was in practice. "We had an unofficial policy on this," he says. "If patients seemed like they were going to be disruptive, you never waited. You took them from the technician working them up directly to the doctor. You don't let them back out into the waiting room, where they could fill other patients' heads with negative comments."

Dr. Aker says his practice schedules disgruntled patients for the end of the day, when they're less likely to negatively affect other patients. "They're marked on our schedule as patients requiring special attention," he notes. "When they arrive, they're quickly escorted away from other patients. When they get worked up in the back, everyone is aware we're giving this patient a lot of TLC."

He recommends searching for problems behind problems. "Often, the disgruntled patient is somebody's mother and the kids have abandoned her, "he says." Or the kids don't call. The support that was there is gone. The husband may have left or passed away, and she's holding all the bad cards. She just feels like no one cares about her. We want to love these patients to the point of confusion.

"We had one woman who was notorious in her community for being unhappy about everything. We ended up becoming very good friends with her. She had no choice. Sometimes, when these patients leave after a visit or a procedure, it's almost like they don't want to leave."

Worth Your Trouble

Turning unhappy patients into goodwill ambassadors for your practice might not affect your surgical outcomes. However, in this era of patient-centered care and the increasing influence of patient-reported outcomes, experts say it should be an important objective. Vocal complaints and negative Yelp reviews can strike like lightning in a world connected by tweets, text messages and online postings. Beyond this reality, the effect of patient satisfaction on your status as a provider dependent on payments from the federal government and health insurance plans demands serious consideration of patient satisfaction.

"The days of paper surveys that collected dust in the corner of the administration office are long gone," says Mr. Fernandez. "Now, more than ever, we must focus on delivering exceptional human-centric care to patients if we want to retain them. They know they have choices."

Dr. Golden notes that a lot of reimbursement matters depend on patient satisfaction scores. "There are well-established outcomes in effective patient communication and enhanced patient satisfaction," he says. "Achieving these outcomes is becoming as important as achieving clinical outcomes. It leads to fewer malpractice lawsuits and increased provider satisfaction, and in the end, a lot less reworking and wasted energy as well." REVIEW

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How to Manage Your Online Reputation

Christine Leonard, Associate Editor

Social media-savvy doctors share their top tips and strategies for representing yourself well online.

People search online for recommendations on everything from the best places to eat to the best hiking trails—and now the best ophthalmologists are also only a few clicks away.

"Evidence-based surveys within the past five years indicate a rise in the number of people using online resources to choose their physicians or providers," says David R. P. Almeida, MD, MBA, PhD, a vitreoretinal surgeon at Erie Retinal Surgery in Erie, Pennsylvania. "We went from about 10 to 15 percent of people searching online for their physicians to closer to 70 percent. That number is just going to keep rising. Soon everyone will Google their doctors, and you have to be ready for that."

Robert F. Melendez, MD, MBA, in practice in Albuquerque, New Mexico, agrees, adding that patients not only search but leave reviews. "Patients are online more and they're reviewing various products and services already, whether it's a restaurant or an Air BnB, and a doctor's office is no different," he says.

"When a patient sees ratings of 4.5 or 3.2 stars for a doctor, that may not be a true indication of the doctor's ability or skill, but the patient's initial perception is heavily affected by that score," he explains. "So for physicians to have the wherewithal to know that patients are searching for them, which they are, they need to be as in control as possible of their online reputations."

Here, these social media experts share what shapes your online reputation, how to improve it, keep tabs on it and make it work for you, and some strategies for avoiding the most common social media pitfalls.

Inevitably Online

If you're new to social media or haven't established an online presence, both Dr. Almeida and Dr. Melendez say one of your first steps should be an internet search of your name to get an idea of what's already out there about you. "How you're seen online matters, even if you have no conscious online presence," says Dr. Almeida. "You have to be aware of what comes up when patients search for you."

"Online review sites create pages on our behalf and it's our job to claim them," says Dr. Melendez. "This is only continuing to grow; I've had several patients in the past few years tell me they found me online."

Dr. Melendez advises "claiming" your online review sites. "Perform a search with the most commonly used

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search engines—Google or Yahoo, for example—and look on the first three pages of results to see which review sites are coming up. Focus on those first," he advises. "Claim them, update your professional photo and make sure your contact information is correct." He adds that it's also a good idea to perform a search using any other names you go by, such as a nickname, to cover all your bases.

A strong practice with a good reputation doesn't necessarily confer good online ratings, and what you find may surprise you, says Dr. Melendez. "You can't let low scores stand," he says. "If you're one of those doctors who has a 2.5 rating out of five, you need to fix that; it doesn't look good."

Raising Low Ratings

While you can't undo a bad review, you can improve your ratings by encouraging patients to rate you when you see them at the clinic, Dr. Melendez says. "Typically, patients—and people in general—won't go out of their way to review anything unless they're extremely happy or extremely unhappy. Our job is to keep everybody happy and satisfied, but we're not perfect and sometimes we run late in the clinic because of an emergency or some other issue like a complicated surgery.

"It's important to communicate with your patient and explain why you're running late, why you made them wait," he continues. "Once you explain, most patients are reasonable and will say, 'Oh! That makes sense.' Then the odds that they'll write a negative review of you are very low. It's not about the score, but about delivering every day in the clinic and OR."

Addressing patients' dissatisfaction before they leave the clinic is key. "The patients who leave unhappy are the ones who will post negative reviews," Dr. Melendez says. "It's a good idea to have your staff let you know if a patient has been waiting a while. The first thing to do is apologize for the long wait and ask if there's anything you can do to make it up to them next time. One solution may be to offer an earlier appointment time so they'll be first in the clinic with no one ahead of them. Once you make it right on the clinic side, you won't have to worry about what they'll write online."

"If it's not something you'd discuss with a patient in the clinic, it's not something you should post online."
—David R. P. Almeida, MD, MBA, PhD

Rating sites are powerful, impression-forming tools for patients, but Dr. Melendez points out that while a five-star rating is outstanding, it's not always necessary—or believable. "A study out of Stanford found that people would rather see a 4.6 than a 5.0 because a 4.6 seems real—a perfect five looks a little fake," he explains. "If your score is above 4.0, I think you're doing well. Everyone's going to have one to five negative comments. If it's 4.5 or higher, that's great. If it's a 5.0, that's outstanding, but it's not always necessary. Consistent feedback is also important. If your latest reviews are several years old, it may be time to fix that."

Negative Comments

When faced with a negative comment online, your first reaction may be to respond right away, but Dr. Almeida says to take a breath first. "Just stop and don't reply," he says. "That's the most important step. You'll be frustrated, but you have to walk away for now. You or your office should call the patient privately and start the communication there. That could lead to the patient coming into the office to discuss the matter further. We know from insurance malpractice studies that most negative issues stem from a lack of communication or a communication breakdown. You can address these issues easily with a phone call. Just don't get into a beef or start a Twitter war."

Your Online Brand

Dr. Almeida says that if you like doing social media, there are many options for cultivating your online profiles. If you don't enjoy being online in this capacity, simple posts about pertinent journal articles, practice updates or conferences you've attended can suffice.

Forming and maintaining your online identity will depend on two basic principles: credibility and honesty, he says. "Your brand represents you and your practice, so you want it to be genuine," he advises. "Don't hand the keys to someone else, such as your office manager or a technician, and ask them to post things on your behalf. That's not your voice, and it's not going to benefit you. Your social media profiles should be as authentic to you as possible."

Dr. Melendez adds, however, that if you're just trying to let people know you're fun and engaging and share some things you do in the community such as teaching, lecturing or attending conferences, then someone in your clinic may be able to run your social media profile, as long as you give them specific guidelines on what to post and what not to post.

With the wealth of information available on the internet, it's also important to separate fact from fiction. "As physicians, it's important to post credible, evidence-based content," Dr.

Almeida says. "Build credibility and trust by posting things that are accurate and true. Don't post an opinion on a topic unless it's been verified by multiple sources. Your sources can come from outside journals, but they should be credible news sources if you're going that route."

Dr. Almeida explains that building trust comes through consistently communicating in effective ways and by posting things of value. "If you're posting what you had for dinner, that may be fun for your friends or people who know you personally, but it's not anything of value," he explains. "Consider who's following your accounts: are they patients, colleagues, administrators, researchers, residents, other doctors? Your content should be of value to your audience. If your practice has a strong focus on patient care or on managing really complex diseases, then posting about new technology may not be as relevant to your practice and therefore won't align with your brand."

Practice Promotion

In a sense, anything you post online is a form of marketing for your practice and for yourself, so representing yourself well across social media is key. Dr. Almeida says you'll be targeting two demographics when you go about promoting your practice: potential and existing patients, and referring colleagues. Then, you need to identify what's of value to each group.

"For patients, disease-specific information is very popular," he says. "What it is, how it's treated and that your office provides care for it are all useful to your patients. In other words, it's high-value, non-offensive, low-risk content. This is a really good route to go.

"For a referral network, you might want to post CME-related content, updates in the field and things you think referring doctors might enjoy reading about," he continues. "If you're a subspecialist, you'll probably want to post thoughtful insight into current topics relevant to all ophthalmologists and optometrists."

Snares of Sponsorship

Experts say you should avoid sponsorship and conflicts of interest at all costs, lest you erode your credibility. "Anything you say will be open to interpretation and may not necessarily be aligned with what you actually meant," Dr. Almeida says. "For example, if you say, 'This new study shows that A is better than B,' depending on how you post that, it's going to be interpreted that you're endorsing A over B, when you're just stating the results of a trial. It's surprising how these can come back to bite you. Word your posts carefully, and again, make sure all of your posts have value.

"You also can't sell stuff," he adds, "even if your clinic sells it. Becoming a sales person for a product or service does not add value and diminishes your credibility. If you want to promote something, you can talk about the studies or evidence for the technique or technology you use, and you can educate people on it, but you can't really hawk stuff. It's just not a good look."

A Targeted Approach

As noted, the type of content you post will be determined in part by your audience. Is your account geared toward patients? Referring doctors? Colleagues? Many ophthalmologists choose to focus on patient education, such as disease states, or doctor education both inside and outside ophthalmology. "If you have a targeted approach, your account will make more sense to those accessing your social media sites," Dr. Almeida says.

Posts about general medical topics are likely to draw a larger, more general audience, while more specialized topics may draw a smaller crowd. Dr. Almeida gives the example of a doctor who specializes in juvenile glaucoma. "You may post really good content, but it might be so niche that it fails to attract a broad audience," he says.

If you have a more specialized focus, or even if you just want to expand your audience, here are three steps you can take:

1. Post content that's specific to your field.

2. Draw some tangents to general ophthalmology or medicine. "If you're that juvenile glaucoma specialist, you might post about recently published articles in pediatric ophthalmology or socioeconomic determinants of health in children or myopia progression in children," Dr. Almeida suggests.

3. Find your personal voice. "If you don't find your personal voice, your account has the potential to become boring," Dr. Almeida says. "Again, you should avoid conflicts of interest and selling things, and you should stay away from politics. There some instances, however, when you should make your voice heard. Generally the medical community remains quiet, but there comes a time when apathy isn't an option and not speaking is tantamount to agreeing or allowing injustice to happen. This third step is much more advanced," he adds. "Stick with the first two until you become more comfortable online and then move on to step three."

To Post or Not to Post

While social media is a powerful tool for networking, increasing your practice's visibility, participating in webinars and online panels and educating patients and fellow doctors, it can also potentially get you into trouble if you post inappropriate content.

"Given how conservative medicine is, there may not be a whole lot to

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Miyata grade (Glistenings)	0[2] (None)	3[8] (High)	0[12] (None)
ABBE value	56[2]	37[9]	55[9]
Refractive index	1.46[3]	1.55[10]	1.47[12]
Mean decentration	0.08 mm[4]	0.78 mm[11]	0.27 mm[13]
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gain initially from having a big online presence, but there's probably a lot to lose if, for example, you don't manage patient privacy properly," Dr. Almeida says. "Patient privacy is among the top pitfalls."

Failing to separate your professional and personal profiles is the next biggest pitfall. "Your practice or professional profile should exist separately from your personal profiles," Dr. Almeida says. "You shouldn't be posting about your kids, what you're having for dinner, or where you went on the weekend on your professional or practice online profile. Posting this type of content may erode your ability to communicate effectively and professionally."

Many younger ophthalmologists, however, feel it's important to share what goes on behind the scenes in a doctor's life, not only to give patients a glimpse into their lives to build rapport, but also to inspire young people to pursue medicine or encourage medical students by being realistic about work-life balance expectations, mental health or starting families in the midst of medical careers. How much or how little you share is entirely up to you; it depends on whom you wish to reach and influence with your social media account, though experts agree the safest route is to maintain separate professional and personal accounts.

Making any kind of political statement on your accounts may also cause problems down the road. "You cannot say, 'Hey, vote for this,' but it would be fine to say, 'Go vote,' " Dr. Almeida notes. "You're allowed to have political opinions—just don't express them online. Your patients or colleagues may be from different parties or hold different views, and the alienation that results from making political statements can be significant and can hinder the patient-physician rapport you're working so hard to build. If it's not something you'd discuss with a patient in the clinic, it's not something you should post online."

Social Media Platforms

There are many social media platforms and each of them has certain strengths and weaknesses. Dr. Melendez says that when you're just starting out with social media, the first question you want to ask yourself is: Am I about producing content or consuming content? In this case, your focus should be on producing content.

"A producer focuses on producing content," he says. "A consumer rarely produces content and mainly consumes it. Twitter is a good example of content consuming, where the vast majority of users might like or retweet or comment, but on the whole, don't contribute much. Facebook is about half and half, and Instagram is more of a 70/30 breakdown for producing/consuming, where most users share photos."

Here are some of the most commonly used social media platforms:

• ***Twitter.*** "Twitter is the ideal starting point for everyone," Dr. Almeida says. "It's a micro blog, and it doesn't require significant time or energy, so you can keep things easily digestible." Twitter limits characters to 280 or fewer, so there's no need to write lengthy discourses on topics. It's a good platform for sharing new studies, medical news or practice updates.

• ***YouTube.*** "It's the most commonly used social media site right now," says Dr. Melendez. "Creating high-quality videos is key. As a physician, I take pride in educating patients and doctors. I post educational videos, with patient consent. Once your video is made, you can share it on other social media platforms such as Facebook and Instagram."

"Many people believe that video currency is the future of social media," adds Dr. Almeida, who creates retinal teaching videos with his colleagues. "Recording the videos takes time, but it's become such an important currency that we may see more and more people doing this."

• ***Facebook.*** "As a classic social media platform, Facebook is still king," says Dr. Melendez. "We're starting to see older individuals using Facebook more often than younger ones. Young people are still on it, but they aren't as active as they once were."

"Facebook probably runs the biggest gamut of the social media platforms," Dr. Almeida adds. "It can be very professional, very unprofessional and in-between. It's become less significant for us in recent years in terms of brand building and practice promotion, just because there's so much disinformation on the site and controversy over the data that Facebook collects from us."

• ***Instagram***—Dr. Melendez says Instagram is the best fit for reaching those aged 18 to 40. It's his social media platform of choice. "I do a lot of teaching, and I have a professional education page where I post educational things about the eyes and our profession." Many of his medical students also use TikTok and Snapchat, he says.

Dr. Almeida doesn't use Instagram that often, but notes that it's a very visual platform. "This platform may not be as relevant for lengthier written content or comments, such as sharing a new publication or study," he says.

• ***LinkedIn.*** Dr. Melendez says that LinkedIn is more formal than most other social media platforms. Its strength lies in network-building. "LinkedIn is for sharing more professional ideas, leadership articles or how to be better professionally and personally, and those are things you don't typically see on platforms like Facebook. On Facebook you could encounter something similar, but it might be alongside a video of a cat drinking milk."

Dr. Almeida notes that you'll likely find other colleagues on LinkedIn, as

well as industry and government reps, who may use this platform to reach out.

Getting Serious

With an already packed schedule, committing to building your online brand may seem daunting. Experts contend, however, that investing the time and effort to do it right is well worth it.

"My recommendation is that if you're going to do it, you have to go all in," Dr. Melendez says. "You can't just create five social media profiles and then let them stagnate. That's analogous to putting a 'for sale' sign on your house and not advertising beyond that. The only people who'll see it are your neighbors and the occasional people who might drive by."

A professional website for you or your practice can also help to shape your online brand by bringing all of your online presences together in one place. "Your practice website should be more than just your practice name and address—that's just the yellow pages," says Dr. Almeida. "It should communicate your brand, what kind of care you deliver, disease-specific information and what services you provide for your community." This is also the spot to add information about yourself, your education, and any awards and publications you have.

Attributes such as key words and search engine optimization often come into play with websites, but Dr. Almeida says you don't have to get that detailed. "There are so many levels you can get into with websites, and if you're enjoying the process, then certainly give those other aspects a try, but they're not necessary now," he says.

If this sounds like a big undertaking, keep in mind that most physicians don't do this alone. "If a bunch of negative results come up when you search online for your name or practice, you can seek out professional services to remedy that," Dr. Almeida says.

Additionally, many practices and physicians hire professionals to build their websites for them. "It's worth it to spend the money to do it right," Dr. Melendez says.

The Bottom Line

"Ultimately, your online reputation matters a great deal," says Dr. Melendez. "Patients are looking for you online. Your social media accounts or your website will ease patient fears about you, as a person. When patients search online for you, they're trying to get to know you: Are you experienced and qualified? Do you look and sound like a nice person? What are your review scores like?" REVIEW

Pseudoexfoliation and Cataract Surgery 2020

Christopher Kent, Senior Editor

The side effects of pseudoexfoliation can make cataract surgery challenging. Here's help.

Pseudoexfoliation has long been known to be a concern when performing cataract surgery. The likelihood of a problematic iris, weakened zonules, postop glaucoma and serious problems occurring years later are issues a cataract surgeon needs to address before, during and after surgery.

Here, surgeons share their experience and advice for making sure these patients have the best outcomes possible.

The Warning Signs

Although surgeons agree that it's possible to be surprised by the presence of pseudoexfoliation when you get to the operating room, most cases can be discovered by noting warning signs during the preop exam.

• ***Look for material on the lens capsule and iris.*** "An eye that has pseudoexfoliation will usually present with pseudoexfoliation material on the pupil margin and the anterior lens capsule that's visible during the slit lamp exam," notes Uday Devgan, MD, FACS, FRCS, chief of ophthalmology at Olive View UCLA Medical Center, an associate clinical professor at the UCLA School of Medicine, and in private practice at Devgan Eye Surgery in Los Angeles.

Amy D. Zhang, MD, a clinical assistant professor of ophthalmology at the Kellogg Eye Center, University of Michigan in Ann Arbor, notes that this material isn't always obvious. "The edges of the iris may have a white fibrillary appearance," she says. "This is most prominently seen at the pupillary border. These can be subtle indications that may be missed on a cursory exam."

• ***Check to see whether the other eye has had zonular issues in the past***. "If the other eye has already had surgery and there was a problem, my guard will be up," says JoAnn Giaconi, MD, a clinical professor of ophthalmology at the Jules Stein Eye Institute and chief of ophthalmology at the Veterans Administration in Los Angeles.

• ***Note the extent of pupil dilation.*** "Pseudoexfoliation patients don't dilate as well as other patients do," notes Dr. Devgan. "Notably, it turns out that the ones who are dilating more poorly tend to have weaker zonular support during surgery, while the pseudoexfoliation patients who dilate better tend to have somewhat better zonular support."

• ***Be alert for a relatively shallow anterior chamber.*** "Another clue, which is a little more subtle, is the anterior chamber depth relative to the axial length," Dr. Devgan points

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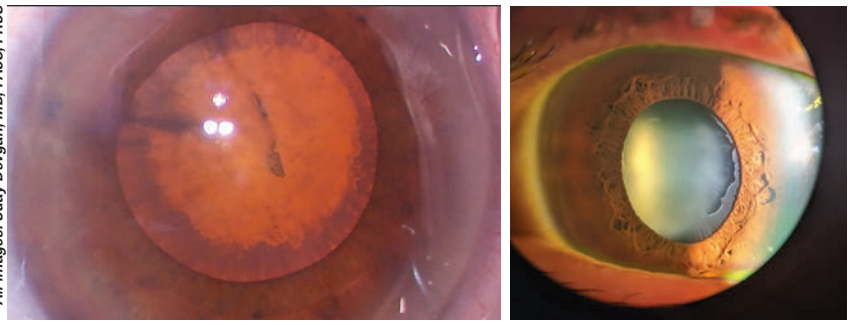
All images: Uday Devgan, MD, FACS, FRCS



Pseudoexfoliation can lead to significant challenges when performing cataract surgery. One of the key warnings that pseudoexfoliation is present is visible material deposited on the anterior lens capsule and iris margin observed during the slit lamp exam.

out. "An average eye with an average axial length should also have an average anterior chamber depth. If you have an average axial length but a very shallow, crowded anterior chamber, that means that the entire zonular support is so weak that the cataract and the iris are being pushed forward into the anterior chamber."

"An anterior chamber depth of less than 2.5 mm has been associated with four-fold increased risk of zonular instability and/or vitreous loss," notes Dr. Zhang. "Also, compare the anterior chamber depth to that of the fellow eye. Pseudoexfoliation may be unilateral, so a difference between the eyes could indicate a problem."

"The other part of this," adds Dr. Devgan, "is that when you get to the OR and the patient lies down, gravity will pull the bag and iris back and the anterior chamber will become really deep. That's because the zonules are so loose that the lens moves forward and back."

• ***Watch for iridodonesis when the eye moves during the slit lamp exam.*** Dr. Giaconi notes that this is another sign of loose zonules.

• ***Look for elevated IOP and optic nerve damage.*** "In many cases of pseudoexfoliation, glaucoma or ocular hypertension are present," Dr. Zhang points out. "So, noticing whether there's an elevation in IOP or signs of optic nerve damage is important."

• ***Consider performing gonioscopy.*** "Not everyone does this, but if you do, check the angle for fibrillary deposits," advises Dr. Zhang. "As a glaucoma specialist, I do this routinely."

Preparing for Trouble

Once you've determined that pseudoexfoliation is present, these strategies can help ensure successful cataract surgery:

• ***Let the patient know that the surgery has a slightly higher risk because of the pseudoexfoliation.*** "I do spend a little time explaining this to the patient, but I'm careful not to dissuade the patient from having cataract surgery," says Dr. Zhang. "You don't want to have to explain the impact of pseudoexfoliation to a skeptical patient after something has gone wrong. Even if a patient already knows that they have pseudoexfoliation, they may not realize that it could impact their cataract surgery."

• ***If pseudoexfoliation is present, consider implanting an anterior chamber lens, and plan accordingly.*** "If the eye has pseudoexfoliation and the patient is older and the lens is denser, I'll plan for the possible use of an anterior chamber lens," Dr. Giaconi explains. "Because these lenses aren't used that often today, our OR doesn't stock all of the options. So, I'll measure the white-to-white distance and calculate the power, and ask the OR to pre-order the appropriate lens so it's available if needed."

• ***Make sure pupil expansion tools will be available in the OR.*** "I make sure we'll have an iris expansion ring on hand, and iris hooks," says Dr. Giaconi. "That way the nurses won't have to go searching for things in the middle of surgery."

• ***Make sure you're comfortable performing an anterior vitrectomy and are prepared to do so.*** "When the patient has pseudoexfoliation, a vitrectomy may be necessary," notes Dr. Zhang. "The incidence of vitreous loss tends to be higher, especially in those patients that have much narrower anterior chambers."

Dr. Giaconi agrees. "Surgeons are often surprised by vitreous in these patients," she says. "You always need to have vitrectomy equipment on hand."

• ***If you think the lens may need to be sutured in, consider referring the patient to someone with extensive experience doing that.*** "I prefer not to suture IOLs in place, even if the lens is obviously loose preoperatively," says Dr. Giaconi. "I only suture a lens once or twice a year, so it may not be in the patient's best interest for me to spend an extra hour and a half doing that. Some high-volume cataract surgeons do this fairly often. If I know of a surgeon who can do it quickly, safely and efficiently, I'll simply refer the patient to that individual."

Surprise PXF in Surgery

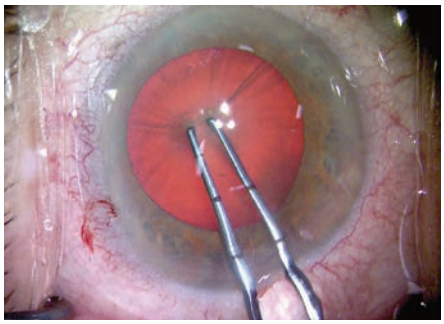
Although it's not good to be surprised by pseudoexfoliation in the OR, it can happen. Dr. Devgan notes that it's sometimes easier to see pseudoexfoliation on the operating table than it is to see it in the clinic. "The patient may not be as dilated in the exam room as in the OR," he notes. "The strength of the dilating drops is very different. Also, when I shine a bright light in the patient's eye in the clinic, many patients become squeamish, so

it's harder to evaluate. In the OR the patient has sedation on board, so you can shine that bright microscope light in their eye and they're very cooperative. As a result, you may see pseudoexfoliation signs on the table that you missed during the exam."

One sign that unexpected pseudoexfoliation is present is a change in anterior chamber depth when the patient is lying down. "Most surgeons won't compare the anterior chamber depth with the patient sitting up vs. lying down during the preop exam," notes Dr. Giaconi. "Often the first time you see the patient in a reclined position is in the OR. If you realize the anterior chamber is deeper when the patient is on the table, you know the patient has zonulopathy and you'll need to proceed with caution."

Another sign is that the anterior capsule wrinkles when pressed. "Suppose the pupil dilation is acceptable, so you start the capsulorhexis," Dr. Devgan says. "If pseudoexfoliation is present, when you poke into the anterior capsule to begin your capsulorhexis, you may notice a lot of radial wrinkles. That tells you right away that you're dealing with loose zonules. In a healthy eye, the anterior capsule is like a trampoline with strong springs; it will be flat and taut, and if you push on it, it will be springy. But if the springs of the trampoline are very loose, poking on the surface causes wrinkles."

Dr. Zhang notes that in terms of surprises, the most common may be a case in which the pupil starts out big on the table but suddenly becomes small. "That leaves you wondering whether you're dealing with pseudoexfoliation," she says. "In that situation, if you weren't prepared to deal with pseudoexfoliation, you have to take each step more slowly. Perform the cataract surgery as you would any other case, but be alert for any sign of vitreous prolapse and zonular laxity. The chance of vitreous loss will be higher in those patients."



Pseudoexfoliation can be missed during the slit lamp exam. One sign a surgeon may encounter during surgery is wrinkling when the anterior capsule is pressed, indicating weak zonules.

Managing a Small Pupil

Because a common effect of pseudoexfoliation is a pupil that fails to expand sufficiently, the surgeon has to decide how to compensate. Many surgeons choose to enlarge the iris with iris hooks, a device such as the Malyugin ring, or a pharmaceutical option such as Omidria (phenylephrine and ketorolac, Omeros).

Dr. Giaconi notes that in terms of a mechanical device, both iris hooks and a pupil expander have pros and cons. "Cosmetically, either option can distort the pupil a little bit postop," she says. "I use the Malyugin ring more often just because it's quicker, but if you plan to prolapse the nucleus through the capsulorhexis and the iris, the ring can sometimes prevent it from prolapsing through. Iris hooks avoid this problem, and they can do a better job of controlling pupil size and shape, but they take longer to use."

Dr. Zhang says she's more inclined to use iris hooks. "If things start dropping, iris hooks are much easier to remove than an entire Malyugin ring," she points out.

Dr. Devgan says he prefers not to use any device or pharmaceutical at all. "I think most surgeons who've done a large volume of cataract surgeries will probably just stretch the pupil to open it up a little further, and then do the capsulorhexis underneath the iris, viewing through the pupil," he says. "We can create a 5.5-mm capsulorhexis, even if the pupil is only 4.5 mm. We don't have to visualize the entire edge directly."

Dr. Devgan adds that he doesn't think a pupil expander is any safer. "I think it may be more traumatic, and more likely to cause damage to the iris than pupil stretching," he says. "In one of my online educational videos I did a comparison; I did one eye using a Malyugin ring and did the other using my [no-device] approach. The capsulorhexis was fine in both eyes, but the iris looked better after using my approach." (You can watch the video at cataractcoach.com/2018/10/31/pupil-stretch-using-capsulorhexis-forceps/)

During the Surgery

These strategies can help the cataract surgery go well and produce a good result:

• ***Iris hooks can be used for capsule support if capsule hooks are not available.*** "In cases of pseudoexfoliation you'll see some areas of zonular laxity," says Dr. Zhang. "Capsule hooks would be ideal to provide capsular support, but when capsule hooks aren't available, I've used iris hooks. They get the job done, although they're not approved for that. When you're using iris hooks for this purpose, aim for a slightly steeper angle, so the pivot of the hook can capture the capsule. The thing that's great about iris hooks is that you can place them anywhere, and use as many or as few as you like."

• ***Make a large capsulorhexis.*** "When zonular support is weak, pseudoexfoliation patients tend to develop capsular phimosis three, six or even 12 months after surgery," Dr. Devgan explains. "That causes the anterior capsule rim to shrink and pull toward the center. A 4-mm capsulorhexis may become fibrotic and scar up, shrinking

to 2 or 3 mm. This can even dislodge the lens. To prevent that, you want to create at least a 5-mm or 5.5-mm-diameter capsulorhexis. This minimizes the impact of any shrinkage."

Dr. Giaconi points out a second reason to make a large capsulorhexis. "A small capsulorhexis can make it more difficult to get the lens out of the bag in an already challenging case."

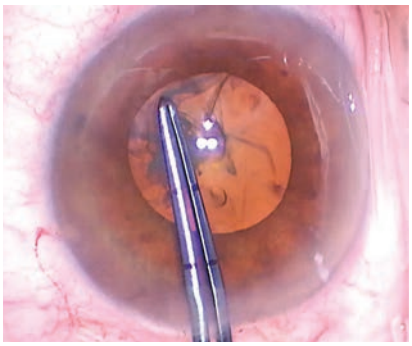
Dr. Giaconi adds that making paired postop anterior capsular incisions in the capsulorhexis can help with potential phimosis. "This may enlarge the capsulorhexis a little bit and distribute the tension, offsetting contraction from postop phimosis," she says.

• ***Consider using a capsular tension ring.*** Dr. Zhang says she finds these helpful when managing a pseudoexfoliation patient. "That raises two questions," she notes. "When during the procedure should you insert it? And in which situations is it not likely to be helpful?

"In terms of timing, if you put it in early in the procedure, you're going to have trouble removing some of the cortex or nuclear material," she says. "If you still have a lot of nucleus present you'll have a harder time visualizing where you're placing it. However, you don't want to wait until late in the procedure to insert it, when you've lost the support of the bag. I usually place it when I've removed most of the cortical material.

"I wouldn't insert a capsular tension ring if there's more than four clock hours of zonular laxity," she adds. "A CTR isn't really designed to support that many clock hours. In that situation you may have to think about other options, such as suturing in an Ahmed segment, or using multiple segments to provide more coverage."

Dr. Devgan agrees. "I wouldn't put a CTR in a pseudoexfoliation patient with 360-degree zonular weakness," he says. "There may not be a benefit there. For those with 360-degree weakness, my preference is getting a three-piece lens, putting the haptics in the sulcus and capturing the optic behind the capsulorhexis so the optic is in the bag. That's great for long-term stability, and it will prevent any phimosis, because the tissue can't clamp down on the lens."



Making a larger-than-normal capsulorhexis is important when pseudoexfoliation is present, both to allow prolapsing the nucleus out of the bag to avoid stressing the zonules during phaco, and to minimize future anterior capsule phimosis.

• ***If the zonulopathy is serious, consider implanting an anterior chamber lens.*** "In these eyes there's a pretty good chance the lens will decenter postoperatively," says Dr. Giaconi. "Putting in a capsular tension ring may delay a problem, but it's not going to prevent the bag from falling. So, if I find a lot of zonulopathy, I'd probably go ahead and put in an anterior chamber lens."

• ***Use a phaco technique that won't stress the zonules.*** "For me, that means avoiding a technique like divide-and-conquer and using something like a quick-chop technique instead," says Dr. Devgan. "An even better option is to bring the nucleus partially out of the capsulorhexis bag, which eliminates any zonular stress." (You can watch a video of this technique at cataractcoach.com/2020/03/21/review-pseudo-exfoliation-cataract-surgery/)

Dr. Zhang says she typically uses horizontal chop in these cases. "I also make my rhexis a little larger so I can partially prolapse the lens out of the bag and further chop the nucleus in that manner," she explains. "My only concern is that sometimes the anterior chamber is very narrow, and if you prolapse the entire lens out, it could cause damage to the endothelium."

"In reality, different techniques are going to work better in different surgeons' hands," notes Dr. Giaconi. "Some surgeons have a very light touch; they may be able to get away with more than other surgeons can."

Dr. Zhang adds that in pseudoexfoliation cases it's good to slow everything down to some extent. "We use Alcon's Centurion system, which lets us set the intraocular pressure we'd like to maintain," she says. "In addition, I slow down the fluid dynamics compared to a normal cataract surgery, in case vitreous does present itself."

• ***Remove excess capsule epithelial cells after phaco—carefully.*** "When you've taken out the cataract and the cortex and you're cleaning up the capsular bag, you may see some hazy lens cells left on the capsule," says Dr. Devgan. "Removing those can help prevent phimosis and capsular contraction. Being thorough is important, but you have to balance that with not damaging the capsule, which is already weak. Remember the first rule of medicine: First, do no harm."

Dr. Giaconi notes that the studies looking at the value of removing these cells have produced mixed results. "Nevertheless, if there's a lot of material on the anterior capsule, I like to use a tool to scrape the cells away," she says. "If you use a tool designed for this purpose, I don't think you'll have a problem in terms of damaging the capsule."

• ***Securing the lens in place has pros and cons.*** "I don't routinely scleral-fixate the lens, although I know some of my colleagues do," says Dr. Zhang. "Normally I wait until a problem has occurred and then fixate the lens. Doing this at the time of the cataract surgery is a lot of extra work to

prevent a problem that may or may not occur. It will make the initial surgery take longer and impact patient comfort as well."

• ***Remember: If a big problem occurs, you don't have to solve it that day.*** "Suppose you're trying to remove the cortex and the whole capsular bag comes out of the eye," says Dr. Devgan. "It's OK to close the eye up and come back in a few days or a month to fixate a lens in the eye. Or, have your colleague who's really good at it do it later. You don't have to do it at the same time."

Postop Management

Pseudoexfoliation patients need to be monitored carefully postop:

• ***Be proactive about a potential postop pressure spike.*** "For uncomplicated cases, a drop of dorzolamide-timolol in the OR immediately following surgery has been reported to help with IOP in the first 24 hours," says Dr. Giaconi. "On the other hand, if the surgery was complicated, and there's no contraindication, I usually give these patients a dose of Diamox in the OR to try to prevent an overnight spike in pressure. I'll also prescribe a few tablets to take home. I tell them: 'If you start to feel a headache coming on, take a tablet.'

"I check these patients the morning after surgery," she adds. "If their pressure makes me uncomfortable, I'll adjust their medications and see them a few days later. If their pressure is fine, I might just see them a week later. I'd probably check them weekly for the first month."

"I may bring these patients back a little bit sooner than an average patient to make sure they're not experiencing a postop pressure spike," agrees Dr. Zhang. "How soon I bring them back depends on their IOP on day one. If it's borderline—in the mid-20s or so—I'd probably bring them back in a couple of days to reassess, and I might start them on a topical drop for pressure control."

• ***Consider keeping your pseudoexfoliation patient on medications longer.*** "I often put my pseudoexfoliation patients on steroids and NSAIDs for a longer time than I would a routine cataract patient," says Dr. Zhang.

Dr. Giaconi adds that she increases postop steroids a little bit if the surgery runs long. "A longer surgery will probably lead to more corneal edema," she notes.

> *"When following up these patients, you won't be able to see the anterior chamber rim, or any phimosis, unless you dilate."*
> *—Uday Devgan, MD*

• ***Monitor these patients for glaucoma.*** "The material that weakens the zonules also clogs up the trabecular meshwork," Dr. Devgan points out. "So, you have to be careful to monitor these patients for signs of glaucoma. Check the IOP; look at the optic nerve; do an OCT of the retinal nerve fiber layer. Stay on the lookout."

• ***Dilate these patients at postop visits.*** "For some other patients you wouldn't dilate at a routine postop visit," Dr. Devgan notes. "However, when you're following-up a pseudoexfoliation patient, you won't be able to see the anterior chamber rim, or any phimosis, unless you dilate. If you see that the anterior capsule remnant has contracted or is phimotic, you can use the YAG laser in the clinic to make some relaxing incisions, for example at 3, 6, 9 and 12 o'clock. That breaks the phimotic ring so it can't clamp down."

• ***Realize that the lens may have problems down the line no matter what you do.*** "I think the average number of years these eyes take to develop a decentered lens is six or seven," says Dr. Giaconi. "Right now I'm not aware of any prospective studies that go out 10 years. However, a recent study conducted at Aravind Eye Hospital in India looked at uncomplicated pseudoexfoliation cases—patients with no zonulopathy where the pupils dilated reasonably well. At five years, it made no difference whether you'd put in a one-piece or three-piece lens, or whether you inserted a CTR."[1]

"The reality is that pseudoexfoliation is a progressive disease," says Dr. Devgan. "You're not stopping its progression by doing the cataract surgery. In some patients, especially those living to 90 or longer, the entire lens and capsular bag may fall back into the vitreous and float there. If it's still very close to the iris when you see the patient, you may be able to retrieve it by yourself; then you'll have to suture the lens in place. If the lens has landed back on the retina, you should call a vitreoretinal colleague."

A Manageable Problem

Dr. Giaconi points out that pseudoexfoliation during cataract surgery isn't the problem it once was. "Today's tools make a difference," she says. "Pseudoexfoliation isn't a potential disaster, as long as surgeons know what they're doing. Our outcomes are better than they were 20 years ago. So take your time, use the right tools, and if a problem is beyond your experience, refer to someone who's accustomed to dealing with it." REVIEW

Drs. Giaconi, Zhang and Devgan report no financial ties to any product discussed.

1. Haripriya A, Ramulu PY, Schehlein EM, et al. The Aravind Pseudoexfoliation Study: 5-year postoperative results. The effect of intraocular lens choice and capsular tension rings. Am J Ophthalmol 2020;219:253-260.

FOR MOST PATIENTS, DRY EYE SYMPTOMS HAVE AN EPISODIC IMPACT

FLARES: THE SPEED BUMPS OF DRY EYE

Most patients with Dry Eye suffer from short-term, episodic exacerbations—***Dry Eye Flares.***[1-3]

Many patients don't suffer from continuous symptoms.[3]

REENVISION DRY EYE

kala PHARMACEUTICALS

References: 1. Brazzell RK, Zickl L, Farrelly J, et al. Prevalence and characteristics of dry eye flares: a patient questionnaire survey. Presented at: AAO 2019: October 12-15, 2019; San Francisco, CA. **2.** Brazzell RK, Zickl L, Farrelly J, et al. Prevalence and characteristics of symptomatic dry eye flares: results from patient questionnaire surveys. Poster presented at: AAOPT 2019: October 23-27, 2019; Orlando, FL. **3.** 2020 Study of Dry Eye Sufferers. Conducted by Multi-sponsor Surveys, Inc.


Early Glaucoma: The Macular Damage Factor

Central vision problems reported by patients with early glaucoma may be attributable to undetected damage in the macula.

Dana M. Blumberg, MD, MPH, New York City

Many physicians managing glaucoma patients have accepted the idea that macular damage only occurs late in the disease. In recent years, however, a number of studies have provided a growing body of evidence that macular damage occurs in glaucoma patients earlier and more frequently than previously believed. Meanwhile, our understanding of how vision is impaired by the disease—especially in early glaucoma—has been lacking. In the clinic, I find it frustrating that what I see in the 24-2 visual field data often doesn't correlate with what the patient is reporting.

Of course, a correlation between visual complaints and visual field data is easy to find when glaucoma is advanced. However, the traditional assumption has been that early glaucomatous damage is primarily peripheral. For that reason, a glaucoma patient's central vision complaints have usually been attributed to other possible factors such as co-existing pathologies. Maybe glaucoma eye drops are causing corneal dryness that could explain visual glare complaints. Maybe the patient has early macular degeneration. Maybe the drops are speeding the development of cataract. Maybe peripheral visual field loss is responsible in some way. Maybe the complaints can be attributed to the way binocular vision combines slightly different images.

With evidence now suggesting that central macular damage might be occurring much sooner than previously thought, I saw a potential explanation for these difficult-to-explain central-vision complaints. So, our group decided to explore the relationship between glaucomatous macular damage and the patient's everyday visual function—especially in early disease.

Here, I'd like to share some of what we've discovered about the presence of macular damage in early glaucoma; how we can miss that damage when we rely exclusively on the 24-2 visual field test; and how that damage may be tied to patient visual complaints that were previously attributed to those other hypothetical causes.

Central Vision Complaints

First of all, it's important to understand that many vision complaints coming from patients with early glaucoma are, in fact, central vision complaints. One 2013 study asked 50 glaucoma patients with mild to moderate disease, visual acuity better than 20/30 and a range of visual field defects in both eyes, to identify one of six Photoshopped images that best approximated their perceptions of their vision difficulties.[1] The six options were: a tunnel of clear vision surrounded by darkness; a tunnel of clear vision surrounded by blur; clear vision with dark patches sprinkled across the visual field; clear vision with blurred patches; clear vision with areas of missing information; and no awareness of altered vision.

Based on traditional ideas about peripheral damage in early glaucoma, we'd expect patients to select the clear vision surrounded by either blur or darkness. Instead, no patients chose the clear tunnel surrounded by darkness and only two patients (4 percent) chose the clear tunnel surrounded by blurriness. No one selected the image with dark patches, but 54 percent chose the image with blurred patches, and 16 percent chose the image with areas of missing

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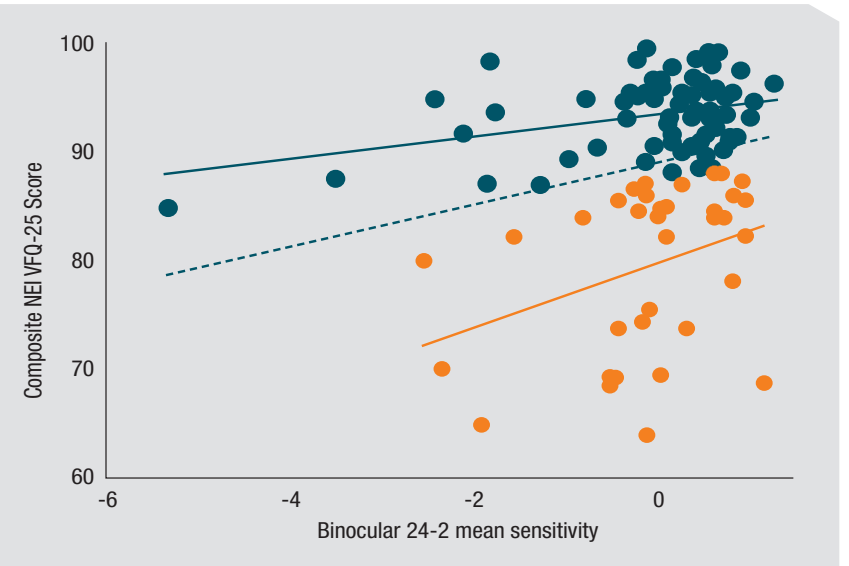
information. (26 percent reported being unaware of any vision loss.) In essence, three-quarters of the patients reported visual symptoms that were more central than peripheral.

As a follow-up, the authors examined the relationship between the presence of visual symptoms and the 24-2 visual field. They couldn't find a clear linear relationship between 24-2 mean deviation and visual symptoms. This supports the clinical observation that visual complaints correlate poorly with 24-2 visual field results in early glaucoma patients.

Another study asked 99 patients with different types and stages of glaucoma (76 percent had primary open-angle glaucoma) to report which of a list of visual complaints they were experiencing.[2] The authors found that the three most common complaints from glaucoma patients were all central vision issues—specifically, needing more light to see well, blurred vision and glare. Peripheral complaints (e.g., difficulty seeing objects off to either side) were much less frequently reported.

Lastly, a third, case-controlled study questioned 221 glaucoma patients about their visual performance under different luminance conditions.[3] Glaucoma patients were found to have significantly more complaints in glare or low-luminance conditions than controls. Circumstances reported to be problematic included driving on a cloudy day, seeing outside at night when there's no moonlight, reading in the sun and adapting to bright or dim light. The idea that glaucoma patients not only have complaints about central vision but also have trouble adapting to light or dark conditions is surprising; these are complaints we normally associate with photoreceptor damage or loss. (In fact, some research relating to macular degeneration is suggesting that difficulty with dark adaptation could be a very early sign of macular degeneration.)

24-2 Mean Sensitivity vs. Visual Function Questionnaire Score



In a 2017 study, patients' scores on the National Eye Institute Visual Function Questionnaire were compared to the patients' binocular mean sensitivity score from the 24-2 visual field test.[4] A subset of patients scored significantly lower than would be anticipated (orange dots). This group had the best correlation between their 10-2 visual fields and NEIVFQ scores, suggesting that patients with disproportionate visual complaints relative to the 24-2 may actually have undetected macular damage.

These findings make it clear that the relationship between the 24-2 visual field—the classic glaucoma functional test—and everyday visual performance in glaucoma patients is not well-understood. Clearly, the relationship is not as straightforward as was previously believed.

Pursuing a Macular Mystery

To delve into this issue, we decided to conduct a series of studies to address the different questions raised by the possible connection between vision complaints from patients with early glaucoma and macular damage.

In our first study we explored whether glaucoma patients with macular damage had worse vision-related quality of life.[4] Patients had early to moderate glaucoma with no evidence of coexisting dry-eye disease or visually significant cataract, based on the LOCS III system. We used patients' 24-2 visual field, which is more of a classic peripheral glaucomatous visual field damage measurement, and the 10-2 visual field, which measures central or macular functional loss. To evaluate patients' quality of life, we had them fill out the National Eye Institute Visual Function Questionnaire, a well-validated measure of vision-related quality of life that not only measures patients' perceptions of their visual loss, but also how it impacts their day-to-day functioning.

Not surprisingly, we found that the 10-2 visual field is a better predictor of the NEIVFQ score than the 24-2 visual field. But the most interesting data appeared when we plotted the binocular 24-2 mean sensitivity, which integrates the two separate eyes into a single score, relative to the NEIVFQ. *(See chart, above.)* A subset of patients had NEIVFQ scores significantly lower than would be anticipated based on the 24-2 visual fields. This group turned out to have the

best correlation between their 10-2 visual fields, focused on the macular region, and their NEIVFQ scores. We concluded that patients with disproportionate visual complaints relative to the 24-2 may actually have undetected macular damage.

Our next study sought to investigate whether macular damage was impacting vision-related quality of life across the different stages of glaucoma.[5] This is a pretty intuitive conclusion to reach in patients with later-stage disease, but we wanted to see if there was a correlation in patients with early disease, whom we haven't traditionally thought of as having macular damage.

To investigate this we looked at 88 eyes of 44 patients with early open-angle glaucoma (defined as a 24-2 mean deviation better than -6 dB). Subjects could not have macular degeneration, had to have less than 2+ nuclear cataract using the LOCS III grading system and minimal to no PCO. We identified the presence of any macular damage in the better and worse eyes, as well as what I'll refer to as peripheral arcuate damage—glaucomatous damage outside of the macula. Then, we looked to see which patients had NEIVFQ scores that were more than one standard deviation below the mean. We found:

- Forty-four of the worse eyes (57 percent) had macular damage; 13 of the better eyes (31 percent) had macular damage.
- Patients with confirmed macular damage in the better eye were 35 times more likely to be in the low-quality-of-life score group.
- Patients with macular damage in the worse eye were 11 times more likely to be in that group.
- Perhaps most interesting, peripheral damage was not an independent predictor for being in the low-quality-of-life-score group.

Our conclusions were first, that macular damage is common in early glaucoma; and second, even in early glaucoma, macular damage can impact vision-related quality of life, while peripheral damage does not.

Diffuse vs. Focal Damage

Next we decided to look at whether the *pattern* of macular damage affected the NEIVFQ score. Two types of macular damage have been described in the existing literature: focal damage, which we can readily see, and diffuse damage. Typically, focal damage is a dense, fairly deep loss of retinal ganglion cells, usually in the inferotemporal macula. This corresponds to a classic superior paracentral visual field defect. Such damage is frequently seen, for example, in normal-tension glaucoma.

Patients with diffuse damage had significantly lower QOL scores than those with focal loss.

Diffuse macular damage—a subtle, diffuse, generalized loss of RGCs in the macula—can be much more difficult to identify. It corresponds to a depressed total mean deviation in the 10-2 visual field. This kind of diffuse damage would be especially difficult to identify without macular OCT; we'd probably look at the 10-2 and conclude that this depression was caused by cataract or dry eye.

To address this, we conducted a cross-sectional prospective study involving 214 eyes of 107 patients representing a wide range of glaucomatous damage.[6] All eyes underwent 10-2 visual field tests and SD-OCT scans measuring both macular damage and the thickness of the RGC plus IPL layers. (We included the thickness measurement because patients with diffuse damage have thinner maculas on average. We wanted to be able to correct for that factor to make sure the thickness alone couldn't account for any differences that turned up between focal and diffuse damage.) All participants also completed the NEIVFQ questionnaire.

The data showed that patients with diffuse damage had significantly lower quality-of-life scores than patients with focal loss (p=0.03), even when adjusted for the average RGC thickness (p=0.02). This tells us that it's not just a matter of the degree of damage, but the type of damage; patients with focal damage had a more recognizable defect, but more diffuse damage had a greater impact on central vision. A possible explanation for this could be that our brain is able to compensate for a focal defect, just as it does for our natural blind spot, whereas diffuse damage might be nearly impossible to compensate for. (A paracentral defect could certainly affect a patient's quality of life, but it might not do so to the same degree as more global, diffuse damage.)

This raises an interesting question: Can diffuse macular damage be seen in 24-2 results (beyond a depressed mean deviation score)? Possibly—but macular damage is very easy to overlook in 24-2 results. Any macular damage would be contained within the four central points, so you might only see one or two depressed points. That might fail to draw your attention.

Our next study evaluated the presence and type of macular damage that was associated with visual problems under either low luminance or glare.[7] As noted earlier, other studies have found that patients with glaucoma reported having visual problems under suboptimal lighting conditions. We decided to see whether macular damage could be a potential driver of

these visual complaints.

We conducted an observational cohort study involving 252 eyes of 126 participants who had mild or moderate open-angle glaucoma, examining the relationship between glaucomatous macular damage and visual difficulty under low luminance conditions. This was measured using the Low Luminance Questionnaire, a validated questionnaire mostly used in the retinal literature to look at macular degeneration symptoms. Subjects could not have macular degeneration; they had to have less than 2+ nuclear cataract using the LOCS III grading system; and minimal to no PCO. As before, we divided the eyes into those with diffuse macular damage and those with focal macular damage. Focal and diffuse macular defects were identified using SD-OCT and both 24-2 and 10-2 visual fields. Findings included:

- Sixty-five percent (n=82) of the 126 better eyes showed evidence of macular damage; 35 percent (n=44) of these eyes did not.
- Of the 82 eyes with damage, 40 percent had diffuse damage and 60 percent had focal damage.
- Diffuse macular damage was a significant predictor of having difficulty in extreme lighting (p=0.0024); difficulty in low lighting (p=0.037); and diminished mobility (p=0.042).
- There was no significant difference between subjects who had focal damage and subjects with no macular damage at all.

Real-world Consequences

Lastly, we looked at a real-world functional outcome by examining whether macular damage would impair facial recognition in patients with good central visual acuity. We conducted a prospective, cross-sectional study involving 144 eyes of 72 participants with a diagnosis of open angle glaucoma in one or both eyes and a visual acuity of 20/40 or better in each eye.[8] We used SS-OCT and 10-2 visual field testing to determine the presence or absence of macular damage and then tested patients using the Cambridge Face Memory Test, a well-validated test from the neurologic literature. The study had very strict inclusion/exclusion criteria; participants had to have good cognitive function, and patients with miotic pupils, cataracts, surface disease, retinal disease or drusen (among other factors) were excluded.

We found that the presence of macular damage predicted diminished facial recognition, regardless of whether we tested the patient's better or worse eye (p<0.0001 in either eye). This was true even after adjusting for potential confounding factors such as glaucoma severity, contrast sensitivity, age and visual acuity.

Since then, we've conducted another study looking at the correlation between facial recognition ability and diffuse versus focal macular damage.[9] The data showed that patients with diffuse damage did significantly worse on the facial recognition test than those with focal damage. Patients with diffuse damage in the better eye recognized 10 fewer faces than those with focal damage; patients with diffuse macular damage in the worse eye recognized an average of 5.5 fewer faces. This remained significant after adjusting for possible confounding factors such as 24-2 mean deviation, age, visual acuity, presence of early cataract, number of drops and contrast sensitivity.

To sum up, our studies to date have demonstrated that:

1) vision-related quality of life, as measured by the NEIVFQ, appears to be driven by diffuse macular damage rather than focal loss;

2) even subtle, diffuse macular damage, easily overlooked in a 24-2 visual field, can cause visual disability;

3) visual complaints relating to low luminance, dim lighting and glare are all significantly associated with diffuse macular damage;

4) facial recognition is affected by the presence of diffuse macular damage.

We believe this provides strong support for the idea that early identification of the presence and type of macular damage is critical to assessing and treating visual disability in early glaucoma. To really assess the patient's visual performance across the disease spectrum, we need to look at the correlation between macular OCT and 10-2 visual fields. Early identification of any type of macular damage, focal or diffuse, is important—but it appears to be particularly important to identify diffuse, generalized macular damage.

Practical Pearls

How might a clinician use this information? Here are a few suggestions:

- ***Run a baseline OCT macular scan on every glaucoma patient.*** I look for any abnormalities on the macular scan and in the central points of the 24-2 visual field. If I see evidence of damage in either one, I'll run a 10-2 test.
- ***Treat early glaucoma patients with macular damage more aggressively***. Once I've uncovered macular damage, I keep a closer watch on the patient and run 10-2 visual fields more frequently.
- ***Let the patient know that any central vision issues they're having may be partly due to the glaucoma.*** Noting that central visual problems can be connected to their glaucoma will reassure the patient that A) the patient isn't imagining these problems; B) you understand what the patient is going through; and C) it's really important for the patient to follow the treatment plan.

• ***If your patient has central vision symptoms that may be the result of macular damage, consider removing a cataract earlier than you otherwise would have.*** You can explain to the patient that you can't correct the macular damage, but you can eliminate the early cataract that's making the problem worse, instead of waiting for the cataract to become more problematic.

Moving Forward

Being able to better understand your patient's visual ability in early glaucoma using office-based testing is a real step forward in ophthalmic care. Once significant damage has been done, we can look at the visual field and say it's obvious that this patient is going to function poorly. But in the early stages of glaucoma, that's been difficult or impossible to do. (This stands in contrast to many retinal diseases where there's a linear relationship between central visual acuity and visual function.)

As doctors, it's hard for us to change our paradigms. We're taught to be careful and to question change, because we don't want to adopt anything unproven that might put our patients at risk. But now, thanks in part to advanced technologies such as OCT, we're getting new insights about diseases like glaucoma, allowing us to look at them and manage them in a more nuanced way. We shouldn't hesitate to use those new insights to help our patients. REVIEW

Dr. Blumberg is an associate professor of ophthalmic sciences at Columbia University Medical Center, part of the Edward S. Harkness Eye Institute in New York. She reports no financial ties relevant to any products mentioned in this article.

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A Clearer Picture of Retinal Imaging

Experts review the pros and cons of the newest imaging devices available for the retina specialist.

Arathi Ponugoti BS, MS, Michael Patrick Kelly, FOPS, and Lejla Vajzovic, MD
Durham, N.C.

Advances in retinal imaging modalities allow us to visualize posterior segment findings to a previously unmet degree. The clinical utility of these imaging techniques is constantly expanding, with new developments in machinery allowing for improvements in patient care. Better fields of view, image clarity/detail and modes of acquisition not only help during diagnosis of retinal disorders but also during screenings and follow-ups. Well-captured retinal images allow us to identify disease severity and stage, compare follow-up visit images to documented findings, track progression of disease between visits, and screen for pathology early. Additionally and importantly, the capture of clear retinal images allows for unambiguous communication between physicians and contributes to the education of trainees.

In this article we'll explore a number of current retinal imaging modalities and their broadened utilities. It's important to keep in mind that many of these imaging techniques and technologies are used in conjunction with each other to gain a fuller understanding of the extent of pathology in a given patient.

Fundus Photography

This old standby has gone through several iterations in recent years that have increased its versatility and usefulness.

• ***Color.*** Standard color fundus photography continues to allow for the documentation of posterior pole findings including the macula and optic disc. These 20 to 50 degree images can be acquired rapidly and provide painless, reproducible, and high-resolution views that are true to size and color. However, these images are limited in their scope and are largely falling by the wayside in favor of widefield fundus imaging that allows for visualization of the retinal periphery, not just the macula and optic disc. Twenty-degree images just barely capture both the optic disc and macula in one image. Standard color fundus images can be useful if there's a need to capture high-magnification images of the macula in the clinic or to get a true-to-scale, color image of the optic nerve.

Optos ultra-widefield tabletop system

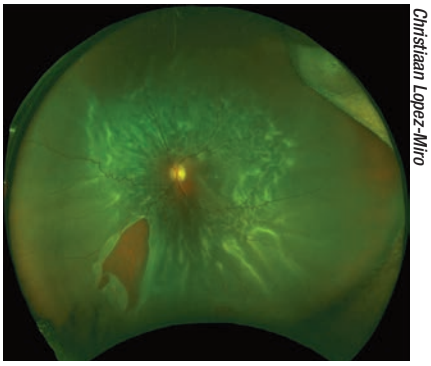

Christiaan Lopez-Miro

Figure 1. Optos ultra-widefield pseudo-color retinal image revealing a total retinal detachment with a large horseshoe tear.

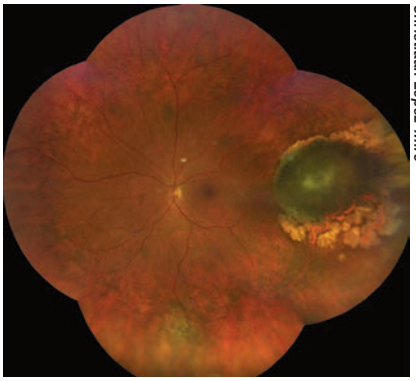
• ***Widefield.*** With the invention of widefield and ultra-widefield fundus imaging systems such as the non-contact tabletop Zeiss Clarus (Carl Zeiss Meditec AG; Jena, Germany) and Optos Daytona (Optos PLC; Dunfermline, United Kingdom), it's become possible to quickly gather high-resolution information beyond the posterior pole. As the peripheral retina is the site of pathology in many retinal diseases, widefield fundus photography has proved transformational for early

This article has no commercial sponsorship.

RetCam 3 Color Fundus Unit

screening, diagnosis and monitoring of an expanded list of retinal diseases. Ultra-widefield imaging allows for imaging of 80 percent or more of the retinal surface area through a 200-degree retinal view. It's now not only possible to assess more peripheral findings in diseases like diabetic retinopathy and macular degeneration, but these systems also allow for imaging and evaluation of choroidal masses, retinal vasculitis, choroidal dystrophies, hereditary retinal disorders and retinal vein occlusions outside the normal limited window of capture in standard fundus photography. Capture and documentation of peripheral lesions such as lattice degeneration, atrophic holes and retinoschisis allows for a more thorough and comprehensive assessment of extent of disease. Widefield fundus imaging has also allowed us to document previously unseen peripheral vascular pathology, thus widening insight into many adult and pediatric retinal diseases.[1]

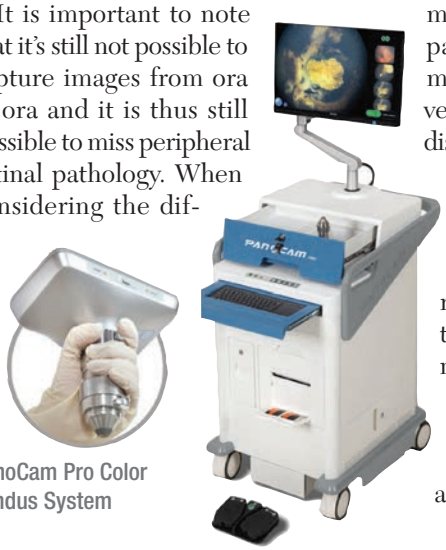
It is important to note that it's still not possible to capture images from ora to ora and it is thus still possible to miss peripheral retinal pathology. When considering the difference between the Zeiss Clarus and Optos Daytona it helps to understand that the Optos is a scanning laser ophthalmoscope and therefore provides a pseudo-color representation of the fundus (*Figure 1*). The Zeiss Clarus, which automatically takes and montages two pictures to approximate the same field of view as Optos, is true-color (*Figure 2*). As such, the Clarus is especially useful in the evaluation of ocular tumors.



Christiaan Lopez-Miro

Figure 2. Zeiss Clarus ultra-widefield color image montaged from four widefield images in a patient with choroidal melanoma after placement of a radiation plaque.

It should also be noted that in patients with undilated eyes the Optos is still able to capture full images with relative ease. For uveitic patients in which the iris has scarred down, Optos is still able to capture a full field of view, allowing for proper assessment of the periphery. In pediatric patients it's important to keep in mind that whereas the Clarus has a very bright flash that some children dislike, the SLO Optos doesn't and, as a result, may be better tolerated by pediatric patients.



PanoCam Pro Color Fundus System

• ***Handheld.*** The advent of portable handheld fundus photography devices has made it possible to not only image newborns in the neonatal intensive care unit and infants in our clinic, but also to image bedridden adults and patients in the OR during exams under anesthesia. The RetCam 3 (Natus Medical Incorporated; Pleasanton, California), Phoenix Icon (Phoenix Technology Group; Pleasanton, California), and PanoCam (Visunex Medical Systems; Fremont, California) are widefield handheld fundus photography systems that allow for evaluation and documentation of retinal findings and changes through the periphery.[2] The use of these devices has extended care significantly to newborns and infants with retinopathy of prematurity within the hospital. They also provide a unique opportunity for evaluation via telemedicine; stitched montages of images can be used to help in this effort.

All three of these devices are contact systems and require the application of gel onto the cornea. Issues with stability can affect image acquisition. Whereas the RetCam 3 and Phoenix Icon are capable of fluorescein angiography, the PanoCam is not. Unlike the RetCam 3 and the Phoenix Icon, the PanoCam is wireless and is thus easier to maneuver.

Fluorescein Angiography

Through the use of either IV or oral fluorescein, fluorescein angiography allows for the visualization and documentation of flow through the retinal vasculature over time. FA is able to reveal the presence of aberrant vasculature all the way through the periphery *(Figure 3)*. Neovascularization, areas of non-perfusion, abnormal vascular findings and areas of leakage can all be detected via FA. There are both tabletop as well as portable options for obtaining FA images. Widefield devices such as the Optos California FA, RetCam 3 and Phoenix Icon are all capable of FA. Heidelberg Spectralis (Heidelberg Engineering; Heidelberg, Germany) is also capable of FA, and has a widefield lens that can be used with the machine. It should be noted that FA images can be obscured by dye leakage; for example,

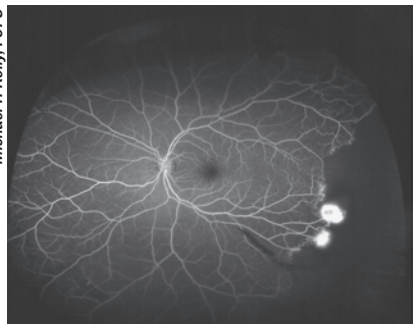

Michael P. Kelly, FOPS

Figure 3. Optos ultra-widefield fluorescein angiography image of sickle cell retinopathy demonstrating peripheral capillary nonperfusion as well as sea-fan neovascularization.

in cases of choroidal neovascularization the fluorescein can leak too much to be able to properly visualize the structure.[3] It's also important to keep in mind that with oral FA, which is generally only used in children who can't tolerate IV FA or for whom it's too difficult to find a vein, it's impossible to obtain arterial phase images with oral FA.[4] Because we can only obtain late-phase angiographic images with oral FA, it is generally only useful in the evaluation of conditions in which there is late leakage such as instances of neovascularization or cystoid macular edema (which can reveal accumulation of dye leakage in the cystic spaces of the macula).

Fundus Autofluorescence

Fundus autofluorescence takes advantage of the fluorescent properties of lipofuscin under certain wavelengths of light to offer views of autofluorescence patterns that reveal the health of the retinal pigment epithelium. In certain retinal disease states, such as age-related macular degeneration, macular dystrophies and retinitis pigmentosa, there is abnormal lipofuscin buildup in unhealthy RPE cells which are unable to properly phagocytose these accumulating granules. In healthy retinas with normal distribution and turnover of lipofuscin in the RPE cell layer, the FAF appears as a black-and-white image of the fundus. Areas in which unhealthy RPE cells can't properly metabolize accumulating lipofuscin will appear brighter. Areas in which RPE cells have died will appear black. FAF is a useful diagnostic tool often used as a complement to FA to diagnose, evaluate and monitor progression of diseases such as AMD, hereditary retinal dystrophies, optic nerve head drusen and astrocytic hamartoma.[5]

Devices that can perform FA can also perform FAF as they use the same wavelength of light. Widefield systems such as the Optos California FA and the Zeiss Clarus can perform FAF, with widefield FAF proving to be particularly useful for the evaluation of certain intraocular tumors and retinal dystrophies. The Heidelberg Spectralis is also capable of FAF with the widefield lens as well as the standard 30-degree and 55-degree lenses (*Figure 4*). Many standard 50-degree color fundus cameras such as Nikon, Topcon and Canon can also perform both FA and FAF.

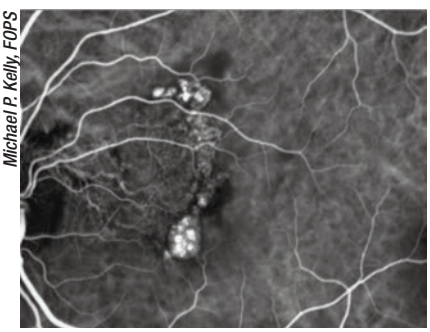

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Figure 4. Fundus autofluorescence image in a patient with Stargardt's disease demonstrating both central hypoautofluorescence surrounded by a hyperautofluorescent halo and irregular hyperautofluorescent flecks in the posterior pole.

Indocyanine Green Angiography

Using a different wavelength of light than both FA and FAF, indocyanine green angiography allows us to see past the retina and into the choriocapillaris and choroid. ICG dye is injected intravenously, flows through the retinal and choroidal circulation, and is then imaged with infrared light that penetrates the retinal layers as the choroidal vasculature fluoresces. As such, ICG provides an angiogram of the choroid and is most useful for evaluation of diseases such as polypoidal choroidal vasculopathy (*Figure 5*), choroidal neovascularization, intraocular tumors, retinal angiomatous proliferation and central serous chorioretinopathy. While some widefield cameras, such as Optos California ICG, can do ultra-widefield ICG, some retinal physicians find it useful to obtain magnified ICG images targeted to the area of interest. On the other hand, widefield ICG can prove to be very useful in the evaluation of vascular alterations in certain uveitic conditions, especially chorioretinal inflammatory disorders such as multifocal choroiditis and birdshot retinochoroidopathy.

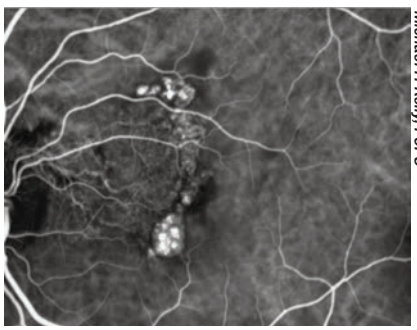
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Figure 5. Polypoidal choroidal vasculopathy with a vessel network and multiple polypoidal lesions are best visualized with indocyanine green angiography.

It's possible to obtain both static ICG images (useful for the evaluation of intraocular tumors and uveitis) as well as dynamic ICG videos (useful for evaluation of NAMD and choroidal neovascularization). In presentations of NAMD in which there are feeder vessels, polypoidal choroidal vasculopathy, or retinal angiomatous proliferation dynamic

information regarding flow can be particularly helpful.

Optical Coherence Tomography

Since its introduction more than two decades ago, posterior segment OCT has become a mainstay in virtually all workups in the retina clinic. Through the use of near infrared wavelength light and the principle of low coherence interferometry, OCT is able to discern the different layers of the retina to provide detailed, high-resolution, 2-D cross-sectional images through the volume of the retina. Morphological changes, as well as alteration, deformation and loss of structure are made clear via OCT. These non-invasive, non-contact scans inform diagnosis, allow for monitoring of disease progression and let us evaluate the response to treatment. The most commonly used type of OCT currently is spectral-domain OCT, which uses a short wavelength of light and a spectrometer as the detector. There are a number of different SD-OCT devices on the market with differing axial resolutions, scanning speeds and features.[6] Some of the most widely used systems are the Zeiss Cirrus, the Heidelberg Spectralis and the OptoVue Avanti (OptoVue; Fremont, California). Swept-source OCT uses a laser that sweeps over a broad range of longer wavelengths allowing for greater penetration through the retina for evaluation of the choroid. SS-OCT also measures the interference spectrum with photodetectors instead of a spectrometer, allowing for faster scanning speeds and the ability to obtain wider field B scans. The Topcon DRI OCT Triton (Topcon, Oakland, N.J.) and the Zeiss Plex Elite 9000 are two SS-OCT systems but are found much less commonly in clinics than SD-OCT systems, which have seemed to retain favor. At this time the Zeiss Plex Elite 9000 is only marketed for research use. Alongside OCT images, systems capture an infrared fundus image via a secondary light source that corresponds with the volume through which the OCT scans were obtained (*Figure 6*).

Figure 7. The Heidelberg Spectralis FLEX system allows for optical coherence tomography and OCT angiography imaging in the operating room during exams under anesthesia.

With the development of the handheld Bioptigen/Leica Envisu C2300 OCT system (Leica Microsystems, Durham, North Carolina) it has become possible to image newborns in the NICU and infants in clinic. This is especially useful for diseases such as ROP, X-linked retinoschisis, Coats', non-accidental trauma and familial exudative vitreoretinopathy. The Bioptigen head is lightweight and well-balanced which makes it easy to maneuver. While the handheld system provides a good virtual biopsy of the retina it doesn't allow for macular thickness maps or RNFL measurements. It should be noted that it's possible to adjust the reference arm to reduce clipping, manually adjust the focus, and adjust the scan length and density when using the handheld Bioptigen and tabletop OptoVue AngioVue. This is especially useful when imaging pediatric patients in which the axial length, refractive error, astigmatism and corneal curvature change with age.[7]

Recently, Leica launched EnFocus, an intraoperative OCT system *(See Product News, p. 62 for more information)*. There's also one OCT device that's in the FDA approval process, the Heidelberg FLEX, in which the camera head is attached to a maneuverable armature allowing for OCT imaging in the OR (*Figure 7*).

Optical Coherence Tomography Angiography

In recent years the development of OCTA has allowed us to obtain three-dimensional, depth-encoded images that can clearly reveal the vessels in which there is flow in the different vascular layers of the retina and choroid. OCTA is an extension of tradi-

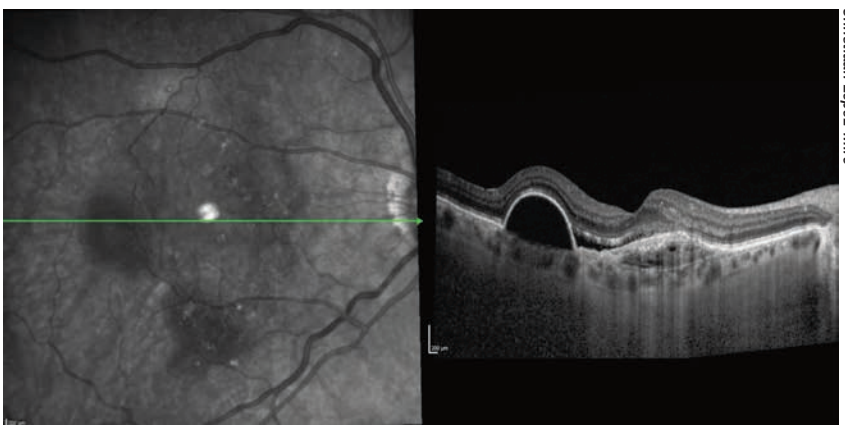

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Figure 6. An OCT image alongside a simultaneously acquired infrared image of a patient with active neovascular age-related macular degeneration based on subretinal fluid and serous retinal pigment epithelium detachment.

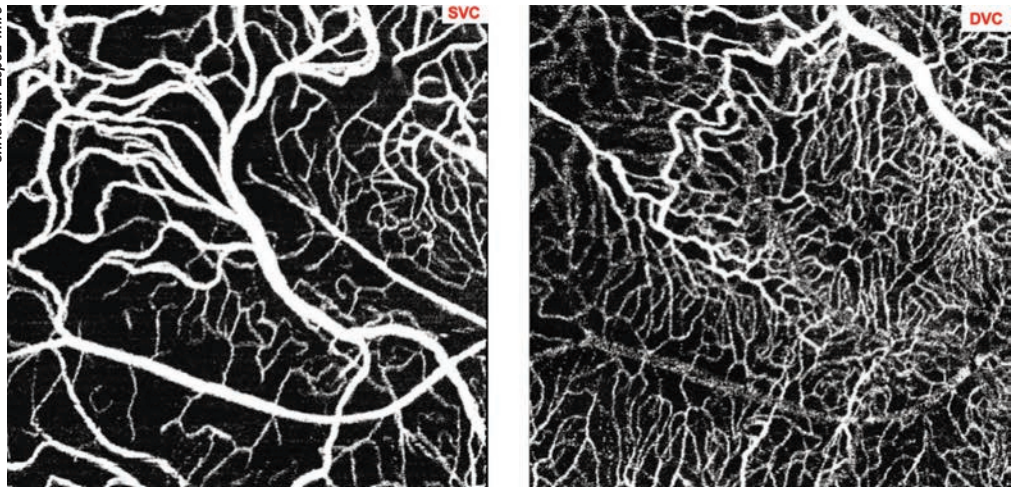

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Figure 8. Superficial and deep vascular complex (SVC and DVC) OCTA images in a pediatric patient with a rare proliferative retinopathy demonstrating an advanced neovascular network with loops and curls as well as loss of fine capillaries.

tional OCT that takes multiple B-scans through each point along the volume of the retina; the plotting of the signal difference from the moving erythrocytes between B scans taken in the same location allows us to obtain a map of blood flow through the retina. In this way it's possible to assess for perfusion defects, abnormal vessel distribution, and pathologic vascular layer features. Unlike FA, OCTA doesn't require either the use of IV or oral fluorescein. OCTA images provide more detail than FA images and allow for assessment of flow and vasculature at all levels of the retina and choroid. It should be noted however that OCTA images cannot detect real time leakage from damaged vessels and have a smaller field of capture (either 3 x 3-mm, 6 x 6-mm, or 12 x 12-mm scan area) thus limiting peripheral and widefield visualization.

OCTA allows for both qualitative and quantitative evaluation of depth-encoded retinal vasculature. Not only is it useful for visualizing and identifying aberrant vasculature such as neovascular membranes, but OCTA can quantify and compare vessel density and FAZ area to better understand the extent of pathology at baseline as well as monitor disease progression.[8]

The four tabletop OCTA devices on the market all differ in scan speed and resolution: the OptoVue AngioVue; Zeiss Cirrus 6000 with Angioplex; Zeiss Cirrus 5000 with AngioPlex; and Heidelberg Spectralis. The Zeiss Cirrus is faster than the Heidelberg Spectralis but doesn't utilize an eye tracking system like the Spectralis. Keep in mind that all three devices define their superficial, deep and avascular layers differently. The Heidelberg Spectralis FLEX, which is currently seeking FDA approval, has made it possible to obtain OCTA images in the OR during exams under anesthesia. This has proven to be particularly useful in pediatric patients with retinal diseases with known neovascular components such as ROP, Coats', and FEVR who often have trouble fixating long enough to obtain a clear OCTA image (*Figure 8*). It should also be noted that while dilation isn't necessary to obtain an OCTA image in adults it makes an appreciable difference in the ability to capture a clear scan in children.

In conclusion, advancements in these retinal imaging modalities continue to expand our ability to diagnose, monitor, and treat retinal diseases in our patients. Through the use of these modalities, often used in conjunction in some combination, we are able to screen for and detect diseases earlier than ever and quickly identify progression in disease that might require changes to treatment plans. The development of new instrumentation and imaging techniques continues to have tremendous impact on access to care, our understanding of retinal disease and clinical practice. REVIEW

Ms. Ponugoti is a medical student completing two research years in the ophthalmology department at Duke University Medical School under the guidance of Dr. Vajzovic, who is an associate professor of ophthalmology at Duke. Mr. Kelly is the director of Duke Eye Imaging.

Dr. Vajzovic receives research funding from Heidelberg. The other authors have no financial interest in the products discussed.

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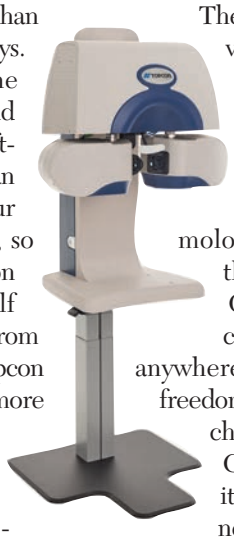
A New Space-saving Autorefraction System

If you've been looking for a refraction solution that can fit into tight spaces, the new Topcon Chronos may be worth a look.

Chronos is a digital refraction system that combines autorefraction, keratometry and subjective refraction in a device that occupies less than four feet of space, Topcon says. The company adds that the system is fully automated, and features guided refraction software called SightPilot, so it can be operated by anyone in your practice. It tests binocularly, so the average patient refraction time is just three and a half minutes (though it can vary from patient to patient), which Topcon says allows providers to see more patients and grow their practice without adding exam lanes or trained technicians.



The system can be controlled via a tablet, laptop or desktop PC, which means that the staff member at the controls can be at a safe distance or even in another room.

For information, visit topconhealthcare.com/products/chronos/.

See Your Practice Better Through the Fog

EyeMD EMR Healthcare Systems recently unveiled its EMR 2.0 system, which it describes as an "all-in-one electronic medical records, practice management and picture archiving and communication system."

The company says that the 2.0 EMR software uses fog-based technology. In fog-based computing, devices such as controllers, switches, routers and video cameras can act as "fog nodes." Then, data generated by a device can be analyzed using one of these nodes without having to be sent all the way back to the cloud.[1] EyeMD EMR says this approach "future-proofs" ophthalmology practices by scaling as the practice's needs evolve. Ophthalmology practices can access their system from anywhere, while allowing them the freedom to choose their hosting architecture, the company says. Customers also have the ability to work through an internet outage uninterrupted.

EyeMD EMR Practice Management is a fully-integrated billing and real-time claims-management system that automates accounts receivables management, its maker says, while producing extensive reports.

For more information on the new system, visit eyemdemr.com or call (877) 2 EYE EMR.

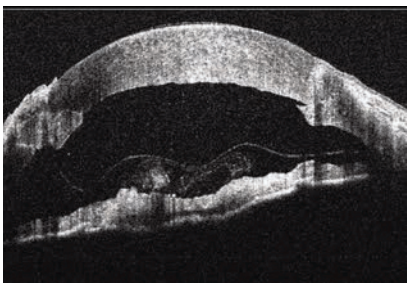
Intraoperative Play-by-Play

Leica recently introduced EnFocus, an intraoperative optical coherence tomography system for its Proveo 8 and M844 F40 surgical microscopes.

The company says the system can show the orientation of donor tissue in real-time in DMEK, the tension on an epiretinal membrane, and placement information for glaucoma shunts. Leica says it can differentiate between artifacts and tissue due to its unique spectrometer technology with dispersion compensation software. Its highly sensitive detector captures more signal, shows fine details even through blood, and can play back the case through acquired OCT scans frame by frame or in video mode to check for such things as residual subretinal fluid, the positioning of a glaucoma drainage device, or whether or not a corneal graft is well-apposed to the host cornea.

For information, visit leica-microsystems.com REVIEW

1. What is Fog Computing? https://www.itprc.com/fog-computing/. Accessed November 19, 2020.



Leica's EnFocus system provides real-time OCT during your procedures.

This article has no commercial sponsorship.

Throbbing pain and redness in his blind eye brings a 54-year-old man to the Wills Eye Emergency Department.

Sarah Amanullah, MD, Tatyana Milman, MD, and Ralph Eagle, MD

Presentation

A 54-year-old Caucasian male presented to the Wills Emergency Room with a four-day history of severe, throbbing right eye pain and redness. He noted that he had been blind in this eye for two years with intermittent pain over the past six months and an acute exacerbation four days prior to presentation. He denied recent eye trauma or surgery. Review of systems was negative for fever, chills, weight loss, chest pain, shortness of breath, abdominal pain, headache or arthralgias.

Medical History

Past medical history was notable for a dental surgery three months prior to presentation, for which the patient took post-procedure oral antibiotics. Ocular history was remarkable for glaucoma of unknown type diagnosed at an outside hospital about two-and-a-half years prior, which was managed by bimatoprost in both eyes. He reportedly lost vision in the right eye six months later. Approximately one year prior to presentation to the Wills Eye Hospital Emergency Room, the practice caring for him closed and the patient stopped taking his glaucoma medications.

Examination

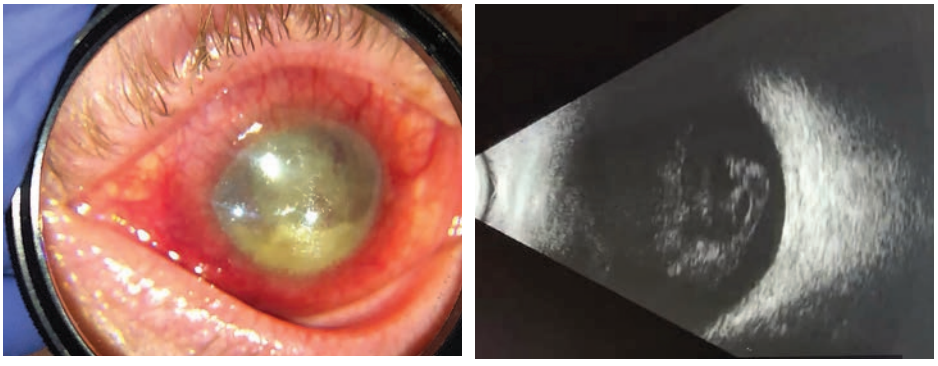


Figure 1. A) Corneal haze with layered hypopyon and prominent conjunctival injection and ciliary flush. B) Vitreous opacities on B-scan ultrasonography.

The patient's vital signs were stable and normal. Ocular examination showed visual acuity of NLP in the right eye and 20/20 in the left eye. IOP by applanation was 36 mmHg OD and 34 mmHg OS. Pupillary examination revealed an afferent pupillary defect OD. Extraocular motility was full. Exam of the right eye *(Figure 1A)* revealed an edematous and erythematous upper lid. The conjunctiva and sclera had 3+ ciliary flush, 2+ injection and no bleb was seen. The cornea was hazy and edematous with microcystic edema and scattered bullae. No epithelial defect, distinct infiltrate or ulceration was noted; however granulomatous keratic precipitates were present. The anterior chamber was shallow with a 3.3-mm, layered hypopyon. The pupil was round and without evidence of sphincter tear. A white cataract was present. There was no view of the fundus. B-scan ultrasonography revealed vitreous debris *(Figure 1B)*. Examination of the left eye was normal, with the exception of trace nuclear sclerotic cataract. The left optic nerve appeared healthy, without notching, hemorrhage or thinning, and had a vertical cup:disc ratio of 0.15. Gonioscopy couldn't be performed OD due to corneal haze. Gonioscopy OS demonstrated an open angle (Spaeth classification D40f).

Based on this information, what's your diagnosis? The diagnosis appears on pg. 64.

Workup, Diagnosis and Treatment

The differential was broad, and included infectious endogenous endophthalmitis, as well as non-infectious etiologies such as sarcoidosis and lens-induced uveitis. Neoplastic etiologies couldn't be excluded, either. The main concern in the emergency room setting was infectious endophthalmitis. The patient underwent a vitreous tap and intravitreal injection of vancomycin, ceftazidime and voriconazole. The patient was admitted for an endogenous endophthalmitis work-up.

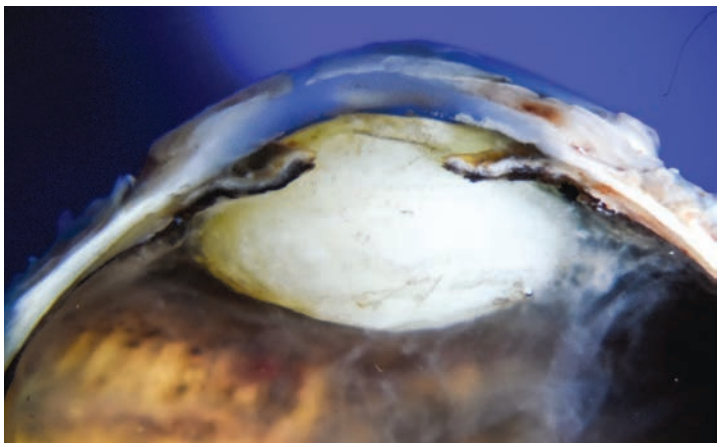


Figure 2. Gross photograph of the enucleated eye demonstrates a swollen white cataractous lens with an inflammatory infiltrate centered around the lens. The anterior chamber angle is closed.

A comprehensive inpatient work-up was notable for elevated Lyme disease IgG and normal IgM, consistent with remote infection. Bacterial, fungal, mycobacterial cultures, HSV1/2, VZV, CMV and Toxoplasma PCR performed on the vitreous tap were negative. Systemic laboratory studies including blood cultures, galactomannan and fungitell were negative. Serologic studies for treponema pallidum, HIV, *Anaplasma*, and *Ehrlichia* were negative. Quantiferon gold was normal. The ESR, ACE and vitamin D levels were within normal limits. Imaging obtained included a transthoracic echocardiogram, which was normal. CT of the facial bones revealed multifocal dental disease.

The patient was treated with intravenous vancomycin. Ocular medications included brimonidine b.i.d. OU, dorzolamide-timolol OU, ofloxacin q.i.d. OD, atropine b.i.d. OD and prednisolone acetate every two hours while awake OD. Although the patient experienced significant relief with topical ophthalmic medications, he continued to have pain in the chronically non-seeing eye and opted for enucleation.

Gross evaluation of the enucleated eye demonstrated a swollen cataractous lens with inflammation centered around the lens. The anterior chamber angle was closed by peripheral anterior synechiae *(Figure 2)*. Microscopic evaluation of the anterior chamber angle demonstrated findings suggestive of chronic post-traumatic angle recession. The lens capsule was ruptured. The lens cortex demonstrated extensive degeneration and liquefaction with Morgagnian globule formation. The lens fibers were infiltrated by neutrophils and focally by the granulomatous inflammation, composed of epithelioid macrophages and rare multinucleated giant cells *(Figure 3A)*. These findings were reminiscent of phacoantigenic uveitis, although a distinct zonal pattern of inflammation was not present.

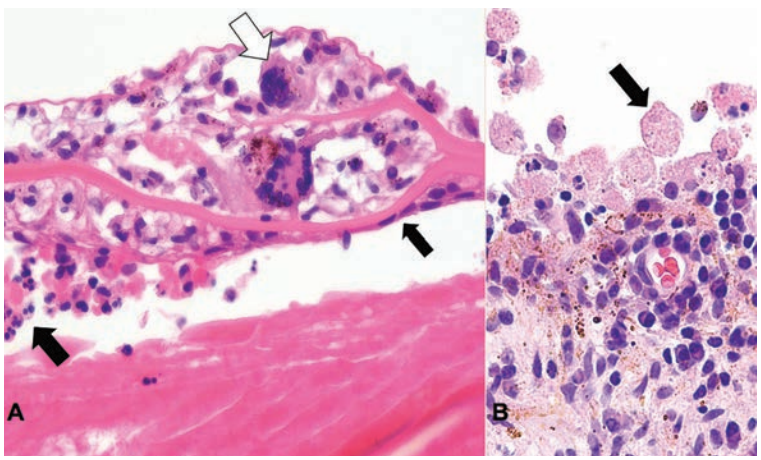


Figure 3. A) Lens capsule is ruptured (thin arrow). Neutrophils surround the lens cortex (wide arrow). Epithelioid macrophages and giant cells are also present (open arrow). B) Macrophages with intracytoplasmic pale pink degenerated lens material (arrow) are present on the surface of the iris (hematoxylin-eosin stain; original magnification x100).

Also noted were numerous macrophages with intracytoplasmic degenerated lens protein in the anterior chamber, compatible with a phacolytic uveitis. *(Figure 3B)*. Additional findings included chronic nongranulomatous iritis and vitritis and end-stage glaucomatous retinal and optic nerve atrophy.

Discussion

Lens-induced uveitis includes a group of intraocular inflammatory diseases characterized by an inflammatory response to lens proteins.

Phacoantigenic uveitis (formerly known as phacoanaphylaxis) is a rare autoimmune condition that occurs when there's an altered immune response to undenatured lens protein, precipitated by disruption of the lens capsule. Phacoantigenic uveitis is a type-3 immune-complex (antigen-antibody) mediated response that results in activation of the complement cascade and a zonal granulomatous response surrounding the lens fibers. Although previously the lens was thought to be immune-privileged, it's now believed to be under immune surveillance. Notably, lens proteins are found in the aqueous humor of normal eyes, and antibodies to lens proteins are found in some individuals who don't have a lens-induced uveitis.[1] The loss of immunologic tolerance to lens proteins has been proposed to lead to phacoantigenic uveitis. In a clinical-pathologic review of 144 patients with phacoantigenic uveitis, the average patient age was 53.[2] The majority were males (61 percent), who presented with NLP vision (78 percent) and low intraocular pressure (58 percent < 9 mmHg).[2] Most cases were associated with trauma (80 percent); however, history of trauma wasn't elicited in 20 percent of patients. The time from trauma ranged from a few days to nearly sixty years. Only 4 percent of patients were diagnosed accurately prior to histopathologic review of an enucleated eye. The five leading clinical diagnoses were phthisis, glaucoma, iritis, endophthalmitis and sympathetic ophthalmia.[2]

Phacoantigenic uveitis (formerly known as phacoanaphylaxis) is a rare autoimmune condition that occurs when there's an altered immune response to undenatured lens protein, precipitated by disruption of the lens capsule.

Phacolytic glaucoma occurs as a result of leakage of

lens proteins from liquified cortex through an intact lens capsule. The lens proteins are then phagocytosed by macrophages, which block the trabecular meshwork, leading to a secondary open-angle glaucoma.

The treatment of lens-induced uveitis is to remove the inciting lens material. The therapy is tailored to the patient, and can include cataract surgery, anterior chamber washout, pars plana vitrectomy or enucleation.[1]

It's important to note that remote trauma in our patient induced angle recession and contributed to the asymmetric glaucoma. It's been documented that 60 percent of eyes with non-penetrating trauma will have some degree of angle recession; however, less than 10 percent of these will develop glaucoma.[3] Interestingly, in those patients who develop traumatic glaucoma, the fellow eye that didn't experience trauma has a 50-percent chance of developing glaucoma, suggesting that patients who develop traumatic glaucoma have an underlying predisposition to it.[3] This observation appears to hold true for our patient in this particular case, who had ocular hypertension in the fellow eye.

In summary, our patient had a remote history of ocular trauma, which led to chronic angle recession and asymmetric cataracts. Histopathology of the enucleated eye showed a lens-induced uveitis, characterized by a mixed forme fruste phacoantigenic zonal granulomatous response and phacolytic macrophagic response. We speculate that lens-induced uveitis in our patient occurred as a result of lens capsular rupture of hypermature cataract, possibly precipitated by pre-existing traumatic lens capsular weakness or microscopic dehiscence. This case highlights the importance of eliciting a history of trauma, even if it's from the distant past, in a patient with asymmetric glaucoma. REVIEW

1. Nche EN, Amer R. Lens-induced uveitis: An update. Graefes Arch Clin Exp Ophthalmol 2020;258:7:1359-1365.
2. Thach AB, Marak GE Jr, McLean IW, Green WR. Phacoanaphylactic endophthalmitis: A clinicopathologic review. Int Ophthalmol 1991;15:4:271-9.
3. Tumbocon JA, Latina MA. Angle recession glaucoma. Int Ophthalmol Clin 2002;42:3:69-78.

REVIEW Advertising Index

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

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

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

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

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

- Hypersensitivity *[see Contraindications (4)]*

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

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

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

6.2 Postmarketing Experience
The following adverse reactions have been identified during post-approval use of Xiidra. Because these reactions are reported voluntarily from a population of uncertain size, it is not always possible to reliably estimate their frequency or establish a causal relationship to drug exposure.

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

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

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

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

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

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

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Novartis Pharmaceuticals Corporation
One Health Plaza
East Hanover, NJ 07936

T2020-87

*In some patients with continued daily use. One drop in each eye, twice daily (approximately 12 hours apart).[3]

†Xiidra is an LFA-1 antagonist for the treatment of dry eye disease. **Pivotal trial data:** The safety and efficacy of Xiidra were assessed in four 12-week, randomized, multicenter, double-masked, vehicle-controlled studies (N=2133). Patients were dosed twice daily. **Use of artificial tears was not allowed during the studies.** The study endpoints included assessment of signs (based on Inferior fluorescein Corneal Staining Score [ICSS] on a scale of 0 to 4) and symptoms (based on patient-reported Eye Dryness Score [EDS] on a visual analogue scale of 0 to 100).[3]

A larger reduction in EDS favoring Xiidra was observed in all studies at day 42 and day 84. Xiidra reduced symptoms of eye dryness at 2 weeks (based on EDS) compared to vehicle in 2 out of 4 clinical trials. Effects on signs of dry eye disease: ICSS (on a scale from 0-4; 0=no staining; 4=coalescent) was recorded at each study visit. At day 84, a larger reduction in inferior corneal staining favoring Xiidra was observed in 3 of the 4 studies.[3]

Indication

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

Important Safety Information

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

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

References: 1. US Food and Drug Administration. Code of Federal Regulations, Title 21, Volume 5 (21CFR349). Accessed April 17, 2020. https://www.accessdata.fda.gov/scripts/cdrh/cfdocs/cfcfr/CFRSearch.cfm?CFRPart=349&showFR=1 **2.** Jones L, Downie LE, Korb D, et al. TFOS DEWS II Management and Therapy Report. *Ocul Surf.* 2017;15(3):575-628. **3.** Xiidra [package insert]. East Hanover, NJ: Novartis Pharmaceuticals Corp; June 2020.

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