SEEING ROTH SPOTS
AS OCULAR SIGN
IN CASE REVIEW

Roth spots may occur in a number of systemic conditions including lym-
phoproliferative disorders. In this case review, a patient’s Roth spots could
have been secondary to underlying anemia and thrombocytopenia as a con-
sequence of HLH status complicated with underlying HIV. Clinicians should
be aware of the ocular manifestations and consider the diagnosis in any pa-
tient fulfilling the diagnostic criteria.

See story on page 35:

Surgical strategies can minimize risk by selecting appropriate patient, optimizing intraoperative view
By Nancy Groves; Reviewed by Kateki Vinod, MD

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Patients under consideration for TM-based MIGS should not have systemic morbidities that may comp-

TM-BASED MIGS

LANDSCAPE SHIFTS
FOR REFRACTIVE-CATARACT SURGERY
AS THE GLOBAL population that is prone to developing cataracts continues to grow, ophthalmologist could be facing challenges as people live longer.

As technology improves, however, patients are more willing to undergo cataract surgery at an earlier stage as the reward becomes greater than any associated risk because it provides an opportunity to improve their quality of life. Eric D. Donnenfeld, MD, shares his thoughts on the ever-changing current landscape.

See story on page 16:

Cataract regimen

A ‘MENTAL’ PICTURE
APHANTASIA CAN ROB ONE OF VOLUNTARILY VISUALIZING PLACES, THINGS

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SEEING ROTH SPOTS AS OCULAR SIGN IN CASE REVIEW

ROTH SPOTS may occur in a number of systemic conditions including lymphoproliferative disorders. In this case review, a patient’s Roth spots could have been secondary to underlying anemia and thrombocytopenia as a consequence of HLH status complicated with underlying HIV. Clinicians should be aware of the ocular manifestations and consider the diagnosis in any patient fulfilling the diagnostic criteria.

See story on page 35: Roth spots

TM-BASED MIGS BEST PRACTICES

Surgical strategies can minimize risk by selecting appropriate patient, optimizing intraoperative view

TRANSCUTANEOUS MIGS BEST PRACTICES

BY NANCY GROVES

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Ruth D. Williams, MD, discusses the presentation she delivered at the 2019 Glaucoma 360 meeting, “Private Equity and Ophthalmology: Will I Be Left Behind?” To watch, go to http://bit.ly/2JzwcIY

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How to close the physician gender pay gap
Gender bias and confidential salary information influence why men earn more than women

by Julie Miller

In Texas, a primary care physician working in a Denton County clinic discovered she was being paid $34,000 less per year than a male physician who performed the same duties. She questioned the matter and was later fired by administrators, who cited poor job performance. The Equal Employment Opportunity Commission (EEOC) brought the doctor’s claim to federal court. In a resolution reached late in 2018, a judge ordered the county to pay the female doctor $115,000 in damages and to correct its compensation policies.

In spite of numerous equal-pay regulations and ongoing EEOC enforcement, female physicians are chronically underpaid compared to their male counterparts. “For every specialty and every geography, there is a significant gap,” says Christopher Whaley, Ph.D., an adjunct assistant professor at the University of California, Berkeley School of Public Health, who has studied the gender pay gap.

CLEAR DATA
Medical Economics found in its survey of primary care physicians that female physicians reported a median annual income of $175,000, while male physicians reported an income of $275,000. In other words, the women surveyed earn 63 cents for every $1 that men earn. At the highest end of the pay scale, 10% of male respondents say they earn $500,000 or more. Whaley, who was the lead author on the Doximity study, says it’s surprising that medicine—with its intensive education requirements and high standards applied uniformly to all professionals—would demonstrate such wide discrepancies in compensation between men and women. “It’s not as if a woman in the study sample had inadequate training,” he says.

REASONS BEHIND THE GAP
The Equal Pay Act of 1963 was the first law making it illegal for employers to pay women less than men for doing the same job. Subsequent state and federal rules have aimed to reinforce pay equality, but the regulatory stick hasn’t been enough to level out earnings. Census Bureau data from 2016 show America’s working women are earning just 80 cents for every $1 that men earn. Implicit bias is often to blame for the historic pattern of discrimination, experts say. For example, women are less likely to be perceived as family breadwinners or as loyal workers willing to put in long hours, says Theresa Rohr-Kirchgraber, MD, FACP, executive director of the Indiana University National Center of Excellence in Women’s Health and a chief physician executive at Eskenazi Health.

Rohr-Kirchgraber has studied gender pay gaps for years. She advises female physicians—many of whom are in fact the breadwinners in their households—to avoid talking about personal issues at work. If a woman declines a meeting invitation because of childcare concerns, for example, it’s in her own best interest to skip the explanation. Talking about outside demands can give the impression that professional duties aren’t a priority.

“Set us up to look as if we’re not as enthusiastic about our jobs,” Rohr-Kirchgraber says. Yet she doesn’t believe men in medicine are deliberately acting with a gender bias, or

Continues on page 9: Addressing transparency
A ‘mental’ picture
Aphantasia can rob one of voluntarily visualizing places, things

By Peter J. McDonnell, MD
director of the Wilmer Eye Institute,
Johns Hopkins University School of Medicine, Baltimore, and chief medical editor of Ophthalmology Times.

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SOON IT WILL be time to pack up the sunscreen, umbrella, and towel and head to the beach. In fact, a good way to get through the cool and wet days of spring is to sit back, close one’s eyes, and visualize sitting in a beach chair surrounded by sand on a hot, summer day and cooled by a gentle, ocean breeze and refreshing beverage.

Some people are able to conjure up such vivid images that, upon opening their eyes, the images are still visible!

One friend tells me her images are not so strong, but it is the positive feelings associated with those images that register strongly.

It turns out that not everyone can escape reality for a few minutes by visualizing a getaway to some beautiful setting.

In the category of learning something new every day, I learned that there are people who have a condition termed, “aphantasia.” When these individuals close their eyes and try to visualize a beautiful beach or the face of a dear parent or beloved child (or anything for that matter), they see nothing.

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I don’t remember learning about this condition, which was named by Adam Zeman, BMBCh, MA, DM, FRCP, a professor at the University of Exeter Medical School. He described a male patient aged 60-plus years who had lost the ability to visualize images following cardiac surgery.

Apparently, one in 50 people has aphantasia. The explanation is unknown, but the condition is presumed to have something to do with some sort of dysfunction in the parietal and frontal lobes.

It can be congenital or (as in the case of the post-heart surgery patient) acquired.

Functional MRIs of the brains of college students show seemingly widespread differences between the brain activation of those who score high compared with low in terms of the vividness of their brain imagery.

BLIND MIND’S EYE
What captured the attention of the BBC World News is that some of the world’s most acclaimed animators, responsible for creating animated films such as “The Little Mermaid,” lack this ability to create mental images. According to the former president of Pixar and Walt Disney Animation Studios, he has a “blind mind’s eye.”

It is interesting that the inability to visualize images is not a barrier to success in a field like animation. However, I wonder whether it makes a difference for surgeons.

As a first-year resident, I vividly recall visualizing every step of cataract surgery (extracapsular extraction in those days) prior to performing my first such operation on a patient. Everything went smoothly in my head the night before and (fortunately) equally smoothly the next morning in the operating room.

I have always taken it for granted that my fellow ophthalmologists used the technique of visualization to help master new procedures. If someone with aphantasia cannot practice in their heads, does that make a difference?

So, dear reader, I ask you to take a few minutes to close your eyes and call upon your brain to conjure up the image of someone or something you care very much about—a loved one, a beautiful beach, the cover of Ophthalmology Times. What happens? ■

References
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.

Check out Xiidra-ECP.com

For additional safety information, see accompanying Brief Summary of Safety Information on the adjacent page and Full Prescribing Information on Xiidra-ECP.com.

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

DOSAGE AND ADMINISTRATION
Instill one drop of Xiidra twice daily (approximately 12 hours apart) into each eye using a single-use container. Discard the single-use container immediately after using in each eye. Contact lenses should be removed prior to the administration of Xiidra and may be reinserted 15 minutes following administration.

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

ADVERSE REACTIONS
Clinical Trials Experience
Because clinical studies are conducted under widely varying conditions, adverse reaction rates observed in clinical studies 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 studies of dry eye disease conducted with lifitegrast ophthalmic solution, 1401 patients received at least 1 dose of lifitegrast (1287 of which received lifitegrast 5%). The majority of patients (84%) had ≤3 months of treatment exposure. 170 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% to 5% of the patients were blurred vision, conjunctival hyperemia, eye irritation, headache, increased lacrimation, eye discharge, eye discomfort, eye pruritus and sinusitis.

Postmarketing Experience
The following adverse reactions have been identified during postapproval 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 cases of hypersensitivity, including anaphylactic reaction, bronchospasm, respiratory distress, pharyngeal edema, swollen tongue, and urticaria have been reported. Eye swelling and rash have been reported.

USE IN SPECIFIC POPULATIONS
Pregnancy
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 pre-mating 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.

Animal Data
Lifitegrast administered daily by intravenous (IV) injection to rats, from pre-mating through gestation day 17, caused an increase in mean preimplantation 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.

Lactation
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. 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.

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

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

NONCLINICAL TOXICOLOGY
Carcinogenesis, Mutagenesis, Impairment of Fertility
Carcinogenesis: Animal studies have not been conducted to determine the carcinogenic potential of lifitegrast.
Mutagenesis: Lifitegrast was not mutagenic in the in vitro Ames assay. Lifitegrast was not clastogenic in the in vivo mouse micronucleus assay. In an in vitro chromosomal aberration assay using mammalian cells (Chinese hamster ovary cells), lifitegrast was positive at the highest concentration tested, without metabolic activation.
Impairment of fertility: Lifitegrast administered at intravenous (IV) doses of up to 30 mg/kg/day (5400-fold the human plasma exposure at the recommended human ophthalmic dose [RHOD]) of lifitegrast ophthalmic solution, 5%) had no effect on fertility and reproductive performance in male and female treated rats.
worse, encouraging it to gain their own financial advantage. “There is plenty of work to go around,” she says. “Guys are just as confused as women as to why this is happening.”

LACK OF TRANSPARENCY
Another reason for pay gap’s persistence is that organizations often keep workers’ salaries and bonuses confidential. Without that data, women can’t quantify discrimination, making it extremely difficult to address. Sharrona Hoffman, JD, LLM, professor of law and bioethics at Case Western Reserve University School of Law in Cleveland, says women in medicine need to start asking questions and advocating for transparency.

“It might seem impolite, but if women are serious about closing the pay gap, they need the data,” Hoffman says.

Ana María López, MD, FACP, president of the American College of Physicians (ACP), says even if an organization won’t reveal comparative compensation data, physicians have a responsibility to do their own research. Other factors determine pay, such as regional market differences, years of experience, or hours of clinical time in proportion to other professional duties. Such data can build a case for negotiating higher pay.

“At my first job as an assistant professor, I remember being told my starting salary,” López says. “I just said, ‘thank you,’ and I had no idea that I could have done research and negotiated anything.” She recommends that physicians explore data from the American Association of Medical Colleges to get a general idea of salary ranges.

Academic medical centers tend to have some safeguards in place to ensure equal pay, so they can be a source of benchmark data, she says. In May 2018, the American College of Physicians published a position statement in the Annals of Internal Medicine addressing equal pay. The statement supports a number of solutions, including increased transparency in compensation data, training to reduce implicit bias, and requirements that women be included on boards and committees.

“We need more inclusive decision-making bodies to come up with better solutions, including moving equity from a lofty goal to something that we practice,” López says.

LET’S TALK ABOUT PAYCHECKS
Conversations about pay don’t have to be confrontational. It makes sense during annual reviews or contract renewals for female physicians to ask whether the organization is at least aware of any gender pay gaps, Hoffman says.

“They might not tell you the truth, and they might squirm a little bit,” she says. “But you have shown that you’re sensitive to the issue.”

Women who suspect gender discrimination can file a complaint with the EEOC, but it’s difficult to prove without supporting data, according to Hoffman, who worked for the EEOC from 1992 to 1998 as a senior trial attorney.

“I don’t remember a single case that was purely pay discrimination, and that’s because it’s very difficult to get that information,” she says.

If a female physician suspects unfair pay, she can speak directly with an EEOC investigator to determine whether an actionable case of discrimination has occurred.

The commission has contact information on its website (https://www.eeoc.gov/). “No ‘proof’ is required at this stage, although of course, the more supporting evidence she has, the better,” James Ryan, spokesperson for EEOC, tells Medical Economics in an email.

BILLING PLAYS A ROLE
In medicine, compensation can be tied to how much revenue a physician brings into the practice. Revenue is a direct function of billing. For example, CPT code 99215 for established patients brings higher reimbursement than CPT 99213, and women might be less inclined to code at the higher level, according to Whaley. Rohr-Kirchgraber agrees and adds that pay gaps are further amplified when women are less assertive than men in their billing practices.

“We might feel sorry for the patient and may be tempted to bill a bit lower,“ she says. “And we don’t appreciate ourselves enough either. We tend not to expect to practice at a higher level.”

But physicians do like to benchmark, so practices might consider sharing productivity numbers in an anonymous ways. The less-productive clinicians should have an opportunity to ask about improving their productivity from those who bill more.

Female physicians are also held to different standards by patients. In soon-to-be-published research, Rohr-Kirchgraber found that female physicians and those from under-represented minority groups tend to score lower in patient satisfaction scores.

Although the study didn’t survey the pa-
MINIMALLY INVASIVE glaucoma surgery (MIGs) represents one of the most exciting innovations in ophthalmology, according to Michele C. Lim, MD. Dr. Lim is professor of ophthalmology and vice chair and medical director of the University of California Davis Eye Center, Sacramento, CA.

With MIGS becoming more commonplace among glaucoma surgeons, Dr. Lim reviewed the literature to provide a summary of safety and efficacy findings.

MIGS STUDY GUIDELINES
FDA guidelines for study design of MIGS devices recommend that the primary endpoint be the percentage of subjects with at least 20% reduction in mean diurnal IOP from baseline and that the secondary endpoint should be the mean diurnal IOP change from baseline.

These guidelines were followed in some of the studies Dr. Lim discussed during the American Glaucoma Society annual meeting earlier this year.

MIGS procedures in which an implant is placed in Schlemm’s canal include the iStent Trabecular Micro-Bypass Stent, the newer iStent inject (both from Glaukos), and the Hydrus microstent (Ivantis). The MIGS literature is “robust” regarding both the iStent and iStent inject, a dual-stent system approved by the FDA in 2018, Dr. Lim said.

COMPARING STUDIES
Focusing on the iStent inject, she discussed two prospective studies in which the system was combined with cataract surgery. In a study by Arriola-Villalobos et al. (n = 20), 86% of patients reached the primary effectiveness endpoint, as did 78% in a study by Hengerer et al. (n = 81).

However, in both studies the mean IOP remained in the mid-teens at follow-up visits 3 to 4 years postoperatively.

Dr. Lim also described two studies of the iStent inject implanted as a standalone procedure. Fea et al. reported that 95% of patients (using no medications) reached the primary endpoint versus 92% of patients taking two medications. In a noncomparative study, Voskanyan et al. found that 72% of patients (using no medications) achieved the primary endpoint.

The mean IOP reduction at 12 months was –13 mm Hg for patients in the iStent cohort and –13.2 mm Hg for those using medication in the Fea et al. study and –14.7 mm Hg in the Voskanyan study.

The most common adverse events reported in these studies were that the iStent was not visible (1% to 13%), the iStent was obstructed (1% to 3%), or that the IOP was elevated (10%).

The Hydrus microstent, which sits in and dilates Schlemm’s canal, received FDA approval in August 2018 and has been the subject of two prospective studies when combined with cataract surgery.

Pfeiffer et al. showed that at 24 months, 80% of the patients in the Hydrus and cataract surgery cohort (n = 50) had a 20% reduction in IOP compared with 46% in the cataract surgery alone group (n = 50). At 24 months, the washed out mean diurnal IOP was 17 mm Hg for the combined procedure patients and 19 mm Hg for those undergoing cataract surgery alone; Dr. Lim noted a medication advantage favoring the Hydrus patients; at 24 months, 73% of this group was not using any hypotensive medications compared with 58% of the cataract surgery group.

Peripheral anterior synchiae was a notable adverse event in the Samuelson et al. study and occurred at a rate of 18% (14.9% nonobstructive, 3.8% obstructive). However, a post-hoc analysis suggested that it was not related to IOP outcomes.

Dr. Lim also discussed bleb-forming MIGS, which require the use of mitomycin-C to suppress fibrosis.

The XEN gel stent (Allergan) received FDA
Glaucoma Laser System

Novartis to integrate lifitegrast into portfolio

**NOVARTIS ANNOUNCED** that it has entered into an agreement with Takeda Pharmaceutical Co. Ltd. to acquire the assets associated with lifitegrast ophthalmic solution 5% (Xiidra) worldwide.

Lifitegrast is the first and only prescription treatment approved to treat both signs and symptoms of dry eye by inhibiting inflammation caused by the disease, said the company in a prepared statement.

The transaction would bolster Novartis’ front-of-the-eye portfolio and ophthalmic leadership.

“[Lifitegrast], with its unique dual benefits, is an example of the type of innovative advances we invest in for the benefit of patients,” said Paul Hudson, chief executive officer of Novartis Pharmaceuticals. “We look forward to leveraging our well-established, commercial infrastructure to bring this medicine to more patients.”

Closing of the transaction is expected in the second half of 2019, subject to customary closing conditions including regulatory approvals.

On closing, Novartis said it plans a smooth transition of operations and integration of lifitegrast into its pharmaceuticals portfolio.

With its anti-inflammatory mechanism of action, lifitegrast is the first dry eye treatment approved to treat both the signs of eye damage and the physical symptoms experienced by patients. Additional benefits of lifitegrast, exhibited in phase III studies, include a timely onset of action and well-tolerated safety profile.

Deal terms include a US $3.4 billion upfront payment with potential milestone payments of up to US $1.9 billion.

As part of the agreement, Novartis noted it expects to be taking on about 400 employees associated with the product.

View the full announcement online at https://bit.ly/2LiCPPC.
Evaluating subthreshold laser technique for CSCR patients

Ongoing study aims to clarify patient selection for endpoint management

By Benedikt Schworm, MD; Special to Ophthalmology Times

Among the more common retinopathies in the United States—along with age-related macular degeneration, diabetic retinopathy, hypertensive retinopathy, and retinal vein occlusion—central serous chorioretinopathy (CSCR) has no treatment that is considered the gold standard.1

Unlike the other conditions, CSCR tends to affect working-age individuals—the mean onset being 45 years of age—and it occurs more frequently in men.1

The exact etiology and pathogenesis is not well understood, but it has been reportedly associated with a range of factors such as corticosteroid exposure, phosphodiesterase inhibitor use, and obstructive sleep apnea.2-4

Interestingly CSCR has also been associated with “type A personality” and those experiencing psychological stress.5,6

An inciting event is thought to trigger an increased permeability of the choroidal vessels and retinal pigment epithelium (RPE) dysfunction—subsequently allowing for the accumulation of exudative fluid in the subretinal space.2,7

It has been reported that more than 80% of CSCR patients will have spontaneous resolution of symptoms within three months, nevertheless, the other 20% often require treatment.7,9

These individuals may have persistent serous macular detachment, vision loss, and subjective impairment.10,11

Although definitions of chronicity vary, a patient can be considered to have chronic CSCR if subretinal fluid has not resolved by three months.

In practice, the classic patient with chronic CSCR presents with reduced visual acuity and contrast sensitivity, visual distortions, and a change in color vision.

CSCR PRESENTATION

Clinically, the retina will have subretinal fluid and RPE irregularities that can also be seen with infrared imaging and optical coherence tomography (OCT). Most RPE irregularities will be seen over a central leakage point.

In patients who have had the condition longer, damage will extend into the outer retinal layers. In a very progressed form of the disease, the patient may have a complete loss of photoreceptors with only the external limiting membrane visible on OCT. Microperimetry on these patients will reveal small scotomas in these areas.

To identify patients with the signs of secondary neovascularization, we take care to look for double layer signs on OCT and typical signs on fluorescein and ICG angiography.

A double layer of the RPE and Bruch’s membrane filled with hyper-reflective material is an indicator for secondary choroidal neovascularization (CNV).

These secondary CNVs in double layers can be visualized more distinctly with OCT angiography.

A secondary neovascularization-
tion calls for a treatment approach using intravitreal anti-vascular endothelial growth factor (VEGF) agents.

**TREATMENT OPTIONS**

In the absence of a gold standard treatment, various strategies have been attempted in CSCR management. Specialists frequently apply laser photocoagulation to the leaking RPE, as directed by fluorescein angiography. Xenon, krypton, and more currently, argon laser has been used. 2, 12-14

The development of subthreshold laser therapy has garnered growing interest as these techniques—including micropulse, selective retinal therapy, and Topcon’s PASCAL with endpoint management (EpM)—can deliver the similar therapeutic benefits without causing visible damage. 15

Photodynamic therapy (PDT) with verteporfin has been used to treat chronic and acute CSCR in patients, as well as, to reduce potential recurrences. We find that PDT with reduced dose (half-dose) is the preferred approach for this method. 16-19

Other drug treatments that have been used for CSCR include intravitreal anti-VEGF, minilacrilocorticoid receptor antagonists, adrenergic blockers, systemic carbonic anhydrase inhibitors, aspirin, *Helicobacter pylori* treatment, and methotrexate. 20

**OUR INVESTIGATION**

My colleagues and I have initiated an investigation evaluating patients with chronic central serous chorioretinopathy who are good candidates for EpM.

Currently, we treat CSCR patients every three months if they present with subretinal fluid, a candidates for EpM.

To see how suitable EpM is in the day-to-day practice of a clinical outpatient service, we have set up trial conditions to follow patients and gather more detail.

We will be looking closely at the anatomical outcomes on OCT as well as patients’ functional vision through visual acuity testing and microperimetry.

We hope to include at least 50 patients. Currently, there are 30 are enrolled. The follow-up period will be a year, and we would like to extend that out to longer intervals so we can examine recurrence after one year.

We know that one of the difficulties in treating CSCR is that it is likely to recur with subretinal fluid—even after other therapies like half-fluence PDT. We observe this on a regular basis.

During our investigation, we want to determine which patients seem to improve the most and if there also are specific subgroups who will derive the most benefit from it. Eventually, we will randomly assign patients to treatment and no treatment or treatment versus another type of treatment to show superiority. First, we want to evaluate the treatment’s effectiveness and improve our technique with the procedure.

We want to ensure it does no harm. We had observed no adverse effects, burns, or scars. It is clearly safe.

**TAKE-HOME**

- **Chronic CSCR patients who have less RPE scarring stand to benefit the most from EpM laser therapy. They have the best chance for a quick and complete resolution of subretinal fluid.**

**CONCLUSIONS**

Through our observations, we believe that chronic CSCR patients who have less RPE scarring stand to benefit the most from EpM laser therapy. These patients tend to have the best chance of a relatively quick and complete resolution of subretinal fluid.

We suspect that if the subretinal fluid bubble is not very large and is centrally located, this approach likely will be significantly beneficial for ehtap.

Patients with leakage points within a 3-mm radius from the fovea appear to do well with EpM’s macular laser pattern.

Patients who have chronic CSCRs with fluid accumulation in multiple locations are more difficult to treat.

An extended recruitment period and a longer follow-up will allow us to include patients with different disease presentation and investigate our data in more detail.

### References


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Dr. Schworm is with the Eye Clinic of the University of Munich, Germany. He did not indicate any proprietary interest. Topcon’s PASCAL laser with EpM is not FDA approved for CSCR.
Personalizing refractive outcomes with presbyopia-correcting IOLs
EDOF, multifocal IOLs providing options for patients with range of visual needs
By Francis S. Mah, MD; Special to Ophthalmology Times

INNOVATIONS IN IOL technology enable refractive-cataract surgeons to deliver near, intermediate, and distance vision, reducing spectacle dependence in presbyopic patients. However, in my experience, personalization of lens selections can further optimize results and maximize patients’ range of vision to meet their visual needs.

During the past five years, I have performed personalized IOL implantations, balancing the benefits of different lenses. I initially mixed and matched +2.75, +3.25, and +4.0 multifocal IOLs (Tecnis ZKB00, ZLB00, and, ZMB00 respectively, Johnson & Johnson Vision).

When extended depth-of-focus (EDOF) IOLs were introduced, I began incorporating those into personalization (Tecnis Symfony, Johnson & Johnson Vision). I now have about 200 patients (400 eyes) with either bilateral Symfony lenses or a Symfony plus a different lens in the fellow eye.

PERSONALIZATION STRATEGIES
In my practice, 40% of the IOLs I implant are premium IOLs. One-quarter of those are toric, while 75% of the premium IOLs are multifocal (ZKB00, ZLB00, ZMB00), pseudoaccommodative (Crystalens or Trulign, Bausch + Lomb), and Symfony IOLs (both toric and nontoric). I personalize at least half of these cases. We explain to patients that they may receive two different lenses, and I think they appreciate that we can fine-tune their vision with this technique.

Depending on preoperative refraction, reader prescription, or glasses add, I discuss with patients what I feel would be best for them. For example, if a patient has +2.75 add in glasses, or is a –3.00 myope, I will recommend a ZLB00 (+3.25 add at IOL plane). Otherwise, I usually implant a Symfony in the first eye.

If the patient is satisfied with both distance and near, I will implant the same lens in the fellow eye. If stronger near vision is desired, I may implant a ZLB00 in the other eye. I have had good outcomes when I place the Symfony in the eye that has astigmatism and then implant the multifocal in the eye with less astigmatism. This reduces the need for astigmatic keratotomy or limbal relaxing incisions.

Interestingly, I find that eye dominance does not matter as much as it might seem. Whether the dominant eye has the lower-add IOL, or the nondominant eye has the more distant-dominant IOL really does not seem to matter. Thus far, I have not had any unhappy patients with this approach. With EDOF lenses, both eyes get the benefit of good distance vision, and eye dominance is less of a factor for the near eye.

A recent paper demonstrates the efficacy of combining an EDOF and mid-add multifocal. In 55 patients with this combination, binocular uncorrected distance visual acuity was 20/16 or better in 70% of patients and 20/20 or better in 97% (Figure 1A). Binocular intermediate and near visual acuity both 20/25 or better in almost all patients three months after surgery (Figure 1B).

‘Personalization is a useful procedure for maximizing the benefits of today’s advanced IOL technologies.’ — Francis S. Mah, MD
if the patient is quite short in stature, has an unusual hobby, or expectation of intensive near work, I may start with the multifocal in the first eye.

In patients with -2.00 D or more of myopia, I also begin with a mid-add multifocal in the first eye because these patients are accustomed to reading up close without their glasses.

In rare cases, I do still implant multifocal IOLs in both eyes. For example, in a recent case I implanted a mid-add multifocal in the first eye of a relatively short, female engineer. She was still dissatisfied with her reading ability, so I implanted the ZMB00 in her fellow eye, after a discussion about the higher risk of glare and halos. The patient was happy with the outcome; with the combination of mid- and high-add multifocals she could easily see the computer and read.

With the array of available lens options, I am much more comfortable offering presbyopia-correcting IOLs to my patients. Not only do I feel confident that I can achieve the spectacle independence they are seeking but I also know that if there is any dissatisfaction after the first-eye surgery, I have options to get the patient to 20/20/20.

**LAYING THE GROUNDWORK**

With advances in lens technology, it is important to keep in mind that patients may require more chair time and discussion about options. Patients are very smart and want to participate in decisions regarding their healthcare. It is rewarding to have higher-level discussions with patients so they understand the process. I also believe they are ultimately more satisfied and may be more understanding if the outcome is not exactly as they expected.

We remind patients they do not have 20-year-old eyes and that our lens options have limitations, but we can decrease their dependence on glasses and contact lenses. I also explain that with multifocal and EDOF lenses, they are more likely to notice glare and halos in dim lighting situations.

It is critical to optimize the patient’s ocular surface before performing measurements. The tear film affects biometry, postoperative vision quality, and, ultimately, patient satisfaction.

**PATIENT SELECTION**

Hyperopes and emmetropes are generally the easiest candidates to start with for personalization and for presbyopia-correcting IOLs in general. We also need to assess patients’ personalities. Patients should be relaxed, while understanding that there are limitations.

I encourage monovision patients to continue with monovision because it is familiar to them. I may not be as likely to use personalization in -2.00-D, -3.00-D, or -4.00-D myopic patients unless they have worn multifocal contact lenses and understand that distance correction reduces reading vision.

In any case involving a premium lens, biometry measurements, axis determination, and IOL power calculations must be meticulous. I prefer the Barrett Universal, Barrett Toric, and Barrett post-refractive calculator (www.ascrs.org).

I also find the ORA System with VerifEye (Alcon Laboratories) to be helpful for intraoperative confirmation of the IOL power especially in post-refractive cases, long eyes, or short eyes.

**TARGET REFRACTION**

When implanting multifocal IOLs, I aim for an outcome as close to plano as possible, but I target -0.20 D with Symfony lenses, which has been successful in my hands. I have not found it helpful to aim for a more myopic target with a Symfony lens in the non-dominant eye; my preference would be to opt for a mid-add multifocal if better near is desired.

It is important to reduce astigmatism as much as possible during the procedure, although I have been surprised by how much astigmatism patients actually can tolerate, especially with EDOF lenses.

Personalization is a useful procedure for maximizing the benefits of today’s advanced IOL technologies. All of my patients who have had personalization are satisfied with their vision and have said that they would do it again.

**Reference**


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Refractive-cataract surgery: Overview of the current landscape

Demographic shifts, improving technology continue to bring patients in at younger age

By Eric D. Donnenfeld, MD; Special to Ophthalmology Times

AS THE GLOBAL population that is prone to developing cataracts continues to grow, ophthalmologist could be facing challenges as people live longer, increasing their odds for cataracts.

Though this is a worldwide issue, in the United States, surgeons are performing about 4 million cataract surgeries each year. It is estimated that there are about 30 million people worldwide who have cataracts of 20/400 or worse, and there are almost 250 million people who have cataracts between the range of 20/60 and 20/200. Cataracts are endemic.1,2

As technology improves, patients are more willing to undergo cataract surgery at an earlier stage as the reward of cataract surgery becomes much greater than the risk associated with it because it provides an opportunity to improve their quality of life. Here are my thoughts on the ever-changing current landscape of cataract-refractive surgery.

Patients’ growing confidence in cataract surgery is a byproduct of better technology. As technology has improved, it has made cataract surgery not only more efficacious but also safer.

When I evaluate cataract surgery, I look at a procedure that has become extraordinarily successful, with much less risk and much greater reward.

‘Cataract surgery, for many patients, has become the ‘fountain of youth’ because they can reverse the aging process.’

— Eric D. Donnenfeld, MD

Cataract surgery, for many patients, has become the “fountain of youth” because they can reverse the aging process and restore natural vision in a way that was not possible before.

When I first started practicing in 1985, cataracts were the defining moment of old age, and postoperative quality of vision was significantly diminished. Therefore, it was common to wait until patients’ visual acuity was 20/70 before performing surgery.

Our goal was to remove the cataract and restore the patient’s vision with glasses. Now we can remove the cataract to improve their quality of vision and remove their refractive error—including hyperopia, myopia, and astigmatism. We can also improve their vision at near as well—with either monovision, extended-depth-of-focus (EDOF), or multifocal IOLs—to resolve refractive error and in some cases presbyopia as well.

EXPECTATIONS CHANGING

During my career, I have noticed an extraordinary increase in patient expectations, and that frightens many cataract surgeons. I view that in a different light and consider demanding patients to be opportunities to meet or exceed their expectations. Demanding patients, while more challenging, also present an opportunity to provide patients with better-quality vision.

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When I evaluate cataract surgery, I look at a procedure that has become extraordinarily successful, with much less risk and much greater reward.

Cataract surgery, for many patients, has become the “fountain of youth” because they can reverse the aging process and postoperative quality of vision was significantly diminished. Therefore, it was common to wait until patients’ visual acuity was 20/70 before performing surgery.

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TAKE-HOME

> While the number of candidates for cataract surgery continues to rise, the number of cataract surgeons is declining. Physicians who are willing to make a commitment to excellence in their practice and go that extra mile can succeed.

DIAGNOSTIC TECHNOLOGY

Refractive cataract surgery began with the advent of optical biometry (IOLMaster, Carl Zeiss Meditec) because it dramatically improved the accuracy of IOL measurements that allow us to achieve emmetropia in significantly more patients than we ever could with previous generations of biometry.

As optical biometry has improved, we have new generations of this technology that provide telocentric keratometry, which is able to locate the fovea and diagnose foveal disease; it can see through dense cataracts and improve the accuracy of IOL power and toric IOL measurements.

Macula OCT (Cirrus-HD OCT, Carl Zeiss Meditec) is another diagnostic technology that I use preoperatively to image macular pathology and health prior to cataract surgery.

When I can view the macula, I can more accurately advise patients on what IOL is in their best interest because I have different levels available to achieve these results. Part of any refractive cataract surgery procedure is having an “escape valve,” a technique for resolving residual refractive error. That “escape valve” might be limbal-relaxing incision, an IOL exchange, LASIK, PRK, or small-incision lenticule extraction (SMILE).

New technologies help improve outcomes, allowing refractive cataract surgery to truly come of age.

Surgical technologies should allow cataract surgery that is extremely accurate, low risk, and effective. That means using advanced diagnostic technology to make certain that we diagnose patients correctly with cataracts, rule out concomitant pathologies, implant the correct IOL with a high degree of accuracy, and treat astigmatism accurately.

Continues on page 18: Landscape
MIGS SURGEONS CAN’T IGNORE
THE DATA IN THE ROOM

Reporting the most medication-free patients and the largest IOP reduction compared to control of any MIGS pivotal trial at 24 months, the Hydrus® Microstent sets a new standard for high quality patient outcomes.¹⁻⁴,*

Delivering a new confidence.
of expectations for patients who have macular pathology, which is difficult to diagnose just by visualizing the retina.

I also use a topographer (Atlas, Carl Zeiss Meditec) to familiarize myself with the health of the cornea and the existence of astigmatism.

Being able to document the cylinder quantitatively and qualitatively is predicated on having a good topography image. It aids in managing both their astigmatism and irregular astigmatism, which may change my choice of IOLs.

Once diagnostic decisions have been made, the next step is the execution of the cataract surgery. In our operating room, we also use a surgical microscope with stereo coaxial illumination (OPMI Lumera, Carl Zeiss Meditec), which provides a great red reflex.

For astigmatism management, we use a computer-assisted cataract surgery instrument (Callisto, Carl Zeiss Meditec), which takes information from the optical biometry to find the steep axis of the cornea and is instrumental for accuracy of toric IOL placement.

Finally, we have adopted lenses IOLs (Alcon Laboratories, Bausch + Lomb, Johnson & Johnson Vision) that have great optics with aspheric optics as well, including EDOF IOLs and multifocal lenses. I have found that low-add lenses provide better-quality vision.

**REIMBURSEMENTS DOWN**

Out-of-pocket spending is now more frequent and is accepted among patients. Patient-shared billing has become an important part of cataract surgery in the United States as refractive outcomes are not covered by traditional insurance.

Providing technology that improves the accuracy of refractive outcomes or treats astigmatism or presbyopia, benefit patients’ quality of life. These are technologies that patients want, and they believe that it’s a worthwhile investment in their future.

There is little that patients will benefit from more than cataract surgery. Many patients are willing to pay out of pocket for the best technology that meets their needs.

As the technology gets better, patients are more willing to use patient-shared billing because the delta between the traditional surgery and the premium surgery has become more significant.

**CONCLUSION**

We anticipate that 2019, in hindsight, will have been another great year for cataract surgery. The number of surgical patients continues to increase, along with their expectations.

The number of cataract surgeons is declining, however. Surgeons who are willing to make a commitment to excellence in their practice and go that extra mile to give patients the quality of vision they desire, will have extraordinarily successful practices, grateful patients, and will be able to practice ophthalmology at the highest possible level.

Refractive-cataract surgery is the future of our profession, and one of the most rewarding aspects of being an ophthalmologist.
In ocular surgery, with penetrating incisions, we inevitably still face postoperative inflammation and pain. Now, a novel potent corticosteroid formulation could help improve that aspect of cataract surgery as well, with enhanced penetration and an easier-to-follow dosing regimen.

**Role of Corticosteroids**

It is important to bring inflammation under control after surgery, and corticosteroids are one option. Left untreated (or undertreated), persistent anterior chamber inflammation can result in complications ranging from photophobia and decreased vision to corneal edema, persistent iritis, and cystoid macular edema (CME).

In a study by Porela-Tiihonen S, et al., up to 35% of cataract surgery patients experienced moderate to severe pain during the hours after surgery. When we see patients on the first postoperative day, we tend to focus on vision and visible signs of inflammation, not on subjective symptoms.

While we are happy that the vision is 20/20, we may overlook that the patient may be in pain. There is no reason for my patients to experience pain if I can prevent it.

**Challenges**

To treat inflammation and pain after surgery, most physicians prescribe a corticosteroid and an NSAID, in addition to an antibiotic to prevent infection. This is an effective combination, and when patients comply with their regimen, preventable complications are rare. However, some options available today do present some challenges.

The first potential problem, in my opinion, is the rash of generics flooding the market, including generic corticosteroids such as prednisolone acetate. Although they meet FDA standards for bioequivalence, they are not as well tested as branded drugs. Another challenge is the potential for some corticosteroids that are effective in reducing inflammation, such as difluprednate, to increase IOP.

Finally, a barrier to effective treatment of pain and inflammation is the dosing of corticosteroids.

Patients generally take their antibiotic, corticosteroid, and NSAID drops 3 or 4 times per day, which can amount to 12 drops per day. This can be inconvenient and unpleasant.

**Decline in Compliance**

We presume our patients may miss some doses of their medications after cataract surgery. Thus, not only do we need to select the drug we think will be most effective, but we also need to educate patients about the potential risks associated with failing to use the corticosteroid drops QID for the full prescribed duration.

**Bid Corticosteroid Option**

The recent introduction of a new corticosteroid formulation, loteprednol etabonate ophthalmic suspension 1% (Inveltys, Kala), addresses some of the challenges we have faced with corticosteroids for cataract patients.

Approved for treatment of inflammation and pain following eye surgery, this novel nanoparticle formulation with proprietary technology (Amplify, Kala) offers a clear set of advantages.

This delivery mechanism offers the superior penetration we need to give patients the best of all worlds: potent and effective control of pain and inflammation, low IOP concerns, and the added benefit of BID dosing.

**Looking Ahead**

Given the potency, efficacy and safety of the loteprednol etabonate ophthalmic suspension 1% formulation, the mucus-penetrating particle may one day make it the preferred choice for control of inflammation and pain after a range of ophthalmic procedures, such as corneal transplantation, refractive surgery, MIGS procedures, and more.
“When using the classic CPC treatment parameters, I prefer to start at a lower power, titrate up just a little until you hear a little crackle, and then decrease the power to just underneath that level,” Dr. Kammer said.

**AVOID THE ‘POP’**
Dr. Kammer tries to avoid hearing a loud “pop” because this is indicative of tissue destruction. In these cases, he typically starts with a power between 1,750 to 2,250 mW (higher watts in patients with lighter pigmentation and lower watts in patients who are more heavily pigmented), with a duration of 2,000 mS and six spots per quadrant.

Surgeons also may want to consider the use of the alternative Gaasterland “slow coagulation technique” that was popularized by glaucoma specialist Doug Gaasterland, MD.

In this treatment paradigm, patients are treated with lower energy per pulse but with longer treatment duration.

Patients typically experience less pain, less inflammation, and less macular edema, albeit with similar efficacy compared to the traditional CPC treatment paradigm, according to Dr. Kammer.

Dr. Kammer also stressed that cyclophotocoagulation should not be relegated to end-stage glaucoma.

In fact, he noted that transscleral CPC is highly effective with a more favorable side effect profile in patients with mild-to-moderate glaucoma.

This has been noted in traditional transscleral cyclophotocoagulation laser therapy as well as with the newer Micropulse cyclophotocoagulation.

Embracing the use of newer techniques, (Micropulse Cyclophotocoagulation, Iridex) offers a less destructive laser modality that provides excellent efficacy with a more tolerable side effect profile.

In fact, due to the fact that this technique does not actually coagulate the underlying tissue, Dr. Kammer prefers to call this Micropulse Cyclo “modification.”

In “modification” technology, a continuous-wave of energy is released in a series of repetitive short pulses. This allows the underlying tissue to be heated up and altered without actually destroying it.

“C
lose attention to details when performing transscleral cyclophotocoagulation (CPC) or phacoemulsification with encyclophotocoagulation can go a long way in preventing complications and ensuring excellent results, according to Jeffrey Kammer, MD, associate professor of ophthalmology, Vanderbilt Eye Institute, Nashville, TN.

With transscleral cyclophotocoagulation, the most vision-threatening complications include hypotony, phthisis, and vision loss. The first step to help avoid these is to carefully select the surgical location.

“If you can avoid the 3 and 9 o’clock locations, you are less likely to cause ischemia and its associated complications,” Dr. Kammer said. “Surgeons also should titrate their power appropriately.

**AVOIDING ISSUES FROM INFLOW PROCEDURES**
CPC for glaucoma requires special finesse for surgery

*By Vanessa Caceres; Reviewed by Jeffrey Kammer, MD*

**take-home**
» A careful use of technique, power parameters, and preventive moves against IOP spikes can make cyclophotocoagulation or phaco and ECP more effective.

**FIGURE 1** Probe axis should be perpendicular to the sclera. (Images courtesy of Jeffrey Kammer, MD)

“AVOID THE ‘POP’

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Embracing the use of newer techniques, (Micropulse Cyclophotocoagulation, Iridex) offers a less destructive laser modality that provides excellent efficacy with a more tolerable side effect profile.

In fact, due to the fact that this technique does not actually coagulate the underlying tissue, Dr. Kammer prefers to call this Micropulse Cyclo “modification.”

In “modification” technology, a continuous-wave of energy is released in a series of repetitive short pulses. This allows the underlying tissue to be heated up and altered without actually destroying it.

Continues on page 21: CPC
Dr. Kammer also shared a Micropulse cyclophotocoagulation technique-related pearl, recommending that surgeons’ probe axis be placed roughly 1 mm behind the limbus and perpendicular to the sclera. This is in contrast to classic transscleral cyclophotocoagulation, where you hold the Gprobe immediately behind the limbus and parallel to the visual axis, he said.

The first Gemini study subject to have surgery performed with the surgical system was treated in March by Steven Vold, MD, medical director of Vold Vision, Fayetteville, AR. “We hope to further validate the long-term treatment benefits associated with performing multiple MIGS procedures during one surgery,” Dr. Vold said. “Our goal of intervening earlier in the disease stage with multiple mechanisms of action is to generate the most efficacy possible while maintaining the optimal safety profile of MIGS. “The [surgical system] targets the three points of resistance in the conventional outflow pathway; this medical technology has the potential to become a leading option in the MIGS space.”

Subjects enrolled in study to review system for MIGS procedures

The largest clinical study to date to evaluate the surgical system, the Gemini study will enroll up to 130 subjects from 10 to 15 medical centers in the United States. Reay Brown, MD, board-certified ophthalmologist and chief medical officer of Sight Sciences, said the company continues to seek technologies suited for their individual patients. “We look forward to further confirming—via this large-scale, prospective, multicenter trial—that our sophisticated technology offers a compelling alternative to traditional treatments,” Dr. Brown said.
Refractive Cataract Surgery

Visual function and IOL glistenings

Steven G. Safran, MD

Dr. Safran is in private practice in Lawrenceville, N.J. He is a paid consultant to Johnson & Johnson Surgical Vision, Inc.

Modern cataract surgery has become refractive surgery, but an additional goal is to ensure that the high-quality vision delivered to patients early after surgery is maintained for the long term.

With this aim in mind, the potential for an intraocular lens (IOL) to develop glistenings and/or nanoglistenings is something that is important to consider when choosing implant technology.

Published reports and my personal experience show that glistenings and subsurface whitening can have negative effects on the optical characteristics of an IOL and can degrade visual function.1-5 Although glistenings and nanoglistenings can occur with any type of IOL, they have been most commonly reported in association with hydrophobic acrylics and particularly with the hydrophobic acrylic AcrySof® IOL.1

Glistenings and nanoglistenings

Glistenings are fluid (water)-filled microvacuoles that form within the IOL optic when the implant is in an aqueous environment.1 The term derives from the defect’s appearance at the slit lamp. Because of a difference in refractive index between the water and the surrounding polymer, light is refracted and scattered at the interface of these substances, thus conferring a sparkling or glistening appearance to the fluid-filled microvacuoles.2 Nanoglistenings, which have also been described in the literature as surface light scattering or whitening, represent the reflection of white light from water that accumulates near the IOL surface in the form of much smaller, more closely spaced but discrete nano-sized fluid-filled vacuoles.1,2

Different ideas have been put forward about the mechanisms leading to the development of glistenings and nanoglistenings and the reasons why the risk varies with different hydrophobic acrylic IOLs. These theories cite differences in material composition as well as in IOL packaging and/or manufacturing processes.1 Certain ocular pathologies and medications may also be risk factors.1,2

Knowledge of the effect of glistenings on the optical properties of an IOL provides a basis for understanding their potential clinical significance. In a bench study, investigators demonstrated how the presence of glistenings in an IOL impairs light propagation through the optic and increases retinal straylight.3 Using experimental methods to induce glistenings in sets of 4 commercially available hydrophobic acrylic IOLs—AcrySof® IOLs, iSymm™ IOLs (HOYA Surgical Optics), enVista® (Bausch + Lomb), and TECNIS®—the researchers evaluated light intensity transmission for IOLs with microvacuoles, which has relevance for maintaining contrast sensitivity. They reported the transmission was 100% for the enVista® IOLs and 98% or higher for the TECNIS® IOLs, but was only approximately 90% for the iSymm™ lenses and fell to as low as 89% for the AcrySof® IOLs. Of the 4 models studied, only the AcrySof® and iSymm™ IOLs were determined to have significant glistenings, which was defined as glistenings associated with straylight levels exceeding those of a healthy 20-year-old crystalline lens. Increased retinal straylight is associated with hazy vision, increased glare hindrance, loss of contrast and color, and halos around bright light sources.2 Consistent with that information, the investigators reported that glistenings had an adverse effect on contrast and suggested that the impact may be most visually significant under low-contrast conditions.3

Whether or not glistenings and nanoglistenings negatively impact visual function has been controversial due to conflicting information in the literature.1 Although investigators have found that they have no detrimental effects on vision, some evidence in the literature indicates otherwise.1,2,4-6 For example, an April 2013 article in the Canadian Adverse Reaction Newsletter noted that Health Canada had received reports of glistenings suspected of being associated with IOLs in 69 patients, including 67 patients who had experienced effects on visual quality or quantity and one patient who had undergone lens replacement to address decreased vision.5

In a recent clinical study, researchers evaluated the presence of glistenings and surface light scattering in hydrophobic acrylic IOLs that were implanted for at least 5 years and the effects of these phenomena on visual and optical performance.1 The investigation included 98 eyes implanted with a monofocal AcrySof® IOL (model SA60AT) and 42 eyes with a monofocal Sensar® IOL (model AR40e, Johnson & Johnson Surgical Vision), which is made of the same hydrophobic acrylic material as the TECNIS® IOLs.6 Slit-lamp examination identified glistenings in 65 of the AcrySof® IOLs, and surface light scattering without glistenings was seen in 33 of the AcrySof® IOLs. AR40e IOLs were not associated with glistenings. Objective tests of optical quality, including straylight, spherical aberration, point spread function, and modulation transfer function, also showed potential negative effects of glistenings and surface light scattering in the AcrySof® IOLs.

The potential visual impact of glistenings is further highlighted by reports describing patients who benefited after undergoing explantation and replacement of an affected IOL.2 One report described 5 patients with an AcrySof® IOL (model MA60BM) who developed decreased visual acuity that was associated with severe IOL glistenings and nanoglistenings.2 Visual acuity in all patients improved after the AcrySof® IOL was exchanged for another implant. These researchers also reported findings from laboratory evaluations that showed decreased light transmission through all of the explanted IOLs relative to an unimplanted AcrySof® IOL. Compared with the control lens, the decrease in light transmission through the
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**INDICATIONS:** TECNIS® 1-Piece IOL lenses are indicated for the visual correction of aphakia in adult patients in whom a cataractous lens has been removed by extracapsular cataract extraction. These devices are intended to be placed in the capsular bag.

**PRECAUTIONS:** Do not resterilize the lens. Most sterilizers are not equipped to sterilize the soft acrylic material without producing undesirable side effects. Do not soak or rinse the intraocular lens with any solution other than sterile balanced salt solution or sterile normal saline. Do not store the lens in direct sunlight or at a temperature greater than 113°F (45°C). Do not autoclave the intraocular lens. Please refer to the specific instructions for use provided with The UNFOLDER insertion system.

**WARNINGS:** Physicians considering lens implantation should weigh the potential risk/benefit ratio for any conditions described in the TECNIS 1-Piece IOL Directions for use that could increase complications or impact patient outcomes. These conditions include severe anterior or posterior segment inflammation or uveitis; patients in whom the intraocular lens may affect the ability to observe, diagnose or treat posterior segment diseases; surgical difficulties at the time of cataract extraction, which may increase the potential for complications (e.g., persistent bleeding, significant iris damage, uncontrolled positive pressure or significant vitreous prolapse or loss); a compromised eye due to previous trauma or developmental defects in which appropriate support of the IOL is not possible; circumstances that would result in damage to the endothelium during implantation; suspected microbial infection; or patients in whom the posterior capsule nor the zonules are intact enough to provide support for the IOL. Children under the age of 2 years are not suitable candidates for intraocular lenses. The TECNIS 1-Piece IOL should not be placed in the ciliary sulcus.

**ADVERSE EVENTS:** In 3.3% of patients, reported adverse events of cataract surgery occurred in less than 1% of patients were secondary surgical intervention (pars plana vitrectomy with membrane peel) and lens exchange (due to torn lens haptic).

**ATTENTION:** Reference the Directions for Use for a complete listing of indications and important safety information.

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**TECNIS Piece**

**Rx Only**

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**WARNINGS:** Physicians considering lens implantation should weigh the potential risk/benefit ratio for any conditions described in the TECNIS 1-Piece IOL Directions for use that could increase complications or impact patient outcomes. These conditions include severe anterior or posterior segment inflammation or uveitis; patients in whom the intraocular lens may affect the ability to observe, diagnose or treat posterior segment diseases; surgical difficulties at the time of cataract extraction, which may increase the potential for complications (e.g., persistent bleeding, significant iris damage, uncontrolled positive pressure or significant vitreous prolapse or loss); a compromised eye due to previous trauma or developmental defects in which appropriate support of the IOL is not possible; circumstances that would result in damage to the endothelium during implantation; suspected microbial infection; or patients in whom the posterior capsule nor the zonules are intact enough to provide support for the IOL. Children under the age of 2 years are not suitable candidates for intraocular lenses. The TECNIS 1-Piece IOL should not be placed in the ciliary sulcus.

**ADVERSE EVENTS:** In 3.3% of patients, reported adverse events of cataract surgery occurred in less than 1% of patients were secondary surgical intervention (pars plana vitrectomy with membrane peel) and lens exchange (due to torn lens haptic).

**ATTENTION:** Reference the Directions for Use for a complete listing of indications and important safety information.

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**INDICATIONS AND IMPORTANT SAFETY INFORMATION for the SENSAR Foldable IOL with OptiEdge Design (AR40E, AR40e, AR40M)**

**Rx Only**

**INDICATIONS:** SENSAR Foldable IOLs with OptiEdge Design are indicated for the visual correction of aphakia in adult patients in whom a cataractous lens has been removed by extracapsular cataract extraction. The lens is intended to be placed in the capsular bag.

**PRECAUTIONS:** Do not resterilize, reuse, or autoclave the lens. Use a sterile balanced salt solution or sterile normal saline. Do not store the lens in direct sunlight or over 113°F (45°C). Refer to the specific instructions for use provided with The UNFOLDER Implantation System. When The UNFOLDER Emerald Series Implantation System is used improperly, the haptics of the SENSAR lens may become crimped or broken.

**WARNINGS:** Physicians considering lens implantation should weigh the potential risk/benefit ratio for any conditions described in the SENSAR Foldable IOL with OptiEdge Design Directions for Use that could increase complications or impact patient outcomes. Do not place in the ciliary sulcus. Lenses <4.0D are not intended, nor should they be used, for a clear lens exchange. Special consideration should be given to the dimensions of lenses at the extreme end of the power range (<4.0D) in relation to the anatomical clearances in the patient’s eye.

**ADVERSE EVENTS:** The most frequently reported adverse event that occurred during the clinical trial of the parent lens model was anterior lens tissue overgrowth, which occurred at a rate of 11.3%.

**ATTENTION:** Reference the labeling for a complete listing of Important Indications and Safety Information.

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**REFERENCES**


Registry taking MIGS device global
Microstent providing reductions in IOP, medication that are durable through 3 years

By Cheryl Guttman Krader

FINDINGS from a “real-world” study show that the multimodal minimally invasive glaucoma surgery (MIGS) device (Hydrus Microstent, Ivantis) safely and effectively treats a variety of glaucoma types, providing reductions in IOP and medication burden that are durable through at least three years, said Jeffrey Whitman, MD.

“It is important to state what is meant by ‘real-world,’” said Dr. Whitman, president and chief surgeon, Key-Whitman Eye Center, Dallas.

“The SPECTRUM registry includes all-comers,” he said. “It is a global, multicenter registry including data from 51 centers in 17 countries, all outside of the United States.”

He presented data from the SPECTRUM registry that was developed to collect outcomes data for patients treated with the MIGS device either in combination with cataract surgery or as a standalone procedure.

Dr. Whitman noted that about 2,500 eyes were enrolled through 2018, and they were implanted with the MIGS device either in a combination procedure with phacoemulsification and IOL implantation or they were phakic or pseudophakic and had standalone glaucoma surgery.

The microstent acts to optimize aqueous outflow by bypassing the trabecular meshwork. It provides precise dilation and scaffolding of Schlemm’s canal over a 90º span that enables consistent aqueous access to multiple collector channels over time.

“The large population of enrolled eyes also represents the full spectrum of glaucoma severity, from mild through advanced, including eyes with glaucoma refractory to prior incisional/filtration surgery,” he added.

Centers contributing to the SPECTRUM registry are located in Europe, North America, South America, the Middle East, and Asia. Almost three-fourths of the nearly 2,500 treated eyes had primary open-angle glaucoma. Other glaucoma types included primary angle-closure glaucoma (9%), pseudoexfoliation glaucoma (7%), and pigmentary dispersion glaucoma (3%).

The patients had a mean age of 71.5 years, 53% were female, and mean baseline mean deviation was –7.2 dB.

In addition to medications, prior glaucoma treatments included filtration surgery in almost 10% of eyes, trabeculectomy in 20%, and iridotomy in almost 8%.

OUTCOMES IN COMBINATION SURGERY COHORT
Dr. Whitman presented outcomes for patients who had combined cataract and microstent surgery, which represented 74% of the eyes enrolled in the SPECTRUM registry. Data were analyzed from 1,119 eyes seen at 12 months, 562 eyes followed to 24 months, and 207 eyes that completed a 36-month visit. Mean baseline IOP for the three cohorts ranged from 18.6 to 19.8 mm Hg and mean number of hypotensive medications being used at baseline was 2.2 or 2.3.

Analyses of change from baseline IOP showed statistically significant reductions at 12 months (–3.6 mm Hg), 24 months (–3.9 mm Hg), and 36 months (–4.2 mm Hg). Similarly, there was a statistically significant and consistent reduction in medication at all follow-up intervals showing that patients on average eliminated use of one medication.

“At all follow-up intervals, approximately three-fourths of eyes reduced medication burden by one or more medications,” Dr. Whitman said. “At 12 months, 58% of eyes were medication-free, and even at three years, more than 42% of eyes were using no ocular hypotensive medications.”

At 12 and 24 months, IOP was ≤21 mm Hg in 95% and 96% of eyes, respectively, and ≤18 mm Hg in 87% and 86% of eyes, respectively. At 3 years, 92% of eyes had an IOP ≤21 mm Hg and IOP was ≤18 mm Hg in 79% of eyes.

Rates of device malposition, hyphema >2 mm, postoperative IOP spikes, and postoperative peripheral anterior synechiae were all less than 1%,” Dr. Whitman said.

Intraoperatively, there were 46 other adverse events (2%), which included IOP spikes, damage to the iris, and cyclodialysis among others. Postoperatively, there were a total of 20 other adverse events, including cases of visual loss, maculopathy, corneal edema/abrasion, and vitreous in the anterior chamber.

At 12 months, 58% of eyes were medication-free. At 3 years, more than 42% of eyes were using no ocular hypotensive medications.
Joint initiative focuses on value of patient input for MIGS therapy

Project involves development of patient-reported outcome measure

By Cheryl Guttman Krader; Reviewed by Malvina Eydelman, MD, and George L. Spaeth, MD

IN 2013, the FDA launched a collaborative project that recognized the value of including information from glaucoma patients in the agency’s evaluation of minimally invasive glaucoma surgical (MIGS) devices.

The project involves participation of the FDA, the bicoastal Centers of Excellence and Regulatory Science and Innovation (CERSI) at University of California San Francisco-Stanford University and Johns Hopkins University, and the American Glaucoma Society (AGS).

Speaking at the AGS meeting in March, Malvina Eydelman, MD, announced that one goal of the dual-armed program has been completed and the second has entered its final phase.

“We, at the FDA, believe that patients’ input can and should inform medical device development and evaluation throughout the product life cycle,” said Dr. Eydelman, director, Division of Ophthalmic, and Ear, Nose and Throat Devices, Center for Devices and Radiologic Health, U.S. FDA, Silver Spring, MD. “Along with that concept, we published two guidance documents defining how patient preference information and patient-reported outcomes can be utilized to assess the safety and effectiveness of new medical devices.

“We have been fortunate to obtain funding from the FDA to allow collaboration between the bicoastal CERSI in this program and to work with the AGS that has been a significant contributor since the project’s inception,” she added.

WHAT PATIENTS WANT

Citing a passage from the Hippocratic Oath and from an article titled “The Value of Autonomy in Medical Ethics” published in 2006, George L. Spaeth, MD, observed that the medical profession has never been very interested in sharing knowledge with patients so that the patients can make decisions likely to lead to what they want.

“As a matter of fact, the idea that physicians may be required to base actions on patient-reported outcomes is one of the most frightening things that comes to mind for physicians,” said Dr. Spaeth, who has participated in the collaborative project as a representative of the AGS and is the Louis J. Esposito Research Professor, Wills Eye Institute, Jefferson Medical College, Philadelphia.

“However, it is time to start thinking about what patients want and what is important to patients,” he said. “If we say that we ought to do MIGS because it results in better patient outcomes, this project will for the first time give us information able to support that statement. It is both enormously exciting and terribly important.”

STATUS UPDATE

The completed project, which was being conducted with the collaboration of the Johns Hopkins CERSI, was designed to determine patient preferences in glaucoma treatment with a focus on MIGS devices. It aimed specifically to answer the question of what outcomes matter most to patients.

Initially, a qualitative study comprising 25 semi-structured interviews with patients with open-angle glaucoma was conducted.

A second larger preference study included 274 patients with open-angle glaucoma recruited at four centers nationwide.

“The manuscript has been submitted for publication, but to highlight some of the interesting outcomes, we found that control of IOP mattered most to patients whereas the reduction in number of drops used was very low on the list,” Dr. Eydelman said.

The second project, which involves the University of California-Stanford University CERSI, has as its goal the development of a patient-reported outcome measure (PROM) that will assess health-related quality of life in patients with mild to moderate glaucoma.

The process for developing the survey tool involves seven phases, of which six have been completed.

First, a physician focus group was convened followed by several patient focus groups with the goal of gathering additional information that was used to develop the questionnaire.

Next, cognitive interviews of item content were conducted, and a web-based PROM was developed.

Then, there was a second round of cognitive interviews, and the information gathered was used to refine the PROM. Now, the modified PROM, is ready for testing at sites throughout the United States.

“The last step in developing this health-related, quality-of-life measure is a field test where patients with mild-to-moderate glaucoma will complete the survey online to assess the questionnaire’s reliability, validity, and responsiveness to treatment,” Dr. Eydelman said.

As “breaking news,” Dr. Eydelman announced that the IRIS Registry will host the questionnaire and AAO’s partner, Verana Health, will use its software for minimizing investigator burden in this study.

At the AGS meeting, Dr. Eydelman put out a call for meeting attendees to become involved as investigators. Glaucoma practitioners who may be interested in being considered as investigators for field testing of the PROM should express their interest via e-mail (ags@aaao.org).

“We need your help to incorporate patient perspectives into the development and evaluation process that informs innovation for MIGS devices,” she said.
Combining MIGS approaches paves way for future glaucoma surgeries

Surgeon sheds light on his experiences with variety of innovative surgery options

By Vanessa Caceres; Reviewed by Won Kim, MD

MICROINVASIVE glaucoma surgery (MIGS) is already a game-changing approach, but there are some ways to raise the bar for even more innovation, according to Won Kim, MD, Walter Reed National Military Medical Center, Bethesda, MD.

Dr. Kim started to combine MIGS procedures in 2013 to see if he could maintain safety while also improving efficacy to achieve lower IOP.

Here is an overview of some ways Dr. Kim has combined MIGS approaches and the results his patients have achieved.

TRABECULAR MESHWORK BYPASS TECHNIQUE WITH SOME FORM OF ECP OR MICROPULSE: Dr. Kim has performed this approach on 31 patients. The average baseline IOP was 21.3 mm Hg on 3.3 medications compared with an average postoperative IOP of 11.8 mm Hg and 2.4 medications. Between postoperative month 1 and year 4, the IOPs have ranged between 11.3 mm Hg and 13.6 mm Hg. Four failures occurred.

Ab interno canaloplasty using a lighted microcatheter combined with a trabecular meshwork bypass technique: Dr. Kim has 19 patients who have had this combination, all of whom had severe visual field loss and four of whom had a failed prior trabeculectomy and/or tube. The average baseline IOP was 20.2 mm Hg with three medications, compared with a range between 11.9 to 13.4 mm Hg between postoperative month 1 and postoperative year 2. At the last follow-up, the mean IOP was 11.8 mm Hg, and patients used 2.4 medications. Two failures occurred.

TWO ISTENTS, ISTENT SUPRA, TRAVOPROST USE: After observing positive results from the MIGS Study Group that were presented at the 2016 American Glaucoma Society meeting, Dr. Kim was inspired to try something similar.

“When the CyPass Supraciliary stent became available, I started combining it first with two iStents and then also with the Ka-hook Dual Blade and Trab 360,” he said.

Overall, the eyes included had advanced field loss, and 11 had had failed prior glaucoma surgery.

Dr. Kim performed this on 33 eyes until the CyPass was recalled. Baseline IOP went from 24.1 mm Hg on 3.6 medications preoperatively to 13.7 mm Hg on 2.7 medications at the last follow-up. Five failures occurred—most in patients who had received glaucoma drainage implants.

COMBINING MIGS PROCEDURES: Dr. Kim shared his overall results among 72 open-angle glaucoma patients in whom he has combined MIGS procedures. Their IOP reduced from a baseline mean of 22.1 mm Hg to a mean postoperative IOP of 12.9 mm Hg at the last follow up.

Complications occurred in five patients who had IOP spikes higher than 40 mm Hg. There were two retinal detachments and one patient with a hyphema that became a vitreous hemorrhage requiring pars plana vitrectomy. Eleven failures required more glaucoma surgery.

AB EXTERNO TRANSCONJUNCTIVAL XEN 45 IMPLANTATION: This approach involves no incisions, and the corneal and anterior chamber remain undisturbed, which aids with visual recovery, Dr. Kim said.

Surgeons can place the Xen supertemporally if desired, which is not possible with an ab interno technique.

Of the 29 patients who have received this approach so far, the mean preoperative IOP was 26.4 mm Hg with 3.8 medications compared with a postoperative IOP of 12.5 mm Hg on 1.6 medications. There were nine bleb needlings, three failures, one case of hypotony maculopathy, and one choroidal effusion.

WON KIM, MD
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This article was adapted from Dr. Kim’s presentation at the 2019 American Glaucoma Society annual meeting. Dr. Kim has no financial disclosures.
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**Special Report**  
CHANGING REALM OF **MIGS & GLAUCOMA SURGERY**

**TM-BASED MIGS**

(Continued from page 1)

promise surgical success—for example, the inability to rotate the head and neck during surgery.

One common concern related to patient selection is whether it is safe to perform TM-based MIGS in patients who are receiving anticoagulation or anti-platelet therapy for cardiac disease or is it safe to perform TM-based MIGS in patients who are receiving anticoagulation or anti-platelet therapy for cardiac disease or anticoagulation or anti-platelet therapy for cardiac disease.

The question of whether to perform phacoemulsification before or after TM-based MIGS is a matter of surgeon preference.

Dr. Vinod also recommends that the corneal wound should be constructed anterior to the limbal blood vessels to minimize the chance of bleeding onto the corneal surface, which can obscure the view intraoperatively.

**RIGHT TIME FOR PHACO**

The second key to minimizing complications with TM-based MIGS is to optimize the intraoperative view of the angle. Performing gonioscopy during surgery is very different from doing so in the office, and there is a learningle curve involved. Novice surgeons may find it useful to practice intraoperative gonioscopy at the end of routine cataract cases to increase their confidence. In general, the microscope is tilted 30° toward the surgeon and the patient’s head is tilted 30° away from the surgeon. The surgeon should be able to comfortably hold the gonioscope in his or her non-dominant hand without exerting excessive pressure on the eye, which can cause corneal striae.

Adequate anesthesia is critical and usually consists of some combination of topical and intracameral agents, Dr. Vinod said.

Beginning surgeons may consider a periocular or retrobulbar block to ensure patient comfort and minimize patient movement.

Based on her experience, Dr. Vinod also recommends that the corneal wound should be constructed anterior to the limbal blood vessels to minimize the chance of bleeding onto the corneal surface, which can obscure the view intraoperatively.

**ROLE OF VISCOELASTIC**

Viscoelastic has several roles in TM-based MIGS—it is used as a coupling agent on the corneal surface as well as to widen the angle, except with a surgical system (Trabectome, NeoMedix Corp.), which has its own infusion.

Viscoelastic can also help to tamponade active bleeding. Overfill may collapse Schlemm’s canal, leading to superficial stent implantation, and underfill may induce corneal striae.

Dr. Vinod noted that her preference is to use whichever viscoelastic already has been opened for the cataract portion of the case. In stand-alone MIGS procedures, she uses sodium hyaluronate 10 mg/mL, which is easiest to remove and less likely to cause an IOP spike postoperatively, she noted.

Final steps that reduce the risk of complications are ensuring a waternight wound closure, ideally with a 10-0 nylon suture, and pressurizing the eye before leaving the operating room.

Dr. Vinod added that these strategies minimize the risk of postoperative bleeding, though hyphema may still rarely occur and typically resolve quickly.

**References**


AcrySof® IQ RestOR® Family of Multifocal IOLS Important Product Information

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

**INDICATIONS:** The AcrySof® IQ RestOR® Posterior Chamber Intraocular Multifocal IOLS include AcrySof® IQ RestOR® and AcrySof® IQ RestOR® Toric and are intended for primary implantation for the visual correction of aphakia secondary to removal of a cataractous lens in adult patients with and without presbyopia, who desire near, intermediate and distance vision with increased spectacle independence. In addition, the AcrySof® IQ RestOR® Toric IOL is intended to correct preexisting astigmatism. The lenses are intended to be placed in the capsular bag. Warnings/Precautions: Careful preoperative evaluation and sound clinical judgment should be used by the surgeon to decide the risk/benefit ratio before implanting a lens in a patient with any of the conditions described in the Directions for Use labeling for each IOL. Physicians should target emmetropia, and ensure that IOL centration is achieved. Care should be taken to remove viscoelastic from the eye at the close of surgery. The RestOR® Toric IOL should not be implanted if the posterior capsule is ruptured, if the zonules are damaged, or if a primary posterior capsulotomy is planned. Rotation can reduce astigmatic correction; if necessary lens repositioning should occur as early as possible prior to lens encapsulation. Some patients may experience visual disturbances and/or discomfort due to multifocality, especially under dim light conditions. A reduction in contrast sensitivity may occur in low light conditions. Visual symptoms may be significant enough that the patient will request explant of the multifocal IOL. Spectacle independence rates vary; some patients may need glasses when reading small print or looking at small objects. Posterior capsule opacification (PCO), when present, may develop earlier into clinically significant PCO with multifocal IOLS. Prior to surgery, physicians should provide prospective patients with a copy of the Patient Information Brochure available from Alcon informing them of possible risks and benefits associated with the AcrySof® IQ RestOR® IOLs. Do not resterilize; do not store over 40°C. Use only sterile irrigating solutions such as BSS® or BSS PLUS®. Sterile Intraocular Irrigating Solutions. ATTENTION: Reference the Directions for Use labeling for each IOL for a complete listing of indications, warnings and precautions.

**KATEKI VINOD, MD**

This article was adapted from Dr. Vinod’s presentation at the 2019 meeting of the American Glaucoma Society. Dr. Vinod did not report any financial disclosures.
MIGS developments continuing to transform glaucoma surgery
Surgeons can anticipate flurry of product releases that will drive innovation

By Cheryl Guttman Krader; Reviewed by Inder Paul Singh, MD

A REDESIGNED INJECTOR for the ab interno gel stent (XEN Gel Stent, Allergan) features ergonomic enhancements that facilitate its usability and allow for improved surgeon control during stent placement, said Inder Paul Singh, MD.

“The current injector is ergonomic and straightforward to use, but the updated version is even more user-friendly and includes features that can be appreciated by new surgeons as well as those who have developed expertise,” said Dr. Singh, president, Eye Centers of Racine and Kenosha, WI.

Modifications to the new injector include a redesigned slider that is smaller and has a smoother surface than its predecessor. In addition, the start position of the slider was moved forward by 8 mm. Surgeons will also feel slightly more resistance as they move the slider to deliver the stent and notice two subtle clicks, one at the midpoint when the needle starts to retract into the sleeve and the second near the end of its travel distance when the needle retraction is complete.

Dr. Singh noted that the smaller, smoother slider enables better grip and movement of the slider button. The reset start position makes the slider button easier to reach.

“Depending on hand size, some surgeons might have had difficulty accessing the slider with their thumb and may have found it necessary to use a second hand to use the injector or look away from the microscope to locate the slider button,” Dr. Singh said. “The smaller size and forward position of the slider button make it easier to engage without any additional maneuvers.”

The increase in slider resistance across its travel distance and the addition of the clicks, which are not mechanically disruptive, provide tactile feedback that allows for real-time confirmation and thus possibly more precise and predictable placement of the stent.

“Now surgeons can feel the progression of the stent’s delivery without having to look at the slider’s position, and the clicks are a nice add-on safety check for surgeons to know when the stent is fully deployed and the device can be withdrawn from eye,” Dr. Singh explained.

THE MIGS ERA
The new injector for the ab interno gel stent is expected to be commercially available during the second quarter of 2019.

Surgeons can look forward to other product releases in the MIGS space as it continues to transform the glaucoma management landscape.

“MIGS has created a new paradigm for glaucoma management in which surgery is being considered earlier as an approach that can decrease the need for topical drops and the compliance, cost, and safety concerns that accompany their use,” he said.

Dr. Singh added that given their proven safety advantages compared with conventional glaucoma surgeries, and with multiple data sets demonstrating good efficacy, surgeons today are less likely to wonder whether or not they should incorporate MIGS.

“With multiple MIGS procedures now available, surgeons are confronted with the question of which procedure to choose for which patient, and they need to become active participants as they aim to pick the right one for each patient,” he said.

Dr. Singh suggested surgeons consider several factors during their decision-making process, but noted it is important to understand where the available procedures work in the outflow pathway.

Explaining how he applies that information, Dr. Singh said that instead of categorizing disease severity based only on the condition of the optic nerve and visual field, he now also judges severity in terms of site or sites of outflow resistance.

Dr. Singh pointed out that conventional rating of glaucoma severity is still important for choosing the target IOP for a particular patient, which may also have implications for choosing a procedure.

“A patient might have pre-perimetric disease and yet have an IOP of 25 mm Hg while on four medications,” he said. “In that situation, I presume that the problem with resistance is not just in the trabecular meshwork but probably also in the Schlemm’s canal and the distal channels.”

“Therefore, I would choose a procedure or

take-home

- As MIGS continues to increase in popularity as a procedure, new products will enter the marketplace that will make surgery easier for physicians and patients alike.

Continues on page 30: Transform
combination of procedures that will address all of those sites of resistance,” Dr. Singh added. Although there are no preoperative diagnostic methods that allow surgeons to pinpoint the site of outflow resistance in a patient with glaucoma, such tools are in development and will likely be available in the future.

In the meantime, Dr. Singh said that based on published data and data he is collecting, the trabecular meshwork is likely not the only site of outflow resistance in patients who are refractory to selective laser trabeculoplasty (SLT). The type of response to SLT may provide an insight into the area of pathology in glaucoma patients.

Lens status is another factor that can influence the selection of a MIGS procedure. While some procedures are approved as stand-alone surgeries, others are indicated only for use in combination with cataract surgery. In addition, a procedure that does not violate trabecular meshwork may be preferred in a patient who is younger, still phakic, and has no sign of cataract.

“Avoiding a procedure that removes or “cuts” the trabecular meshwork in this situation allows for the opportunity to perform SLT later or place a trabecular bypass stent if the patient develops a cataract in the future,” Dr. Singh explained.

Reimbursement can also be an issue, he noted. “When all other factors are equal, surgeons are often forced to choose the procedure that is covered for the patient and may actually end up ruling out a procedure if it is not reimbursed at all and the patient cannot pay out-of-pocket,” Dr. Singh explained.

**BECOMING A MIGS SURGEON**

As glaucoma patient care has entered the MIGS era, Dr. Singh encouraged colleagues to become a comprehensive MIGS surgeon. Although it is not necessary to learn all of the available procedures, he recommended learning at least one within each category.

“If you handcuff yourself to one procedure, you limit your ability to help the spectrum of patients that you will encounter in practice,” he said. “Just as we have many pharmaceutical options, we now need to avail ourselves of the multiple surgical options.”

Comfort level with the required surgical technique and follow-up care (i.e., bleb management) are factors that can help surgeons choose the specific procedures they will adopt. As they build their toolbox and recognizing that patients may need to undergo multiple glaucoma procedures over time, MIGS surgeons also need to be prepared to spend time with patient counseling and expectation building.

“MIGS has increased the number of options we have in our therapeutic ladder, and so the breadth of our patient counseling conversations about the current options for glaucoma management and future needs has also increased,” Dr. Singh concluded. “We need to set the expectation that more than one surgery now or in the future may be necessary to halt the progression of the disease.”

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**INDER PAUL SINGH, MD**

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Dr. Singh is a consultant to, does research for, and/or is a speaker for Allergan and other companies that market or are developing MIGS procedures.

(FIGURE 1) Ab interno canaloplasty (ABiC) demonstrating evidence of increased flow.

(FIGURE 2) OMNI 180 blanching.

(FIGURE 3) Xen in a premium IOL patient (Crystalens).

(FIGURE 4) iStent inject flow and blanching. (Images courtesy of Inder Paul Singh, MD)
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Family of surgical codes evolving to align procedure payment
Differentiating across categories instrumental to establishing accurate value

By Lynda Charters; Reviewed by Cynthia Mattox, MD

AS SURGEONS are aware, the Current Procedural Terminology (CPT) system—maintained/copyrighted by the American Medical Association—comprises five-digit codes that define all physician services ranging from testing codes to examination visit codes to surgical codes.

Of these, the Category I codes are the main codes for which payments are easily made, according to Cynthia Mattox, MD.

She explained that there are criteria to determine if physicians can have a Category I code, which mandates use of an FDA-approved drug if a Category I code is involved and the surgery must be performed extensively countrywide by multiple providers, and have well-documented reported efficacy in the peer-reviewed literature.

CPT codes are used in conjunction with ICD-9-CM or ICD-10-CM numerical diagnostic coding during the electronic medical billing process.

“These criteria have recently been stepped up and the bar is higher,” said Dr. Mattox, who spoke on behalf of David Glasser, MD, at the recent American Glaucoma Society annual meeting and is immediate past president of the organization.

CODE VALUATION
A code value is established after a CPT code has been established and described by the CPT Committee. The code valuation system, which was first introduced in 1992, is the resource-based relative value system. Then a different committee, which is comprised of volunteer physicians from all medical specialties, attempts to devise a relative value unit that encompasses a number of factors, i.e., the physician work involved in the procedure, the practice expense, and an amount to cover professional liability insurance.

The value of these factors is then combined with the entire spectrum of medical treatment to obtain a value that is relative to all other specialties, for example, appendectomy and breast cancer surgery. The committee bases its decisions on information provided by the various societies for each medical specialty after a random survey of physicians who perform the procedure or test. The committee then makes a payment recommendation to Centers for Medicare and Medicaid Service (CMS), which ultimately makes the final decision on the code valuation.

The value determined by the CMS now is added to the proposed rules in July of each year, then a period is allowed for comments about the valuation, and the ultimate determination of the service’s value is published in the November Final Rule, Dr. Mattox explained.

“Physician work is complicated, but in this system the time required to perform the service, the intensity and technical difficulty of the service, the mental judgement involved in the service, and the stress related to potential harm to the patients are all involved in the formula,” she said.

This combination of factors is reported by physicians in a survey, the results of which are synthesized by a team at the American Academy of Ophthalmology. Once the components are determined, a conversion factor that comes out annually is implemented that applies to all medical specialties.

Among the factors mentioned previously, Dr. Mattox demonstrated how important the practice expense is in the equation.

“It is substantial, almost half of the full value of the code,” she said. “The practice expense includes the postoperative visits and the technician time and cost.”

CATEGORY III CODES
These codes differ from those described previously in that they are designed to be temporary codes for new technologies (iStent, Glaukos; XEN Gel Stent, Allergan) for glaucoma surgery.

“Inclusion in Category III is intended to allow time for more data collection, more efficacy, and perhaps an FDA pivotal trial,” Dr. Mattox said. “When the codes are developed, they are automatically assigned to a non-covered list of codes in the Medicare system. Our goal, if we want access to these technologies, is to have the non-covered status removed to allow them to be covered.”

Coverage of new technologies is accomplished region by region with the involvement of each the numerous Medicare carriers. Coverage still involves the scientific data presented to the medical directors at the Medicare carriers; coverage can involve a consensus of a society or organization or conversations between a medical director and colleagues.

The bottom line is that a great deal of effort is involved in procuring Category III coverages implemented. Dr. Mattox pointed out that no set rules are involved in how the medical directors in the various regions decide on coverage or pricing of the procedures.

The Category III codes are not specific for a device, and difficulties may arise when trying to determine where a device fits within an existing code.

Dr. Mattox explained that the valuation that is in place and historical shows a great deal of intraoperative time and a lot of differentiation in the payment.

In December, via a CPT assistants’ guidance document, the canaloplasty code (66174) was issued and is the proper code for a novel glaucoma treatment system (OMNI, Sight Sciences).

“Our family of surgical codes is evolving,” Dr. Mattox concluded. “Each move to a new Category I code requires a re-evaluation of entire categories of code. There will be some inequities until the area evolves further.

“The ultimate goal is to align procedure payment in a fair fashion and make payments relative again to the intensity, time, and postoperative care,” she said.

CYNTHIA MATTOX, MD
cmattox@tuftsmedicalcenter.org
Dr. Mattox has no financial interest in any material presented in this report.
I didn’t realize
STARS
were little dots that twinkled

—Misty L, RPE65 gene therapy recipient

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PEDIG focusing on binocular activities for amblyopia

Group provides update on possible role of computer game rather than patching, eye drops

By Steve Lenier; Reviewed by Michael Repka, MD, MBA

Focusing on the treatment of amblyopia with binocular activities, Michael Repka, MD, MBA, provided updates on behalf of the Pediatric Eye Disease Investigator Group (PEDIG).

“Rather than doing patching or eye drops in an eye, the child might be able to play a computer game, and that is pretty exciting for kids and their parents to hear,” said Dr. Repka, past network chairman of PEDIG.

PEDIG is a group of ophthalmologists and optometrists who perform pediatric eye care. There are currently more than 100 sites in the network, with more than 300 pediatric ophthalmologists and pediatric optometrists in the United States, Canada, and the United Kingdom.

Supported by funding from the National Eye Institute, the investigators collaborate on developing and launching trials, and disseminating the results to the ophthalmology community.

**VIDEO GAME AID**

Dr. Repka described a first-generation game, Hess Falling Blocks, a binocular video game similar to Tetris, where the child would watch the falling blocks through red-green glasses. By coloring the blocks, investigators could have the child see some blocks with the good eye, some with the bad eye, and some with both eyes.

Contrast could be lowered in the good eye, so that the child would pay attention to those blocks seen by the bad eye, which remained at full contrast. The strategy was that by playing the game, the bad eye would be stimulated, and the visual acuity would improve.

The contrast can be slowly raised in the better eye to the point where the child can see out of both eyes. This approach would only apply to children who have some degree of binocularity, both eyes working together. It cannot be used with strabismus larger than a microstrabismus.

PEDIG investigators conducted two studies with Hess Falling Blocks, one with kids 5 to 12 years old, and one with kids 13 to 16 years old. Treatment was playing the game on a tablet for an hour a day for 16 weeks. A control group wore a patch over the stronger eye for two hours per day, so the trial compared conventional therapy with the new therapy.

The visual acuity outcome for both the younger group and the older group favored patching (the control group) slightly. The eyes of the children playing the game improved, but not by much, and they improved less than the eyes of the children in the patching control group.1,2

Investigators determined engagement was poor, leading to low compliance. In the older age group, only 13% reached 75% of the assigned time.

Researchers are now studying a game called Dig Rush, featuring underground miners digging for gold. For the randomly selected trial with this game, researchers had the children play the game for 8 weeks.

The control group was not being patched or receiving any other treatment besides correct glasses, so researchers did not want to extend the treatment any longer. There was a safety outcome at 4 weeks. The study group was children 7 to 12 years old, and researchers looked to see if their vision improved. This game also did not work, even though compliance was better.3

Researchers are recruiting subjects 4 to 7 years old to participate in the Dig Rush study, following the theory that amblyopia should be easier to treat in a younger group.

Dr. Repka also discussed a surgical trial on intermittent exotropia, where eyes occasionally drift out. The study looked at two different approaches: surgery on both eyes, or surgery on just the eye that drifted out. The study group was followed for 3 years, and results were termed as a suboptimal surgical outcome.

Researchers measured the outcomes over time, 12 months, 24 months, and 36 months, to see how the children did. They found a difference in the two surgical approaches, although the children who had bilateral lateral rectus surgery did a little worse than children who had recession-resect surgery on only one eye. The difference was small and not statistically significant.4

**References**


**TAKE-HOME**

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**Roth spots may be ocular sign of hemophagocytic lymphohistiocytosis**

Clinicians should be aware of unusual but characteristic signs, symptoms, findings

**Neuro-Connection** By Andrew G. Lee, MD; Tonse A. Kini, MD; Randy Igbinoba, MPH; Bayan A. Al Othman, MD; Helen Li, MD

**HEMOPHAGOCYTIC** lymphohistiocytosis is a rare disease with a range of ocular findings, and a study has revealed a case which also included the formation of Roth spots in the eyes.

The patient was a 33-year-old African-American male with a history of human immunodeficiency virus (HIV) and hypertension who presented with fever, splenomegaly, and bilateral vision loss. Multiple Roth spots were found bilaterally by ophthalmoscopy. The patient was found to have hypertriglyceridemia, elevated serum ferritin, pancytopenia, and elevated soluble interleukin 2 receptor levels. A bone marrow biopsy confirmed hemophagocytic lymphohistiocytosis. Hemophagocytic lymphohistiocytosis is rare and can be a life-threatening, multisystem, inflammatory syndrome caused by overactive macrophages and lymphocytes. Though ocular involvement in hemophagocytic lymphohistiocytosis is known, to our knowledge, this is the first case of Roth spots as the presenting ocular sign of hemophagocytic lymphohistiocytosis, as described in bacterial endocarditis, they may occur in a number of systemic conditions, including lymphoproliferative disorders.

The extraocular motility was normal, and confrontation visual field testing showed a central scotoma OD that was normal OS. External and anterior segment was normal. Intraocular pressure measured 12 mm Hg in both eyes (OU).

Ophthalmoscopy revealed multifocal large blot hemorrhages with pale centers consistent with Roth spots OU. There was a large hemorrhage over the macula OD consistent with 20/400 vision (Figure 1).

Optical coherence tomography (OCT) of the macula demonstrated a large subinternal limiting membrane hemorrhage, dome elevation OD, and a small subinternal limiting membrane hemorrhage OS (Figure 2).

Hematologic evaluation showed serum white blood cell count: 0.25k/ul (4.5–11 k/ul); red blood cell count: 2.13 m/ul (4.4–6 m/ul); platelet count: 10 k/ul (150–400 k/ul), hemoglobin: 6.3 gm/dl (14–18 gm/dl), hematocrit: 19%, CD4%: 13% (37–47%), reticulocyte count: 3.2% (0.5–2.1%), triglyceride: 731 mg/dl (Reference <150 mg/dl), serum ferritin: 85,951 ng/ml (range 30–400 ng/ml).

The patient had a history of HIV and hypertension on active antiretroviral therapy (HAART), admitted for fever and refractive pancytopenia, reported acute, painless, bilateral central vision loss.

Physical examination revealed the patient was a poorly nourished cachectic male. He also has concurrent intermittent epistaxis, melena, and severe generalized fatigue. Medications include emtricitabine, tenofovir, darunavir, cobicistat, folic acid, metaprolol, and ondansetron. Social history was significant for smoking and marijuana use. His family history was noncontributory. Neuro-ophthalmic examination showed best-corrected visual acuity of 20/400 in his right eye (OD) and 20/70 in his left eye (OS). Pupils were regular and reactive and were 4 mm in dark and 3 mm in bright light without anisocoria or relative afferent pupillary defect.

**TAKE-HOME**

> While Roth spots have been classically described in bacterial endocarditis, they may occur in a number of systemic conditions, including lymphoproliferative disorders.

**CASE PRESENTATION**

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Continues on page 37: Roth spots
Deep learning predicts OCT measures of diabetic macular thickening

Study: AI can detect swelling, severity of that swelling in macula of patients with diabetes

By Steve Lenier

Deep learning is capable of automatically predicting OCT-equivalent measures of macula thickening from color fundus photos and could significantly benefit tele-ophthalmology.

The researchers performed a retrospective analysis on 17,997 CFPs and their associated OCT measurements, taken from the phase III RIDE and RISE studies in DME, to develop and assess the performance of deep learning algorithms. Large amounts of data collected during clinical trials such as these are very valuable for developing AI algorithms.

Results were presented relating to four different DCNN models:
DEEP LEARNING

(Continued from page 36)

Two models to detect the presence of clinically significant MT, using the cutoff points on time-domain OCT (TD-OCT) of CFT of 250 μm and 400 μm

Two models to detect the presence of clinically significant MT, using the cutoff points on TD-OCT of CST of 250 μm and 400 μm

The authors say their study showed DL models can accurately identify which CFPs are associated with a clinically significant level of MT.

RESULTS

The study showed that the best deep learning algorithm was up to 97% accurate in detecting DME severity using CFPs alone. These results show there is potential for AI to increase screening capacity via telemedicine, according to Genentech.

CONCLUSION

According to this study, DL is capable of automatically predicting OCT-equivalent measures of MT from CFPs and could significantly benefit tele-ophthalmology screening programs, contributing to earlier diagnoses of abnormal MT, timely referral to specialists, faster recruitment of patients into clinical trials, and enhanced visual/health outcomes among individuals with diabetes.

Reference


ROTH SPOTS

(Continued from page 35)

400ng/ml). Serum soluble interleukin (IL) 2R was markedly elevated at 17412 unit/ml (Reference: 45–1105), CD163 was high at 8744 ng/ml (Reference: 387–1785). Hemophagocytic histiocytes were present on bone marrow biopsy consistent with the diagnosis of HLH.

An MRI of the brain and spine showed chronic anemia changes with diffuse abnormal bone marrow signal. CSF analysis was normal. Serum PCR was positive for cytomegalovirus (CMV) and Epstein-Barr virus (EBV). A CT scan of the abdomen showed hepatomegaly, worsening splenomegaly with infarctions confirmed by USG. The patient was treated with platelet and RBC transfusions, HAART for HIV, etoposide, dexamethasone, and intravenous immunoglobulin (IVIG). Despite treatment, the patient’s condition deteriorated due to acute respiratory failure, and vancomycin-resistant Enterococcus sepsis, and he died from organ failure.

DISCUSSION

Our patient meets the diagnostic criteria for HLH including fever, splenomegaly, hypertriglyceridemia, elevated serum ferritin, cytopenia, elevated soluble IL2-R level (12,114) and a diagnostic bone marrow biopsy demonstrating hemophagocytic histiocytes. Nonspecific retinal hemorrhages have been described in HLH and two of these cases were virus-associated HLH. 1, 2, 3

Yao et al. reported multifocal retinal hemorrhages interspersed with numerous detachments of the pigment epithelium and macular edema. 2 Hemorrhage involving the nerve fiber layer was found in a patient with CMV-associated HLH by Liao and Thompson. 2

Roth spots are white-centered retinal hemorrhages that appear in a variety of disease processes and most commonly occur within the periphery of the retina. 4

Roth spots in HLH can have been reported previously and could be secondary to the panortside and infections that occur during the course of the disease. Argyraki et al. reported a single case of Roth spots in an HLH patient with endocarditis. 5

Although Roth spots were classically described in bacterial endocarditis, they may occur in a number of systemic conditions including lymphoproliferative disorders. Our patient’s Roth spots could have been secondary to underlying anemia and thrombocytopenia as a consequence of HLH status complicated with underlying HIV, which is again independently found to be associated with Roth spots. Clinicians should be aware of the ocular manifestations of HLH and should consider the diagnosis in any patient fulfilling the diagnostic criteria.

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The Division of Ophthalmology at the University of Vermont College of Medicine, in alliance with the University of Vermont Medical Center, is seeking an academic neuro-ophthalmologist. This individual must have completed a board approved 3- or 4-year ophthalmology residency or a 3-year neurology residency and a clinical neuro-ophthalmology fellowship, and be board certified or board eligible, and eligible for medical licensure in the State of Vermont. The successful applicant will be appointed at the Assistant/Associate Professor level in the Clinical Scholar Pathway, commensurate with years of experience and accomplishments.

Duties will include providing clinical care to neuro-ophthalmology patients, teaching the principles of ophthalmology to medical students and undergraduate students in Allied Health programs, providing teaching experience for residents in training, developing basic and/or clinical research, and performing additional departmental and/or sectional administrative duties as assigned by the Chair of the Department of Surgery.

This is a full-time, 12 month, salaried, faculty appointment and carries with it attending staff privileges at The University of Vermont Medical Center. Salary is competitive and commensurate with years of experience and accomplishments.

Located in Burlington, the University of Vermont Medical Center serves as Vermont’s only academic medical center. Burlington is a vibrant community located on the shores of Lake Champlain, between the Adirondack and Green Mountains. With year-round recreational opportunities, safe communities and excellent schools, this progressive community has been frequently cited as one of the most livable cities in the U.S. The University is especially interested in candidates who can contribute to the diversity and excellence of the academic community through their research, teaching, and/or service. Applicants are requested to include in their cover letter information about how they will further this goal.

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DUREZOL® (difluprednate ophthalmic emulsion) 0.05%
Initial U.S. Approval: 2008

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

1 INDICATIONS AND USAGE
1.1 Ocular Surgery
DUREZOL® (difluprednate ophthalmic emulsion) 0.05%, a topical corticosteroid, is indicated for the treatment of inflammation and pain associated with ocular surgery.

1.2 Endogenous Anterior Uveitis
DUREZOL is also indicated for the treatment of endogenous anterior uveitis.

4 CONTRAINDICATIONS
The use of DUREZOL, as with other ophthalmic corticosteroids, is contraindicated in 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.

5 WARNINGS AND PRECAUTIONS
5.1 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, IOP should be monitored.

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

5.3 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 beyond 28 days 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.

5.4 Bacterial Infections
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. If signs and symptoms fail to improve after 2 days, the patient should be reevaluated.

5.5 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).

5.6 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 culture should be taken when appropriate.

5.7 Topical Ophthalmic Use Only
DUREZOL is not indicated for intraocular administration.

5.8 Contact Lens Wear
DUREZOL should not be instilled while wearing contact lenses. Remove contact lenses prior to instillation of DUREZOL. The preservative in DUREZOL may be absorbed by soft contact lenses. Lenses may be reinserted after 10 minutes following administration of DUREZOL.

6 ADVERSE REACTIONS
The following serious reactions are found elsewhere in the labeling:
- Elevated IOP [see Warnings and Precautions (5.1)]
- Posterior subcapsular cataract formation [see Warnings and Precautions (5.2)]
- Secondary ocular infection [see Warnings and Precautions (5.4)]
- Perforation of the globe [see Warnings and Precautions (5.3)]

6.1 Ocular Surgery
Ocular adverse reactions occurring in 5% to 15% of subjects in clinical studies with DUREZOL included corneal edema, ciliary and conjunctival hyperemia, eye pain, photophobia, posterior capsule opacification, anterior chamber cells, anterior chamber flare, conjunctival edema, and blepharitis. Other ocular adverse reactions occurring in 1% to 5% of subjects included reduced visual acuity, punctate keratitis, eye inflammation, and iritis. Ocular adverse reactions occurring in less than 1% of subjects included application site discomfort or irritation, corneal pigmentation and striae, epikeratitis, eye pruritis, eyelid irritation and crustsing, foreign body sensation, increased lacrimation, macular edema, sclera hyperemia, and uveitis. Most of these reactions may have been the consequence of the surgical procedure.

6.2 Endogenous Anterior Uveitis
A total of 200 subjects participated in the clinical trials for endogenous anterior uveitis, of which 106 were exposed to DUREZOL. The most common adverse reactions of those exposed to DUREZOL occurring in 5% to 10% of subjects included blurred vision, eye irritation, eye pain, headache, increased IOP, iritis, limbal and conjunctival hyperemia, punctate keratitis, and uveitis. Adverse reactions occurring in 2% to 5% of subjects included anterior chamber flare, corneal edema, dry eye, iridocyclitis, photophobia, and reduced visual acuity.

8 USE IN SPECIFIC POPULATIONS
8.1 Pregnancy Teratogenic Effects
Pregnancy Category C
Difluprednate has been shown to be embryotoxic (decrease in embryonic body weight and a delay in embryonic ossification) and teratogenic (cleft palate and skeletal anomalies) when administered subcutaneously to rabbits during organogenesis at a dose of 10-12 mcg/kg/day. However, since use of corticosteroids is contraindicated in most active viral diseases of the cornea and conjunctiva, difluprednate during human pregnancy has not been evaluated and cannot rule out the possibility of harm, DUREZOL should be used during pregnancy only if the potential benefit justifies the potential risk to the embryo or fetus.

8.2 Lactation
It is not known whether topical ophthalmic administration of corticosteroids could result in sufficient systemic absorption to produce detectable quantities in breast milk. Systemically administered corticosteroids appear in human milk and could suppress growth, interfere with endogenous corticosteroid production, or cause other untoward effects. Caution should be exercised when DUREZOL is administered to a nursing woman.

8.3 Pediatric Use
DUREZOL was evaluated in a 3-month, multicenter, double-masked trial in 79 pediatric patients (39 DUREZOL; 40 prednisolone acetate) 0 to 3 years of age for the treatment of inflammation following cataract surgery. A similar safety profile was observed in pediatric patients comparing DUREZOL to prednisolone acetate ophthalmic suspension, 1%. DUREZOL is not indicated for intraocular administration.

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

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T2017-52
April 2017
INDICATIONS AND USAGE

DUREZOL® (difluprednate ophthalmic emulsion) 0.05% is a topical corticosteroid that is indicated for:

- The treatment of inflammation and pain associated with ocular surgery.
- The treatment of endogenous anterior uveitis.

Dosage and Administration

- For the treatment of inflammation and pain associated with ocular surgery instill one drop into the conjunctival sac of the affected eye 4 times daily beginning 24 hours after surgery and continuing throughout the first 2 weeks of the postoperative period, followed by 2 times daily for a week and then a taper based on the response.

For the treatment of endogenous anterior uveitis, instill one drop into the conjunctival sac of the affected eye 4 times daily for 14 days followed by tapering as clinically indicated.

Most Common Adverse Reactions

- Bacterial infections – 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. If signs and symptoms fail to improve after 2 days, the patient should be re-evaluated.

- Viral infections – Employment of a corticosteroid medication in the treatment of patients with a history of herpetic 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 use. Fungus invasion must be considered in any persistent corneal ulceration where a steroid has been used or is in use.

- Contact lens wear – DUREZOL® Emulsion should not be instilled while wearing contact lenses. Remove contact lenses prior to instillation of DUREZOL® Emulsion. The preservative in DUREZOL® Emulsion may be absorbed by soft contact lenses. Lenses may be reinserted after 10 minutes following administration of DUREZOL® Emulsion.

For additional information about DUREZOL® Emulsion, please see Brief Summary of Prescribing Information on adjacent page.

Eligible commercial patients now pay as little as $30*

Not actual patients.


Explore the potency and demonstrated efficacy of DUREZOL® Emulsion at durezolhcp.com.

IMPORTANT SAFETY INFORMATION

Contraindications

DUREZOL® Emulsion, as with other ophthalmic corticosteroids, is contraindicated in 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 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. If this product is used for 10 days or longer, IOP 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 sciera, perforations have been known to occur with the use of topical steroids. The initial prescription and renewal of the medication order beyond 28 days 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.

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INDICATION FOR USE. The iStent inject® Trabecular Micro-Bypass System Model G2-M-IS is indicated for use in conjunction with cataract surgery for the reduction of intraocular pressure (IOP) in adult patients with mild to moderate primary open-angle glaucoma.

CONTRAINDICATIONS. The iStent inject is contraindicated in eyes with angle-closure glaucoma, traumatic, malignant, uveitic, or neovascular glaucoma, discernible congenital anomalies of the anterior chamber (AC) angle, retrobulbar tumor, thyroid eye disease, or Sturge-Weber Syndrome or any other type of condition that may cause elevated episcleral venous pressure.

WARNINGS. Gonioscopy should be performed prior to surgery to exclude congenital anomalies of the angle, PAS, rubeosis, or conditions that would prohibit adequate visualization of the angle that could lead to improper placement of the stent and pose a hazard.

MRI INFORMATION. The iStent inject is MR-Conditional, i.e., the device is safe for use in a specified MR environment under specified conditions; please see Directions for Use (DFU) label for details.

PRECAUTIONS. The surgeon should monitor the patient postoperatively for proper maintenance of IOP. The safety and effectiveness of the iStent inject have not been established as an alternative to the primary treatment of glaucoma with medications, in children, in eyes with significant prior trauma, abnormal anterior segment, chronic inflammation, prior glaucoma surgery (except SLT performed > 90 days preoperative), glaucoma associated with vascular disorders, pseudoxfoliative, pigmentary or other secondary open-angle glaucomas, pseudophakic eyes, phakic eyes without concomitant cataract surgery or with complicated cataract surgery, eyes with medicated IOP > 24 mmHg or unmedicated IOP < 21 mmHg or > 36 mmHg, or for implantation of more or less than two stents.

ADVERSE EVENTS. Common postoperative adverse events reported in the randomized pivotal trial included stent obstruction (6.2%), intraocular inflammation (5.7% for iStent inject vs. 4.2% for cataract surgery only), secondary surgical intervention (5.4% vs. 5.0%) and BCVA loss ≥ 2 lines ≥ 3 months (2.6% vs. 4.2%). CAUTION: Federal law restricts this device to sale by, or on the order of, a physician. Please see DFU for a complete list of contraindications, warnings, precautions, and adverse events.


TRANSFORMING MIGS IN MORE WAYS THAN ONE.

Optimized Outflow: Two multi-directional stents designed to restore natural outflow
Clinically Proven: Significant IOP reduction across a wide range of clinical studies
Procedural Elegance: Predictability and precision to meet the needs of your practice
Proven Safety: Safety profile similar to cataract surgery alone

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