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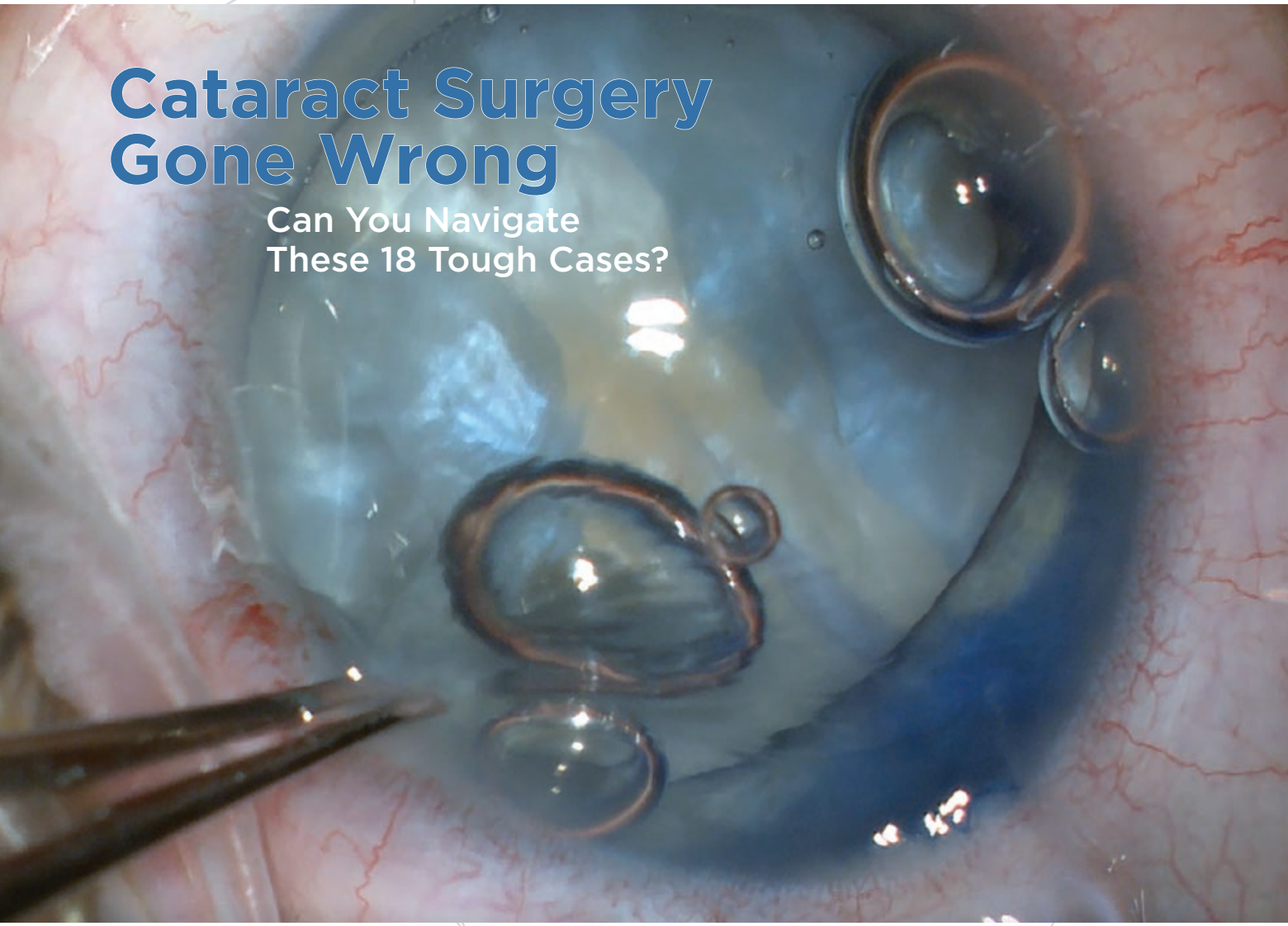

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Mitchell P. Weikert, MD, Academy fellow since 1999, joined ophthalmologists from 137 countries to attend AAO 2016 in Chicago.

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Mitch Jackson, MD
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Cynthia Matossian, MD
Matossian Eye Associates, NJ

The nice thing about the OPD-Scan III placido disk rings is they are in black and white and easy for patients to understand. If the circles aren't crisp and sharp, there's something wrong. If they're warped and irregular, most people can understand that this is a diseased tear film and therefore treatment is needed.

Larry Patterson, MD
Eye Centers of Tennessee

There are a few things that I really need in my practice; none of my surgical coordinators, nor I, ever want to perform cataract surgery on anyone without the OPD. It's one of the reasons that we detect OSD. Previously, I didn't always notice with the slit lamp how dry their ocular surface was.

Neda Shamie, MD
Maloney Vision Institute, CA

The OPD allows you to determine the impact of the ocular surface disease on the visual system, and in turn, gives you points to talk about with the patient. The mires and the measurements help gauge not just your decision on what you can offer the patient, but to also create a more reasonable expectation for the patient.

Toby Tyson, MD
Tyson Eye, FL

We're seeing more and more ocular surface disease; maybe it's because we're finally noticing it, but probably because we now have ways to treat it. I do find that the OPD really helps us out. The OPD mires quickly show you and your technicians any corneal distortions.

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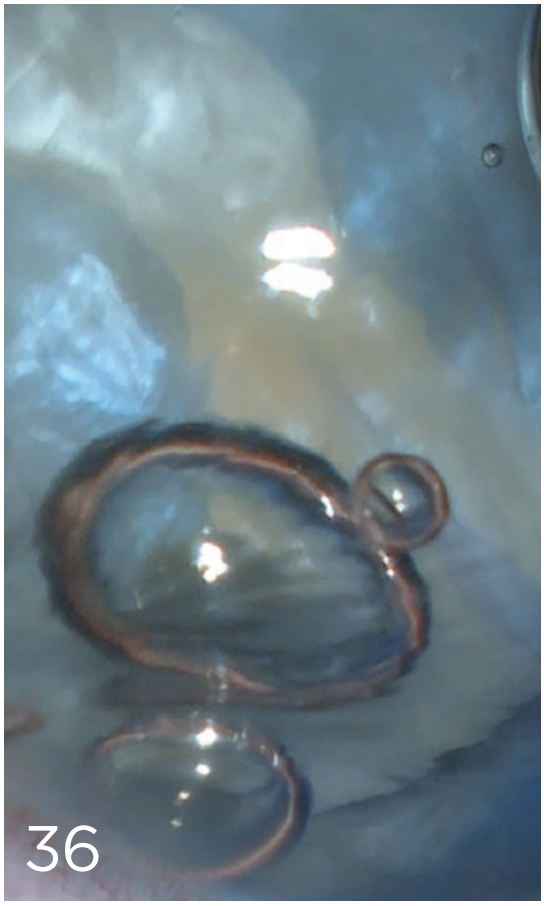

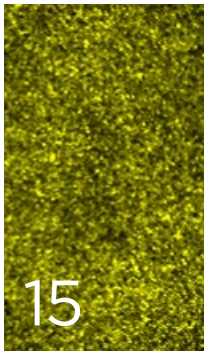

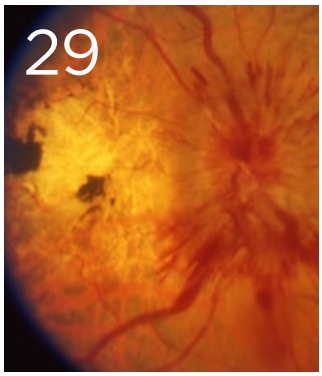

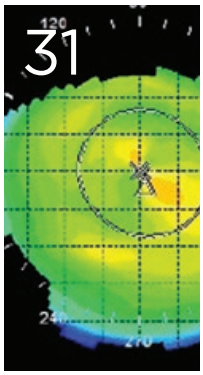

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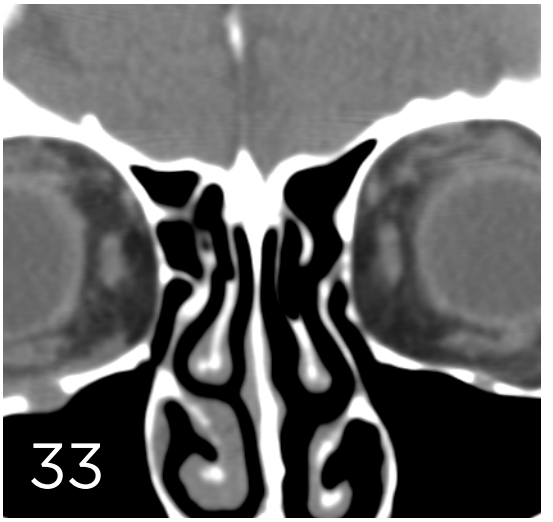
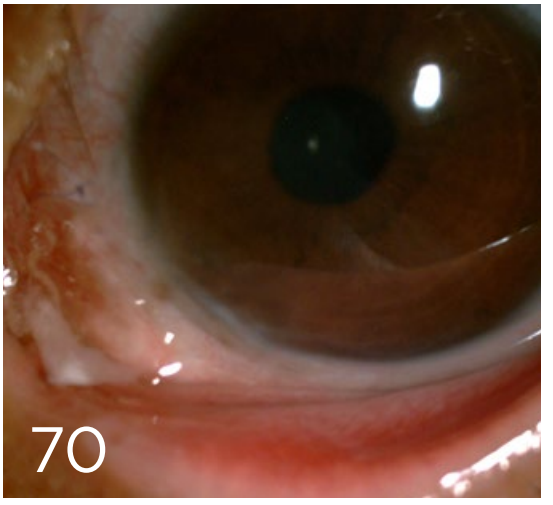
Rosa Braga-Mele, MD





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Contributing Writers

Mark Mrvica, Kelly Miller
M.J. Mrvica Associates, Inc.
2 West Taunton Ave.,
Berlin, NJ 08009
856-768-9360
mjmrvica@mrvica.com
Advertising Sales

AMERICAN ACADEMY OF OPHTHALMOLOGY®
655 Beach St.
San Francisco, CA 94109
866-561-8558, 415-561-8500
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Letters

Why Attend the Mid-Year Forum?

Last spring was my second year attending the Mid-Year Forum (MYF), and from personal experience, I can say that there are three great reasons to attend: advocacy, education, and connections. Although we all make a big difference with daily clinical work, I'd encourage everyone to go national with their passion for patient safety and our profession. If we don't show up in D.C., our voices will go unheard.

During Congressional Advocacy Day, we trek around the U.S. Capitol (during the beautiful cherry blossom season), meeting with representatives and their staff. During these meetings, we have opportunities to inform our nation's leaders about the goals and challenges of our profession and explain how pending legislation affects our patients. When you see how various bills are introduced and passed, you may think of the *Schoolhouse Rock!* episode "I'm Just a Bill," but hopefully this experience will be as enlightening for you as it was for me! Attendees can take this understanding back home to effectively advocate at the state level for quality patient eye care.

Lastly, the MYF provides great opportunities to meet leaders within our field, particularly at fun events like the OphthPAC and Surgical Scope Fund receptions. The connections you will make with both leaders and peers are valuable because they allow you to share experiences and learn about other states' issues, all in a less formal setting.

I have had the opportunity to attend two MYFs so far, and I plan to advocate for my profession at as many of these meetings as I can in the future. I'd encourage all to attend!

Paul O. Phelps, MD
Member, Academy Young Ophthalmologist Advocacy Subcommittee
Chicago

2019 MID-YEAR FORUM

The Mid-Year Forum will take place April 10-13. During this annual meeting in Washington, D.C., Academy members and ophthalmic leaders gather to discuss critical issues facing ophthalmology. The event also includes Congressional Advocacy Day and the spring meeting of the Academy Council. Mid-Year Forum 2019 is open to all Academy members.

For registration and event information, visit aao.org/mid-year-forum.

To learn about the Advocacy Ambassador Program for Academy Members-in-Training, visit aao.org/mid-year-forum/advocacy-ambassador-program.

Opinion

RUTH D. WILLIAMS, MD

From the Ground Up: Building Community

I'm the granddaughter of wheat farmers in northeastern Montana, the great-granddaughter of Swedish immigrants. In my favorite picture of my dad (now 89), the 7-year-old is wearing mud-spattered overalls with big holes at the knee and grinning with wild joy. The flat expanse of a 340-acre homestead is the backdrop, and though the photo is a monochrome one, I imagine the golden, mature wheat fields and the breath-stealing blue western sky.

Like many of us—including those born in large cities—I am a child of farm values. Grit, resilience, persistence, hard work, cheer, and gratefulness are typical qualities of ophthalmologists. And there are other parallels: Changes in the practice of ophthalmology can be compared to the evolution of the American farm. Like the wheat farms in my family, most ophthalmology practices once were small and, often, family-run. The ophthalmologist provided eye care for the local community and was part of a loosely knit network of independent physicians.

Like the family farm, solo and small ophthalmic practices still thrive in some settings, but they are slowly giving way to larger, more complex organizations. Many small groups are developing strategies that include adding partners or locations, joining groups together, or engaging private equity. Vantage EyeCare is one of the largest private ophthalmology groups. Julia Lee, the chief executive of the group, explains that "becoming a practice of more than 100 providers has allowed us access to important conversations in our community about more effective health care delivery, accessibility, and meaningful ways we can move the needle on cost without sacrificing quality."

This makes me think of the writer and environmental activist Wendell Berry, who is also a farmer in Kentucky. He writes about consolidation and the mechanization of agriculture and suggests that large-scale farming can cause decay in local communities. In an interview, he said, "We must support what supports local life, which means community, family, household life—the moral capital our larger institutions have to come to rest upon. If the larger institutions undermine the local life, they destroy that moral capital just exactly as the industrial economy has destroyed the natural capital of localities—soil fertility and so on. Essential wisdom accumulates in the community much as fertility builds in the soil."[1]

The practice of ophthalmology faces similar challenges. As our practices evolve, it's easy to lose our ties to the community. How do we preserve our essence as we become part of and subject to a large system?

First, every ophthalmology group needs core values that guide decisions and transcend changes in leadership. In an interview at the Mid-Year Forum Advocacy Ambassador program, Keith Carter referred to "culture building," noting that it involves a set of values that define an organization. Second, our professional organizations, including the Academy, set expectations for quality care, professionalism, ethics, and transparency (see "All About Trust," Current Perspective, November). Third, and most importantly, ophthalmologists are leaders, and our opportunity to shape and lead ever-larger practices is unprecedented.

As Berry put it, "There can be no such thing as a 'global village.' No matter how much one may love the world as a whole, one can live fully in it only by living responsibly in some small part of it."[1] As ophthalmologists, our small part is the practice in which we provide eye care and the health systems, large or small, that we help shape. And—as Berry reminds us—going forward will require tenacity. In his poem "The Farm," he advises:[2]

Stay years if you would know
The work and thought, the pleasure
And grief, the feat, by which
This vision lives.

1 Snell MB. *New Perspectives Quarterly.* 1992;9(2):29-34.

2 Berry WE. *A Timbered Choir: The Sabbath Poems 1979-1997.* Washington, D.C.: Counterpoint; 1998.

Current Perspective

DAVID W. PARKE II, MD

RCTs: The Gold Standard's Future

Randomized clinical trials (RCTs) have long been appropriately the "gold standard" for clinical research. Properly designed and conducted, an RCT provides information that is accepted by stakeholders as statistically and clinically valid. In a randomized trial, participants are distributed by chance to different groups to compare different drugs, devices, or treatment plans. In order to be valid, the different arms of the trial should be comparable, with specific inclusion and exclusion criteria, and be powered (by an appropriate sample size) to address the predetermined study objectives. Ophthalmology has a rich history of RCTs —from Arnall Patz' trial of oxygen in preterm infants at risk for retinopathy of prematurity to clinical trials of new immunomodulating drugs.

Typically, drugs under development will undergo four phases of clinical trials. Phase 1 is a small trial to study purely safety and side effects. It is not powered or designed to study efficacy, and every person receives the drug—but at different doses. Phase 2 trials—true RCTs—are small scale, typically double-masked, and designed to explore effectiveness as well as safety and dosage. Phase 3 RCTs constitute large scale studies of effectiveness, safety, dosage, and comparisons to placebo or treatment alternatives. There are many design variants for phase 3 trials, and they are the largest, longest, and most expensive of the three phases. Phase 4 trials occur after the FDA has approved a drug and are meant to provide "real-world" evidence of safety and to identify rare adverse events not evident in phase 3. They are a form of postmarket surveillance studies.

RCTs have drawbacks, however. These particularly include:

Cost. The typical cost for phases 1-3 varies between $15 million and $60 million with occasional trials exceeding $500 million. Ophthalmology trials are among the most expensive, on average. The cost per patient in a trial can exceed $50,000.

Time. Each RCT phase has two major time sinks—time to enroll and time to follow the patients. Phase 3 trials typically run 2-4 years. Challenging enrollment processes and criteria can prolong the study.

As a result, studies show that 86% of clinical trials don't finish on time, and nearly half of trials don't meet their initial recruitment goals.

This was a subject of some discussion at the 36th annual J.P. Morgan Healthcare Conference in early January. The meeting included about 9,000 attendees representing over 450 companies and included leaders in the life sciences industry, emerging companies, technology innovators, and the investment community.

David W. Parke II, MD
Academy CEO

While clinical trials are only a small part of the total cost of drugs and devices, they are a critical step in the development and approval pathway. Getting answers quickly and with high-credibility data benefits company, physician, and patient alike.

The Academy's IRIS Registry may have an important role to play. As a vast repository of clinical data, it can identify potential study-eligible patients and help monitor and facilitate patient enrollment in RCT phase 2 and phase 3 trials. It can have a particular utility in phase 4 or postmarket surveillance studies. The IRIS Registry can help monitor and analyze what is happening in the real world of drug and device use to recognize or search for previously unrecognized safety issues and compare outcomes from rigidly conducted RCTs to what is seen in real-world clinical practice. As an example, IRIS Registry studies have demonstrated that clinicians employ anti-VEGF drugs differently in clinical practice than in clinical trials—and the treatment results can be different. This helps inform and modify subsequent recommendations for patient management.

RCTs remain the gold standard. New registry data analytic capabilities should serve to provide a real-world perspective on the application of RCT results and thus benefit all parties engaged in patient care.

EXTRA **MORE ONLINE.** For more about the IRIS Registry, see aao.org/eyenet/article/all-about-trust?november-2018.

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References: 1. Silverstein SM, Rana V, Stephens R, Segars L, Pankratz J, Shivani R, et al. Effect of phenylephrine 1.0%-ketorolac 0.3% injection on tamsulosin-associated intraoperative floppy-iris syndrome. *J Cataract Refract Surg.* 2018;44(9):1103-1108. **2.** Rosenberg ED, Nattis AS, Alevi D, et al. Visual outcomes, efficacy, and surgical complications associated with intracameral phenylephrine 1.0%/ketorolac 0.3% administered during cataract surgery. *Clin Ophthalmol.* 2018;12:21-28. **3.** Bucci FA Jr, Michalek B, Fluet AT. Comparison of the frequency of use of a pupil expansion device with and without an intracameral phenylephrine and ketorolac injection 1%/0.3% at the time of routine cataract surgery. *Clin Ophthalmol.* 2017;11:1039-1043. **4.** Visco D. Effect of phenylephrine/ketorolac on iris fixation ring use and surgical times in patients at risk of intraoperative miosis. *Clin Ophthalmol.* 2018;12:301-305. **5.** Walter K, Delwadia N. Miosis prevention in femtosecond cataract surgery using a continuous infusion of phenylephrine and ketorolac. Presented at: 2018 American Society of Cataract and Refractive Surgery (ASCRS) and American Society of Ophthalmic Administrators (ASOA) Annual Meeting; April 13-17, 2018; Washington, DC. **6.** Matossian C. Clinical outcomes of phenylephrine/ketorolac vs. epinephrine in cataract surgery in a real-world setting. Presented at: American Society of Cataract and Refractive Surgery (ASCRS) and American Society of Ophthalmic Administrators (ASOA) Annual Meeting; April 13-17, 2018; Washington, DC. **7.** Al-Hashimi S, Donaldson K, Davidson R, et al. Medical and surgical management of the small pupil during cataract surgery. *J Cataract Refract Surg.* 2018;44:1032-1041. **8.** Gayton JL. E-poster presented at: 15th International Congress on Vision Science and Eye; 2017 Aug 10-11; London, UK. **9.** Katsev DA, Katsev CC, Pinnow J, Lockhart CM. Intracameral ketorolac concentration at the beginning and end of cataract surgery following preoperative topical ketorolac administration. *Clin Ophthalmol.* 2017;11:1897-1901. **10.** Waterbury LD. Alternative drug delivery for patients undergoing cataract surgery as demonstrated in a canine model. *J Ocul Pharmacol Ther.* 2018;34:154-160.

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News in Review

COMMENTARY AND PERSPECTIVE

RETINA

Imaging Provides Cellular Views of Retinal Layers

IN A MILESTONE FOR IMAGING THE retina's deepest layers, NEI researchers have successfully used adaptive optics (AO) combined with indocyanine green (ICG) angiography to visualize the entire photoreceptor/retinal pigment epithelium/choriocapillaris complex in living human eyes.[1]

Simultaneous visualization. In the AO-ICG study, simultaneous imaging of the three retinal layers revealed that the dye localized not only to the choroidal vasculature but also to the retinal pigment epithelium (RPE) cells.

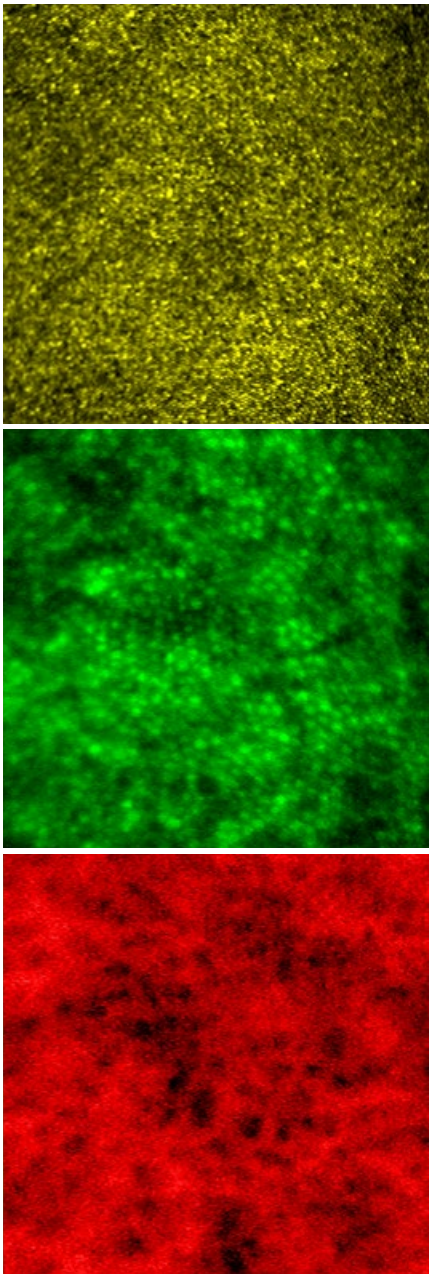
"This is a unique interaction that was unexpected," said senior investigator Johnny Tam, PhD, at the NEI. "Typically, when people think of angiography they think of blood vessels, but this work is interesting because it shows a nonvascular structure, the RPE, that's interacting with the dye."

Improved resolution. The addition of adaptive optics, to correct for wavefront aberrations, improved the resolution achievable with ICG and scanning laser ophthalmoscopy to approximately micrometers, sufficient to visualize and even quantify cells in the outer retinal layers, Dr. Tam said.

Moreover, by subtracting the light emitted by the dye in RPE cells, the researchers were able to detect the weaker fluorescent signal emitted by the tiny vessels of the choriocapillaris, he said. "This ability to see the choriocapillaris is not currently possible with conventional ICG," he said.

Additional findings. The researchers also reported the following:

- After 23 healthy subjects received an intravenous injection of ICG, the dye was rapidly taken up by the RPE cells, peaking within several seconds. Further exploration of this dynamic process could lead to insights about drug pharmacokinetics in the retina, the researchers wrote.
- A second, smaller peak occurred a mean of 18.31 seconds (SD ± 2.98 seconds) after the first peak, reflecting the dye's recirculation from the systemic circulation. Additional injections did not affect the subjects' individual recirculation times. The researchers suggested that this might eventually allow retinal recirculation times to be used as an individualized biomarker for monitoring systemic vascular perfusion.
- RPE cell spacing and the flow voids in the choriocapillaris averaged 3.1 and 3.7 times larger, respectively, than they were in the tightly packed cone photoreceptor layer. Variations in these ratios over time might eventually enable individualized tracking, at a cellular level, of retinal disease progression, the researchers wrote.
- In a single patient with retinitis pigmentosa, AO-ICG showed intact RPE and choriocapillaris layers underneath areas where photoreceptors had been lost. The borders between areas with healthy and absent photoreceptors were abrupt, rather than gradual. "This data provides a powerful tool for revealing



VISUALIZATION. *Cone photoreceptors (top) appear as tiny, bright punctate spots of varying intensity. Fluorescence shows RPE cells (center) in the initial minute after ICG is injected intravenously. At bottom is the choriocapillaris. All images taken simultaneously at the same location on the retina.*

Johnny Tam, PhD, NEI

the cellular status of disease in the living human eye," they wrote.

Other applications. Improved imaging is seen as a major need for the advancement of regenerative therapies for eye disease, according to the NEI, which currently funds five imaging projects through its Audacious Goals Initiative. Adaptive optics is being used to improve other types of advanced retinal imaging, including multiply-scattered light imaging, and angiography using optical coherence tomography. Insights from these and other techniques, such as conventional angiography, will be complementary to AO-ICG, Dr. Tam said.

"We see our combined approach as allowing us to start to validate some of the intriguing findings that we see with conventional ICG. We want to go back to existing data and then collect data in new ways and interpret it all in ways that we didn't think about previously," he said.

The ultimate goal would be to apply the cellular-level discoveries from AO-ICG to already familiar imaging modalities, Dr. Tam said.

"Generalizing our results to standard ICG is something we're very interested in. I think that as we start to compare our AO technique with standard ICG, we can take from the concepts that we've learned with AO-ICG and start to apply that toward clinical practice."

—Linda Roach

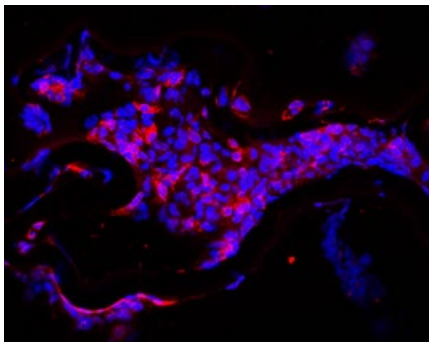
1 Jung H et al. *Commun Biol.* Published online Nov. 14, 2018.

Relevant financial disclosures—Dr. Tam: None.

CATARACT

PCO, Lens Cells, and Inflammation

RESEARCHERS HAVE COME A BIT closer to figuring out the primary cause of fibrotic posterior capsular opacification (PCO), an undesirable outcome of cataract surgery. They report a cascade of events triggered by surgical trauma, starting with the transformation of remnant lens epithelial cells (LECs) into signaling centers that promote inflammation.[1]



INFLAMMATORY CASCADE. *Remnant LECs five days following surgery, stained for cyclooxygenase 2 (red), which catalyzes a key step in prostaglandin synthesis. The cell nuclei are stained blue.*

And while the researchers haven't connected all the dots, they speculate that postsurgical inflammation may

TRAUMA

Amniotic Membrane in Severe Ocular Chemical Injury

RESEARCHERS HAVE FOUND THAT COMBINED AMNIOTIC membrane transplantation (AMT) and medical therapy does not accelerate healing in severe ocular chemical injury.[1] However, the data also show that routine medical therapy leads to a quiet, conjunctivalized cornea and deep fornices with minimal complications, making ocular surface reconstructive surgeries—including stem cell transplantation—possible.

Patients and intervention. For this randomized study, 60 eyes of 60 patients with Roper-Hall grade IV ocular chemical injury were enrolled in the trial with a minimum follow-up of 12 months. Patients were assigned to two groups: Group 1 (30 eyes) received topical preservative-free lubricating gel and drops, chloramphenicol, betamethasone, homatropine, oral vitamin C, and doxycycline; Group 2 (30 eyes) received AMT on the entire ocular surface in addition to the medical treatment provided in Group 1.

Outcome measures. The main outcome measure was the time to complete corneal epithelialization. Secondary outcome measures were best-corrected visual acuity (BCVA) and neovascularization in the central 5 mm of the cornea. Patients were examined on postoperative days 1, 3, 7, 14, and 28; biweekly until three months; monthly until one year; and quarterly thereafter. They were also assessed for the development of complications, such as glaucoma and symblepharon formation.

Results. Mean follow-up time was 20.3 ± 2.5 months (13 to 24 months). Corneal epithelial defects healed within 72.6 ± 30.4 days (21 to 180 days) in Group 1, versus 75.8 ± 29.8 days (46 to 170 days) in Group 2. Mean BCVA was 2.06 ± 0.67 logMAR (0.4 to 2.6) versus 2.06 ± 0.57 logMAR (1 to 2.9) in Groups 1 and 2, respectively ($p = .85$). Group 1 developed more central corneal neovascularization (22 eyes; 73.3%) compared to Group 2 (16 eyes; 53.3%). This, however, was not statistically significant ($p = .108$).

Assessment. "AMT has been reported as a treatment option in the management of the ocular chemical injury," said coauthor Medi Eslani, MD, at the University of Illinois College of Medicine in Chicago. However, he noted, "Most of the previous studies are nonrandomized with a mixed population. Based on this trial, AMT does not offer any advantage over conventional medical therapy alone in terms of corneal epithelial healing, final visual acuity, and neovascularization in patients with severe ocular chemical injury."

—Arthur Stone

1 Eslani M et al. *Am J Ophthalmol.* Published online Nov. 9, 2018.

Relevant financial disclosures—Dr. Eslani: None.

Melinda K. Duncan, PhD

play a key role in the onset of PCO, which affects a wide range of adults (25%-70% of patients) and nearly 100% of children 10 years after surgery.

Starting with mice. To understand the mechanisms by which ocular trauma results in fibrotic PCO, the researchers surgically removed the lens fiber cells in mice, leaving behind the lens capsule and attached LECs. They then compared the levels of all mRNAs expressed by LECs immediately following surgery and 24 hours later.

While, as expected, many genes associated with fibrosis are upregulated, the researchers' comparison revealed that LECs robustly activate the innate immune response within hours of cataract surgery.

An unexpected finding. "That lens cells have the capability of becoming signaling centers for ocular inflammation was surprising, because the lens is classically thought of as an immune-privileged site," said Melinda K. Duncan, PhD, at the University of Delaware in Newark. "But here, lens cells are making huge amounts of cytokines associated with the innate immune system."

Two implications to consider. First, if the remnant LECs prove to be primary drivers of postsurgical inflammation, they could be targeted to directly reduce this side effect of surgery, Dr. Duncan said. "Second, if we can shut down the inflammatory response by lens epithelial cells, we can test the idea that inflammation is a trigger for fibrotic PCO. If that is the case, inhibiting that inflammation could be an approach to reducing fibrotic PCO."

Up next. The researchers hope to identify the precise mechanism by which surgery induces this process. Their most recent results have shown the likely upstream trigger is a signaling cascade initiated immediately after surgery, leading to the activation of "immediate early response" transcription factors.

"We anticipate that this trigger will involve a receptor that we could anticipate blocking clinically," Dr. Duncan said. However, she said, researchers are "likely two to five years away" from identifying the relevant pathways. "Our goal is to identify a therapy that could be instilled into the eye during surgery to block this cascade."—*Miriam Karmel*

1 Jiang J et al. *Invest Ophthalmol Vis Sci.* 2018; 59(12):4986-4997.

Relevant financial disclosures—Dr. Duncan: None.

DRUG DELIVERY

Drug Delivery Via Microneedle Patch

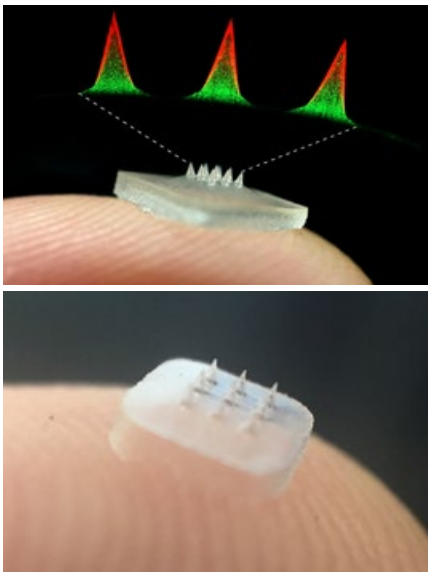
A TEAM OF BIOMEDICAL ENGINEERS has demonstrated the effectiveness of an eye-contact patch equipped with double-layered microneedles for both rapid and controlled drug delivery directly into the eye.[1] The patch, intended to overcome the limitations of systemic, topical, and intraocular injection, is as easy to apply as a disposable contact lens. While not yet tested in human eyes, it promises a paradigm shift for long-term treatment, allowing patients to manage their ocular disorders at home.

"Our work provides a new strategy for efficient drug delivery into the eye, with the help of dissolvable tiny microneedles," said Peng Chen, PhD, at Nanyang Technological University in Singapore.

Building on earlier success. Dr. Chen and his colleagues recently developed microneedle-based skin patches to manage obesity.[2] Their ease of use and effectiveness in transdermal drug release "inspired us to further explore microneedle applications in eye disease treatment," he said. The researchers tested the eye patch in mice with corneal neovascularization, but it has applications for other ocular diseases, he said.

A one-two punch. The patch consists of multiple pyramid-shaped microdrug reservoirs attached to a polymeric contact lens–like substrate. The microneedle tips are thinner than a human hair and a fraction the length of a grain of rice.

Using corneal neovascularization as the disease model, the researchers applied the patch to mouse corneas for a quick burst of an anti-inflammatory compound, followed by sustained release of an antiangiogenic monoclonal antibody. The biphasic release achieved an approximately 90% reduction of neovascular areas with a single 1-gram dose. The result far surpassed human clinical studies that have shown the need for repeated high-dosage topical drugs to treat corneal neovascular disease.[3,4]



RESERVOIRS. *Each needle has two separate reservoirs: The fast-dissolving inner core (green) is covered by a outer layer (red) that provides a slower release of medication.*

Looking ahead. Dr. Chen hopes to find clinical collaborators to launch a clinical trial. In the meantime, he said, "We are continuing to work on optimizing the eye patch for better practical use in human eyes." —*Miriam Karmel*

1 Than A et al. *Nat Comm.* 2018;9(1):4433.
2 Than A et al. *Small Methods.* 2017;11(1): 1700269.
3 Ferrari G et al. *Cornea.* 2013;32(7):992-997.
4 Bock F et al. *Graefes Arch Clin Exp Ophthalmol.* 2008;246(2):281-284.

Relevant financial disclosures—Dr. Chen: Singapore A*STAR Biomedical Research Council: S; Singapore National Research Foundation: S; Singapore Ministry of Education: S; Singapore Ministry of Health: S.

Than Aung, MBBS, PhD

See the financial disclosure key, page 8. **For full disclosures,** including category descriptions, view this News in Review at aao.org/eyenet.

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Journal Highlights

NEW FINDINGS FROM THE PEER-REVIEWED LITERATURE

Ophthalmology

Selected by Stephen D. McLeod, MD

Cost-Effectiveness Comparison of DMEK and DSAEK

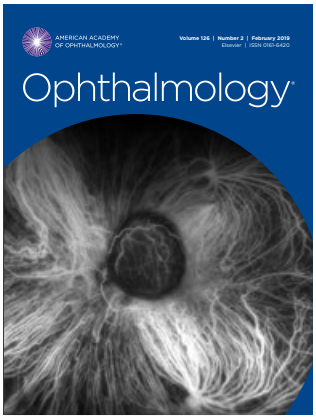
February 2019

Gibbons et al. studied the cost effectiveness of Descemet membrane endothelial keratoplasty (DMEK) and Descemet stripping automated endothelial keratoplasty (DSAEK) and found DMEK to offer superior cost effectiveness, with similar cost but greater utility.

The base case in this study was a 70-year-old man undergoing his first endothelial keratoplasty for bilateral Fuchs endothelial dystrophy. Costs were compared for a 15-year time horizon. The costs and incidences of complications were derived from Medicare reimbursement data, average wholesale prices, and PubMed literature in English. All costs were discounted 3% per annum and were adjusted for inflation to 2018 U.S. dollars. Uncertainty was assessed by deterministic and probabilistic sensitivity analyses. The primary outcomes were incremental cost-effectiveness ratios and incremental cost-utility ratios, measured in cost per quality-adjusted life-years (QALYs).

For the 15-year period, DMEK was superior to DSAEK with respect to QALYs, generating an extra 0.4 QALYs overall. DMEK also was more cost-effective for improving visual acuity, from the societal and third-party payer perspectives. Probabilistic sensitivity analyses, which included variations in costs and rebubble rates, showed that cost savings were greater with DMEK than DSAEK in 38% of iterations. Moreover, in 98% of the models, DMEK costs were within the societal willingness-to-pay threshold of $50,000/QALY.

Despite the favorable findings for DMEK, performing this procedure can be challenging because of the steep learning curve. The economic model in this study was designed for cases that were equally amenable to DMEK and DSAEK. However, the authors acknowledge that some patients are not suitable candidates for DMEK.



Pathologic Features of VA Decline in Patients With CNV: Five-Year Results

February 2019

In a cohort study of patients from the Comparison of Age-Related Macular Degeneration Treatments Trials (CATT), **Jaffe et al.** looked at associations between macular morphology and visual acuity (VA) through five years of anti-VEGF treatment. They also sought to determine the retinal anatomic features that contributed to the VA results. They found the relationships between VA and morphology that had been identified in year 1 were sustained or strengthened by year 5. Strong contributors to VA decline from year 2 to year 5 included new foveal scar, choroidal neovascularization (CNV), retinal thinning, and the presence of intraretinal fluid (IRF) or subretinal hyper-reflective material (SHRM).

The study cohort included CATT participants with active CNV secondary to age-related macular degeneration and with a VA of 20/25 to 20/320. During CATT, patients were assigned randomly to receive ranibizumab or bevacizumab for two years; after this, treatment was at the discretion of each patient's ophthalmologist. Outcomes of interest were VA, morphologic features on optical coherence tomography, and lesion size and foveal composition on fundus photography and fluorescein angiography.

Of the 914 participants alive at the five-year mark, image gradings and VA data were available for 523 (57%). At this time point, 66% of eyes had SHRM, 60% had IRF, 38% had subretinal fluid (SRF), and 36% had subretinal pigment epithelium (RPE) fluid. Mean foveal center thicknesses were 148 µm for the retina, 125 µm for the subretinal tissue complex, 103 µm for RPE + RPE elevation, 11 µm for SHRM, and 5 µm for SRF. Factors that were independently associated with poorer VA were SHRM ($p < .001$), thinner retina

($p < .001$), greater CNV lesion area ($p < .001$), foveal center pathology ($p < .001$), and IRF ($p < .05$). The adjusted mean number of VA letters was 65 for nongeographic atrophy; 64 for nonfibrotic scar; 62 for no pathology in the foveal center; 61 for CNV, fluid, or hemorrhage; 56 for fibrotic scar; and 53 for geographic atrophy (GA).

The presence or worsening of the following pathologic features in years 2 to 5 was linked to greater loss of VA from baseline to 5 years: GA area, foveal GA, foveal scar, foveal CNV, foveal IRF, SHRM, retinal thinning, and CNV lesion area. Such factors were present even in patients whose treatment remained aggressive.

Childhood Intermittent Exotropia Outcomes: PEDIG Report

February 2019

Donahue et al., of the Writing Committee for the Pediatric Eye Disease Investigator Group (PEDIG), reported comparative long-term outcomes for bilateral lateral rectus recession (BLRc) and unilateral lateral rectus recession plus medial rectus resection in the same eye (R&R) as primary treatment for intermittent exotropia (IXT). By the three-year mark, there were no substantial differences in the incidence of suboptimal surgical outcome between these approaches. As a result, the authors do not recommend one procedure over the other.

This randomized multicenter trial included 197 children (aged 3 to <11 years) with basic-type IXT. The largest deviation by prism and alternate cover test, at any distance, ranged from 15 to 40 prism diopters (PD), and near stereoacuity was at least 400 seconds of arc. Patients were assigned randomly to receive BLRc (n = 101) or R&R (n = 96). During follow-up visits, which occurred every six months until three years postoperatively, a study-certified examiner who was masked to treatment assignment obtained measurements of stereoacuity, exotropia control, and ocular alignment. The main outcome measure was suboptimal surgical outcome by three years, defined as any of the following: exotropia of ≥10 PD (distance or near) according to the simultaneous prism and cover test (SPCT); constant esotropia of ≥6 PD (distance or near) per SPCT; loss of ≥2 octaves of stereoacuity from baseline at any follow-up exam; or reoperation.

The cumulative probability of suboptimal surgical outcome within three years was 46% (n = 43) for the BLRc group and 37% (n = 33) for the R&R group (95% confidence interval [CI], –6% to 23%). Nine patients (10%) in the BLRc group (eight of whom had a suboptimal outcome) needed reoperation, as did four patients (5%) in the R&R group (three of whom had a suboptimal outcome). Six of the 9 reoperations in the BLRc group were for recurrent exotropia, whereas 3 of the 4 reoperations in the R&R group were for esotropia. Among participants with three full years of follow-up, 29% of the BLRc group (25 of 86) and 17% of the R&R group (13 of 77) underwent reoperation or had a suboptimal outcome by three years (95% CI, –2% to 13%). With respect to improving IXT control and reducing deviation magnitude, the benefits of the two procedures were similar.

The authors acknowledged that three years is a relatively short assessment period; follow-up will continue for another five years.

—Summaries by Lynda Seminara

Ophthalmology Glaucoma

Selected by Henry D. Jampel, MD, MHS

Exfoliation Syndrome and Chronic Obstructive Pulmonary Disease

January/February 2019

Exfoliation syndrome (XFS) and chronic pulmonary obstructive disease (COPD) share some elements of pathophysiology, notably the process of elastin repair and extracellular matrix (ECM) modeling. Given this link, **Taylor et al.** set out to determine whether patients with XFS were at greater risk of having COPD and vice versa. They found that patients with XFS were more likely to be diagnosed with COPD, particularly if they were smokers, but that those with COPD were not at elevated risk of developing XFS. They also found that patients with both COPD and XFS had significantly better survival rates than did those with COPD alone.

The researchers evaluated 2,943 patients with XFS, 20,589 patients with COPD, and 162 patients with both illnesses. All were older than age 50 and had been treated between 1996 and 2015. Medical records were drawn from the Utah Population Database. Controls were selected and matched by sex and birth year to patients in a 5:1 ratio. Conditional multivariable logistic regression was used to calculate the odds ratio (OR) to estimate risk of COPD in patients with XFS. Model covariates included race, obesity, and tobacco use.

The results show that the risk of a COPD diagnosis was increased in XFS patients compared to that of non-XFS controls (OR = 1.41, 95% confidence intervals [CI] 1.17-1.70; $p < .0004$), with a subset of patients who used tobacco at a 2.2-fold increased risk (OR = 2.17, 95% CI 1.15-4.09; $p = .02$). Overall 10-year survival rates were better in COPD patients who had XFS than in those who did not (76% and 43%, respectively), perhaps because the diagnosis of XFS moved these patients into the health care system at an earlier point in their lives.

The findings add to the understanding that XFS is more than an ophthalmic disease, the researchers said. They also noted that the finding that COPD risk was particularly elevated in those XFS patients who used tobacco suggests that tobacco is the "insult" that leads to degradation of ECM metabolism, thus increasing COPD risk.

—Summary by Jean Shaw

Ophthalmology Retina

Selected by Andrew P. Schachat, MD

SS-OCT Angiography Imaging of Geographic Atrophy

February 2019

Thulliez et al. used two different swept-source optical coherence tomography angiography (SS-OCTA) scanning patterns to image geographic atrophy

(GA), with the goal of determining whether the patterns provided similar measurements in eyes affected by age-related macular degeneration (AMD). They found that the two patterns strongly correlated on measurements of area and enlargement rate (ER), and they suggest that all macular GA can now be imaged with 12 × 12 mm SS-OCTA scans, which provide a 40-degree field of view (FOV).

For this prospective case series, the researchers enrolled 25 patients (32 eyes) with GA secondary to dry AMD. They compared the area and ER measurements obtained when the same GA lesion was imaged using 6 × 6 mm and 12 × 12 mm scan patterns on the same SS-OCTA machine. Images were obtained at baseline and at the six- and 12-month marks—and at baseline, the atrophic lesions had to be fully contained within the 6 × 6 mm scan pattern.

The results showed that lesion area and ER measurements for both scan patterns were comparable for all eyes in all patients through the 12 months of the study. As a result, the researchers said, the 12 × 12 mm SS-OCTA scans can now be considered the ideal single imaging modality for the detection and follow-up of GA, as they provide a wider FOV and provide information on both structure and flow. The researchers cautioned, however, that it is not possible to assess hyperautofluorescence patterns at the margins of GA with this technology.

—Summary by Jean Shaw

American Journal of Ophthalmology

Selected by Richard K. Parrish II, MD

Sarcoidosis-Related Uveitis: Progression to Systemic Disease

February 2019

Ma et al. studied the clinical course and disease characteristics of sarcoid uveitis with the goal of understanding the timing and potential risk factors of its progression to systemic sarcoidosis. They found that concurrent undiagnosed systemic sarcoidosis is common at the time of uveitis onset and recommended that clinicians maintain a high degree of suspicion for systemic disease during and after the detection of uveitis.

This study was a single-center retrospective review of records for 113 patients with concomitant uveitis and presumed (n = 69) or biopsy-proven (n = 44) sarcoidosis. Gathered data included the rate and timing of the development of symptomatic systemic sarcoidosis in relation to the onset of uveitis. The authors compared and contrasted demographics, uveitis characteristics, treatments, and visual outcomes between patients who remained systemically asymptomatic and those in whom symptomatic systemic sarcoidosis developed.

In 89 patients (79%), uveitis was the initial presenting sign of sarcoidosis. Among patients with presumed sarcoidosis, 23 had symptoms of concurrent undiagnosed systemic sarcoidosis at uveitis onset, such as a dry cough, exertional dyspnea, or erythema nodosum. Over time, symptomatic sarcoidosis developed in 29 patients in an organ that was not involved at uveitis onset. The median time from uveitis detection to the development of symptomatic systemic sarcoidosis was 12 months. All patients received topical corticosteroids for intraocular inflammation, and more than half also received regional treatment. Neither group had substantial deterioration of visual function, nor were there meaningful associations between any uveitis characteristic and the progression to extraocular sarcoidosis.

Diabetes Itself May Not Impair Recovery After Cataract Surgery

February 2019

Although studies suggest that the risk of pseudophakic cystoid macular edema (PCME) after routine cataract surgery is higher for patients with diabetes, this may relate more to diabetic retinopathy than to diabetes alone. In a post-hoc analysis of data from two double-blind randomized controlled trials, **Danni et al.** compared outcomes of uneventful cataract surgery between nondiabetic patients and those with diabetes but no retinopathy. For nearly all outcomes assessed, there were no substantial differences between the groups.

This study included 276 eyes (266 patients) that underwent routine cataract surgery. Patients with type 1 or 2 diabetes (56 eyes) were compared with nondiabetic patients (220 eyes). Clinical evaluation was performed by the operating physician, and a research technician recorded data attained before surgery and on postoperative day 28. Demographics and baseline ophthalmic and surgical parameters were comparable for the study groups.

The following outcomes were similar for patients without and with diabetes, respectively: increase in aqueous flare (6.3 ± 16.4 vs. 3.7 ± 8.9 photon units/ms; p = .282), increase in central retinal thickness (CRT; 12.0 ± 38.2 vs. 5.9 ± 15.8 µm; p = .256), and improvement in corrected distance visual acuity (0.57 ± 0.31 vs. 0.53 ± 0.35 decimals; p = .259).

In eyes that received steroid monotherapy (n = 64), the increase in CRT was 38.1 ± 72.8 µm for those without diabetes and 7.8 ± 6.6 µm for those with diabetes (p = .010). In eyes of patients on nonsteroidal anti-inflammatory drug (NSAID) monotherapy (n = 157), the increase in CRT was 5.7 ± 18.4 µm for nondiabetic patients and 6.2 ± 20.5 µm for diabetic patients (p = .897). Among the 55 eyes that received steroid and NSAID therapy, CRT increased 3.6 ± 4.1 µm in nondiabetic patients and 2.9 ± 3.2 µm in patients with diabetes (p = .606). Within 28 days of the surgery, PCME was reported for eight eyes; of these, seven were in the nondiabetic group. On day 28, intraocular pressure was nearly identical for the study groups.

The only outcome with a significant between-group difference was the change in CRT among patients on steroid monotherapy. Therefore, patients with optimally managed diabetes may not be at greater risk of PCME. In light of the relatively small sample size, the authors urged caution in drawing conclusions from their study. Longer follow-up may shed light on differences in macular edema kinetics between patients with and without diabetes.

—Summaries by Lynda Seminara

JAMA Ophthalmology

Selected and reviewed by Neil M. Bressler, MD, and Deputy Editors

Association of Cataract Outcomes With Surgical Experience

January 2019

Some evidence suggests that the quality of patient care may be lower in the latter stages of a physician's career. Of particular concern is the technical proficiency of surgeons, given the neurophysiologic changes that occur naturally with aging. In a large population-based study that addressed this matter for cataract surgery, **Campbell et al.** found no correlation between late career stage and the risk of adverse surgical events.

The study included data for 499,650 cataract operations performed in Ontario, Canada, from 2009 through 2013, which represented all ophthalmologists who performed the surgery in the province during this period. Linked health care databases were used to study cataract surgery complications while controlling for patient-, surgeon-, and institution-level covariates. The authors focused on four serious adverse events: dropped lens fragments, posterior capsular rupture, suspected endophthalmitis, and retinal detachment. Surgeons were grouped by career level, with early-, mid-, and late-career phases defined as <15 years of experience, 15-25 years of experience, and >25 years of experience, respectively.

Random-effects logistic regression models were used to evaluate the association between late-career stage and the risk of adverse events, controlling for both patient-level and surgeon-level covariates and for institution type. In a secondary analysis, surgeon age was the variable of interest. Analyses were adjusted for secular trends.

During the study period, late-career surgeons performed 143,108 (28.6%) of the surgeries, and their work was not associated with higher overall risk of surgical adverse events (odds ratio [OR], 1.06 vs. midcareer surgeons). In a sensitivity analysis in which surgeon volume was removed from the model, the result was similar (OR, 1.10). An association was observed between late career stage and the risk of suspected endophthalmitis (OR, 1.41) and dropped lens fragment (OR, 2.30).

The authors noted that, in future studies, it may be worthwhile to consider the frequency of secondary surgery as another indicator of the quality of primary surgical care.

Ultrawide-Field Imaging for Assessing Diabetes Severity

January 2019

Substantial retinal pathology can exist beyond the 7 standard fields of the Early Treatment Diabetic Retinopathy Study (ETDRS), which include only about two-thirds of the retinal surface. Ultrawide-field (UWF) imaging allows for evaluation of up to 82% of the retinal surface in a single image. **Aiello et al.** looked at a large body of evidence to evaluate the reliability of UWF imaging relative to that of 7-field ETDRS for assessing the severity of diabetic retinopathy (DR). The authors observed exact agreement for 59% of eyes and agreement within 1 step for 97%—findings that may justify using UWF in future clinical trials.

For this cross-sectional study, the investigators included modified ETDRS 7-field images and UWF images captured with the Optos 200Tx system. All images were from adults with type 1 or type 2 diabetes (mean age, 62.2 years). Images were evaluated by trained graders who were masked to the clinical data. κ statistics were used to measure agreement among ETDRS 7-field images, UWF images, and UWF images masked to include only the ETDRS 7-field area.

Among the 742 eyes with graded ETDRS 7-field and UWF images, 359 (48.4%) initially had exact agreement and 653 (88.0%) had agreement within 1 step (weighted κ, 0.51). After open adjudication by an independent senior grader who examined all images that had a discrepancy of more than 2 steps, there was perfect agreement for 435 eyes (59.0%) and agreement within 1 step for 714 eyes (96.9%). Hence, concordance between the two imaging modalities was substantial (weighted κ, 0.77).

Of eyes that were 2 or more steps discrepant, 116 were available for adjudication. The ability of ETDRS and UWF masked images to accurately detect DR was considered similar for 59 eyes (50.9%), better with 7-field ETDRS for 22 eyes (19.0%), and better with UWF masked images in 31 eyes (26.7%). For 12.5% of eyes, the severity grade was at least 1 step higher with UWF unmasked versus UWF masked images. Predominantly peripheral DR lesions were present in 41.0% of eyes, indicating that the actual DR severity was at least 2 steps higher for 11.0% of eyes. Disparity for individual eyes was similar for these imaging modalities. *(Also see related commentary by Stephen S. Feman, MD, in the same issue.)*

iStent May Reduce the Need for Glaucoma Drugs After Cataract Surgery

January 2019

Wang et al. compared postoperative use of ocular antihypertensive drugs among patients who had cataract surgery alone and those who underwent cataract surgery and received the iStent Trabecular Micro-Bypass (Glaukos). They found that, by 20 to 24 months following surgery, the standalone group needed substantially more glaucoma medications.

For this retrospective longitudinal study, the authors included patients enrolled in a U.S. managed care network who had cataract surgery plus the iStent (n = 1,509 bilateral; n = 1,462 unilateral) as well as a control group that received bilateral cataract surgery only and was matched (1:1) to patients who had bilateral iStent/cataract surgery. All procedures were performed between 2012 and 2016. The main outcome measure was the number of topical ocular antihypertensive agents used postoperatively versus preoperatively (baseline).

Diagnoses of those who underwent iStent/cataract surgery were primary open-angle glaucoma (78.4%), narrow angles (12.8%), and secondary glaucoma (8.8%). At baseline, 41.2% of this group were not receiving a topical glaucoma agent, and 29.5%, 14.7%,

and 14.6% were receiving 1, 2, or ≥3 agents, respectively. Among the 22.8% of iStent/cataract surgery participants who completed at least two years of postoperative follow-up, the authors observed an increase (to 64.7%) in the number who required no drops by 20 to 24 months postoperatively ($p < .001$, χ^2 test). Patients using at least one topical agent at baseline had a mean reduction of 1.01 and 0.61 in the number of medications by 20 to 24 months after bilateral or unilateral surgery, respectively (both $p < .001$, paired t test). Sustained reduction in medication use was more common for patients who had at least three medications at baseline versus only one medication (hazard ratio, 1.68).

Compared with matched controls who underwent cataract surgery alone, those with the combination procedure had a greater reduction in the mean number of drops used by month 20 to 24 (0.99 vs. 0.49; $p < .001$, paired t test). Moreover, a larger percentage of the iStent/cataract surgery group were receiving no drops by the 20- to 24-month mark (73.5% vs. 55.3%; $p < .001$; χ^2 test).

These findings support those of smaller studies showing that the iStent in combination with cataract surgery reduces dependence on ocular antihypertensive drugs following surgery.

—Summaries by Lynda Seminara

OTHER JOURNALS

Selected by Deepak P. Edward, MD

Ocular and Brain Injury in Pediatric Trauma Patients

Journal of AAPOS
2018;22(6):421-425

In a large retrospective study, **Gise et al.** evaluated the relationship between traumatic brain injury (TBI) and sight-threatening ocular injury. They found that nearly 55% of pediatric trauma patients with ocular comorbidity were found to have TBI. The most common ocular injuries in patients with TBI were orbital fractures and contusions of the eye or adnexa.

For their research, the authors used the U.S. National Trauma Data Bank registry to review records of pediatric patients who were hospitalized for trauma from 2008 through 2014. Ocular injuries were categorized by type and location. TBI was identified by relevant ICD-9 codes (for skull fracture; intracranial injury; shaken baby syndrome; injury to the optic chiasm, optic pathway, or visual cortex; and head injury not otherwise specified).

Of the 58,765 pediatric patients (< 21 years of age) with concomitant trauma and ocular injury upon admission, 32,173 (54.8%) were diagnosed as having TBI. The majority were 12-18 years of age (41.3%), and 69.8% were boys. The most common ocular injuries associated with TBI were contusions of the eye/adnexa (39.1%) and orbital fractures (35.8%). Globe ruptures were not significantly associated with TBI and occurred in only 5.1% of cases.

With regard to age distribution, younger children were more likely to be injured at home, particularly during a fall, while adolescents were more likely to be injured as a result of a motor vehicle accident. With regard to racial distribution, blacks and Hispanics were most likely to be injured during an assault, while whites were more likely to have self-inflicted or unintentional wounds. Whites also were more likely to be injured in a motor vehicle accident. Firearm-inflicted trauma was highest among blacks, and Hispanics had the greatest risk of being injured because of being struck by a motor vehicle.

These findings demonstrate that TBI is common among trauma patients with concurrent ocular injury. Demographic patterns may help to identify patients with the greatest risk of TBI, leading to earlier diagnosis and treatment.

RNFL Thickness and Brain Neurodegeneration

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2018;1(7):e184406

In a study of elderly patients without dementia, **Méndez-Gómez et al.** explored the relationship between thickness of the retinal nerve fiber layer (RNFL) and alterations in brain regions that are prone to neurodegeneration. The authors found that greater RNFL thickness correlated with better findings during magnetic resonance imaging (MRI), not only in the brain's visual pathways but also in areas linked to Alzheimer disease processes.

For this investigation, the authors conducted a cross-sectional analysis of participants in the population-based Three-City Study in France. Brain volume was evaluated for 104 patients, and diffusion tensor imaging was analyzed for 79 patients. The mean age of the 104 participants was 80.8 years; 56.7% were women.

Global RNFL was assessed by spectral-domain optical coherence tomography. T1-weighted MRI images were used for measurement of global white and gray matter fractions and the hippocampal fraction. Microstructural brain alterations were determined from diffusion tensor imaging at various locations, including the level of posterior thalamic radiations, limbic system tracts (the fornix and cingulum bundles), and the posterior limb of the internal capsule (control region). Linear regression models were applied, and adjustments were made for relevant confounders.

Results of these assessments showed that a thicker global peripapillary RNFL was associated with better diffusion tensor imaging variables in the global and hippocampal part of the cingulum, a region of the brain associated with neurodegeneration noted in Alzheimer disease. No significant associations were found between the RNFL and the diffusion tensor imaging variables in the control region located outside the visual pathway, nor were any significant associations found with global MRI variables.

Axonal thickness of the retina, which can be measured quickly and easily, may allow for early-stage detection of neurodegeneration in the brain. The authors acknowledged that more research is needed to confirm the potential utility of RNFL thickness as an indicator of early degeneration of the brain in presymptomatic elderly adults.

—Summaries by Lynda Seminara

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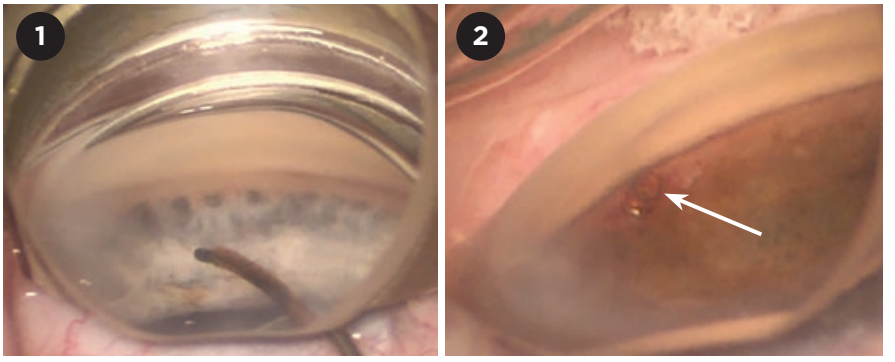
CyPass Update: What Now?

Wednesday, Aug. 29, 2018, was "the day that rocked the glaucoma world," as Thomas W. Samuelson, MD, describes it. That's when Alcon urgently called for a "voluntary medical device market withdrawal" of its CyPass microstent, a minimally invasive glaucoma surgery (MIGS) device.

Two months later, the voluntary withdrawal was changed to an FDA Class 1 recall.



IN PLACE. *The CyPass during surgery (Fig. 1) and after implantation (Fig. 2).*

Unfamiliar Territory

CyPass was pulled from the market because of safety concerns based on five-year data from the COMPASS XT study, which indicated a higher rate of endothelial cell loss (ECL) in patients who underwent cataract surgery and received a CyPass than in those who had cataract surgery alone.

"In the field of ophthalmology, we had not experienced a device withdrawal like this before," said Michelle R. Butler, MD, who practices in Dallas. And it stunned ophthalmologists who had experienced success with the device.

For instance, John P. Berdahl, MD, who practices in Sioux Falls, South Dakota, estimated that he had implanted more than 60 CyPass devices since the FDA's initial approval, with good results. "I found that patients with moderate glaucoma and intraocular pressures [IOPs] on the lower side of the teens benefited from CyPass because we were able to create a conduit from the anterior chamber to the suprachoroidal space, allowing us to bypass Schlemm's canal and drain the aqueous internally," he said.

Initial upheaval, then guidelines. Cynthia Mattox, MD, president of the American Glaucoma Society, said her top priority was disseminating information to the members as quickly as possible. She stayed in touch with the Ophthalmic Mutual Insurance Company (OMIC) and Alcon, and she participated in conference calls with investigators.

Initially, the recall sparked considerable confusion among clinicians, especially those who had implanted the device in their patients, Dr. Mattox noted.

But in short order, the American Society of Cataract and Refractive Surgery (ASCRS), the FDA, and OMIC issued guidance for clinicians.[1-3] That guidance continues to be updated as needed. (See "Where We Are Now.")

A CyPass Primer

CyPass is one of several MIGS devices developed to serve as a minimally invasive alternative to conventional glaucoma surgery. These newer surgical options can allow patients to reduce their medication burden and modestly improve overall pressure control while avoiding some of the complications associated with traditional glaucoma surgery, Dr. Butler said.

Given their favorable safety profile and modest efficacy, the various MIGS devices have gained popularity in the treatment of patients with mild to moderate glaucoma.

How it differs. "Many of the MIGS devices [and procedures] are Schlemm's canal–based," said Dr. Butler. "CyPass was the first MIGS device to use an entirely new outflow pathway," giving clinicians another option for many patients.

Initial approval. CyPass received

BY LORI BAKER-SCHENA, EDD, MBA, CONTRIBUTING WRITER, INTERVIEWING **JOHN P. BERDAHL, MD, MICHELLE R. BUTLER, MD, CYNTHIA MATTOX, MD,** AND **THOMAS W. SAMUELSON, MD.**

Michelle R. Butler, MD

approval from the FDA on July 29, 2016, based on two-year safety and efficacy data from the COMPASS trial.[4] In this study, 374 patients received the CyPass in combination with cataract surgery, and 131 patients underwent cataract surgery alone (controls). At 24 months, 77% of the microstent subjects achieved greater than 20% unmedicated IOP lowering versus 60% of control patients.

In addition, mean reduction in IOP was 7.4 mm Hg for the CyPass group versus 5.4 mm Hg in the control group, with 85% of microstent subjects not requiring IOP-lowering drugs at 24 months.

At this point, Dr. Butler said, the rate of ECL was 11.2% in the CyPass patients and 7.9% in controls.

Call for additional safety data. After the FDA approved CyPass, it mandated an additional three years of safety data be collected from these patients. Named the COMPASS XT trial, this study included 200 CyPass patients and 53 cataract controls.

Troubling results. The COMPASS XT study uncovered a significant difference in ECL between CyPass recipients and the control group at 48 and 60 months. At month 48, the CyPass group experienced an 18.4% rate of ECL, versus 7.5% in the control group. At the 60-month mark, those rates of loss were 20.4% in the CyPass group and 10.1% in the control group.

Pinpointing the problem. An ASCRS task force, which included Drs. Berdahl and Samuelson, wrote up a preliminary statement that provided both an analysis of the COMPASS XT results as well as recommendations for clinicians.

The task force noted a correlation between CyPass implantation depth and the rate of ECL, with the number of device rings visible used to grade implantation depth. ECL was 1.39% per year for eyes with no rings showing, 2.74% per year for eyes with one ring showing, and 6.96% per year for eyes with two to three rings showing.

Additional findings. On a positive note, no patients in COMPASS XT required corneal surgery during the five years of the trial. One case of corneal edema was documented; it resolved by the completion of the study.[5]

Where We Are Now

Here is a brief compilation of guidance for clinicians, drawn from ASCRS, the FDA, and OMIC:

Product return. Return unused devices to Alcon.

Notify affected patients and conduct baseline exams. The clinician should promptly 1) notify patients who have received a CyPass that the device has been withdrawn and 2) conduct a baseline examination to document the device's position and determine the patient's risk.

Assess device positioning. ASCRS recommends documenting the presence or absence of contact between the corneal endothelium and the device, the position of the device lumen anterior to Schwalbe's line, and the number of retention rings visible in the anterior chamber.

The FDA's language is as follows: "Eye care providers should . . . assess device positioning by visualization of the number of retention rings visible on the proximal end of the device. Patients with two or more rings visible on examination should be evaluated for ECL as soon as possible."[2]

Develop a monitoring plan. Without clear evidence of corneal decompensation, no action other than clinical monitoring is recommended in patients who have one ring (or no rings) of the CyPass visible in the anterior chamber by gonioscopy, the ASCRS task force said.

The task force report also pointed out that while there is a greater risk of corneal ECL in patients with two or three rings of the CyPass device visible in the anterior chamber by gonioscopy, "not all eyes will experience clinically meaningful ECL." It added, "Without clinically significant evidence of corneal decompensation, no action other than monitoring is indicated."

Specular Microscopy

Dr. Samuelson, president of ASCRS and in practice in the Minneapolis area, noted that the ASCRS guidelines recommend that specular microscopy be considered for those patients at increased risk (two or more rings visible or the lumen of CyPass is above Schwalbe's line). In contrast, the FDA recommends using specular microscopy to evaluate all CyPass recipients until the rate of ECL stabilizes.

What if you don't have a specular microscope? In its latest recommendations,[3] OMIC suggests the following:

- Identify practices or academic centers where counts are available, and determine the cost of the count.
- If the exam does not indicate any relevant problems, tell the patient that you do not feel a count is needed at this time.
- At the same time, give the patient the option of having the count done, and explain the cost.
- Document all of the above.

What About Device Revisions?

What about patients with CyPass devices who fall into the high-risk category due to the number of retention rings visible on the proximal end of the device?

After the first few weeks of implantation, it is difficult to reposition or remove the device because of fibrosis, and such manipulation carries a risk of complications, Dr. Butler cautioned. For these high-risk patients, ASCRS recommends trimming the proximal end.

However, as Dr. Butler pointed out, relatively few surgeons have experience trimming a CyPass. Doing so requires a bimanual technique to stabilize and trim the stent and additional help to hold the gonioprism in place for visualization. She added that the decision to trim a high-risk stent must be weighed against the risk of the procedure itself.

For its part, the FDA says, "Based on the endothelial cell density levels, and other factors such as age and time postimplantation, the surgeon should determine if additional surgical interventions (that is, trimming, repositioning, or removal) are appropriate."

Weighing the Risks

"Perspective is important" when considering the ramifications of the withdrawal, Dr. Samuelson said. "Interestingly, none of our traditional glaucoma devices [or procedures]—such as long tubes or trabeculectomy—has been held to a safety standard that compares the procedure to the safety of cataract

surgery alone. That is a high bar."

"It is important to keep things in perspective," Dr. Mattox agreed. "Glaucoma is a long war—and [with] each of these little battles you fight, you may not win everything, but you need to keep fighting for the patient's vision." Dr. Mattox added, "We don't want to see so much reaction to this recall that we stifle the whole field. Ultimately, with iterations and proper risk management, both patients and doctors will benefit from new technology. However, it is important that we remain transparent so we can learn and optimize the options for patients."

Patients with moderate or more severe disease who have received a CyPass might possibly still benefit from the device, Dr. Samuelson said. And with regard to evaluating risk, he added that there are other more traditional procedures to treat glaucoma, "yet those may pose at least as much—if not more—risk in terms of endothelial cell loss. Interestingly, this has not been studied."

Dr. Samuelson also cited an article[6] that asserted that damage to the corneal endothelium may actually be caused by the glaucoma disease process itself as well as by treatment alternatives. However, none of the existing glaucoma surgical devices has five-year ECL data to serve as a comparator to data generated by the COMPASS XT study. The authors called for more research on ECL as it relates to both glaucoma and its various treatments.

Confidence in the Process

Dr. Berdahl noted that he has not "given up hope" that CyPass could be reintroduced to the marketplace. "Upon analyzing the [COMPASS XT] data, I wasn't worried from a patient standpoint. My read on the data was that there is a significant loss of endothelial cells in the CyPass patients, but it hasn't turned into a clinical problem. Alcon acted on the side of caution."

Looking back over the CyPass recall, Drs. Berdahl and Samuelson praised the cooperation that took place among physicians and organizations as the recall rolled out.

"The process worked well in this scenario," Dr. Berdahl said. "The FDA approved the device while mandating extension studies. A negative safety signal was noted, and the device was withdrawn from the market."

For his part, Dr. Samuelson concluded, the system "is working just like it was intended [to]. Based on subclinical findings, Alcon was able to act swiftly and effectively to stop implantation. The FDA has cast a big safety net—all before any clinical signs [of harm were identified]. Now we are in this regroup mode trying to identify why patients are losing cells."

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Dr. Berdahl is a glaucoma and cornea specialist at Vance Thompson Vision in Sioux Falls, S.D. *Relevant financial disclosures: Alcon: C,L; Allergan: C,L; Glaukos: C,O.*

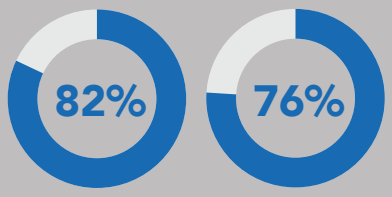
Dr. Butler is a glaucoma specialist with Glaucoma Associates of Texas and assistant professor of ophthalmology at UT Southwestern Medical Center, both in Dallas. *Relevant financial disclosures: Allergan: L.*

Dr. Mattox is a retired glaucoma specialist and current president of the American Glaucoma Society. *Relevant financial disclosures: Alcon: C,S; Allergan: C,S; Ivantis: C; New World Medical: C; Santen: C.*

Dr. Samuelson is a glaucoma/anterior segment specialist, founding partner of Minnesota Eye Consultants, and current president of ASCRS. *Relevant financial disclosures: Alcon: C; Glaukos: C,O; Ivantis: C,O; Santen: C; Sight Sciences: C.*

See disclosure key, page 8. **For full disclosures,** see this article at aao.org/eyenet.

EXTRA **MORE ONLINE.** For a discussion of CyPass positioning and the need to monitor patients, see aao.org/interview/cypass-withdrawal-from-cornea-surgeon-s-perspectiv.



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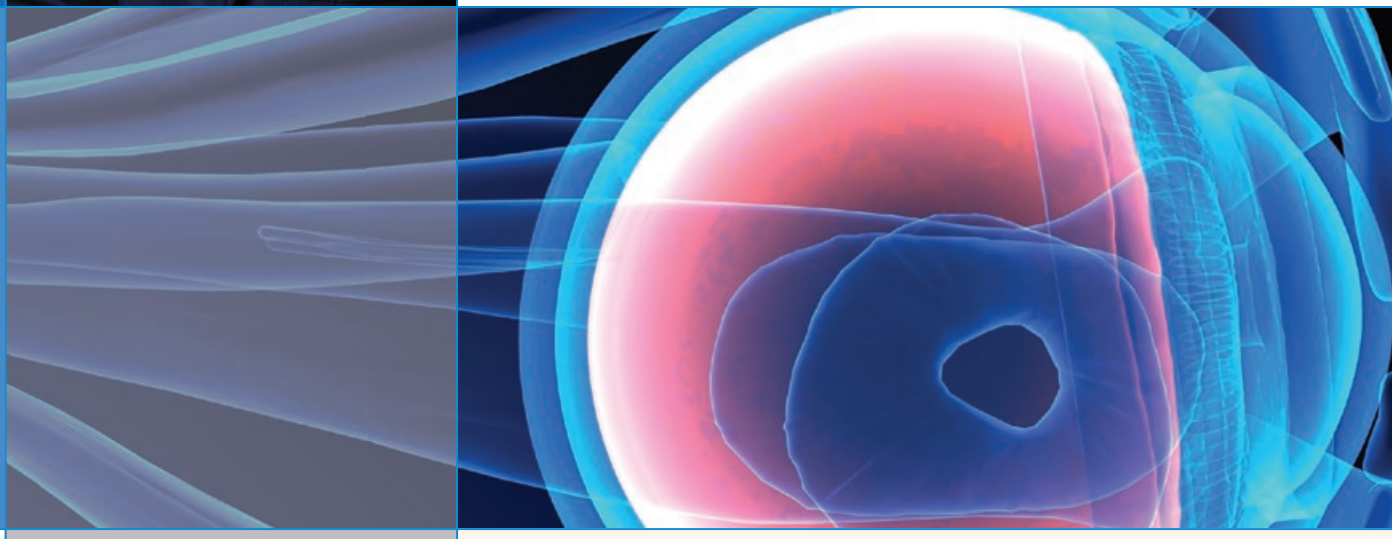

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Drug Tx for Thyroid Eye Disease

Until now, the diplopia, proptosis, and other sequelae of thyroid eye disease (TED) have been thought to be irreversible. Surgical interventions, while continually improving, haven't typically returned patients to the level of visual function or aesthetics they experienced before disease onset.

"We can never restore them to normal with surgery," said Jennifer A. Sivak-Callcott, MD, who practices in Morgantown, West Virginia. "We can decompress the eye, move the eye muscle insertions, and line the eyes up, but the muscles aren't going to contract normally. Our goal in doing strabismus surgery is to stop patients from seeing double when [they are] looking straight ahead or down."

Breakthrough Therapy

Enter teprotumumab (Genmab/Roche), a new immunomodulatory agent that has received Fast Track, Breakthrough Therapy, and Orphan Drug designations by the FDA, based on results of a phase 2 study of patients with TED.

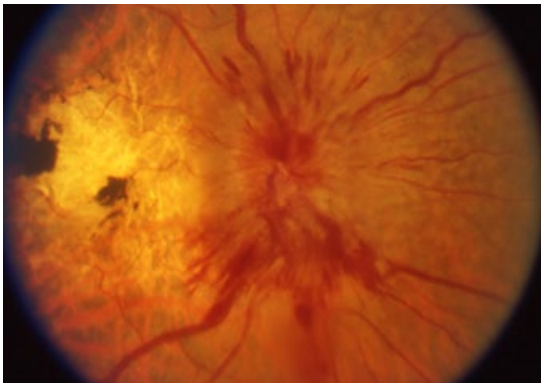
Reversing proptosis. In late 2017, the study, published in *The New England Journal of Medicine* (*NEJM*), reported that teprotumumab reduced and even reversed the sequelae of TED.[1] "It's the first medical treatment shown in any study to actually reduce proptosis," said Dr. Sivak-Callcott.

"It's very exciting," said lead investigator Raymond S. Douglas, MD, PhD, at Cedars-Sinai Medical Center in Los Angeles. He added that the drug "is really going to change how we think about this disease from start to finish, although there aren't yet any other clinical studies of this drug." (A confirmatory phase 3 study of 76 patients is under way.)

Mechanism of action. With thyroid disease, the body makes antibodies against the thyroid gland. "These receptors are similar to receptors in orbital tissues, including the progenitor cells," said Dr. Sivak-Callcott. "So in thyroid eye disease, you develop an autoantibody that attacks the thyroid and the soft tissues of the orbit."

Teprotumumab "is designed to block the IGF-1 [insulin-like growth factor] receptor and turn this receptor into 'stealth mode,' so the immune system doesn't see it," said Dr. Douglas. "It goes right at the heart of the molecular distinction of this autoimmune disease, instead of treating downstream cytokines or other inflammatory markers. This drug, in a sense, targets the match that starts the forest fire of TED."

Teprotumumab targets the IGF-1 receptors throughout the body, not just those in the thyroid, noted Elizabeth A. Bradley, MD, at Mayo Clinic College of Medicine and Science in Rochester, Minnesota.



NEW ERA. *Ideally, drug treatment will allow clinicians to intervene long before the occurrence of sequelae such as proptosis—or even vision loss because of compressive optic neuropathy (shown here).*

Results. The phase 2 trial of teprotumumab spanned 22 centers across the United States and Europe. Of the 87 patients in the intention-to-treat group, 42 received teprotumumab, and 45 were controls. At week 24, 29 of the 42 (69%) of those who received teprotumumab had positive results, versus 9 of 45 (20%) of those given a placebo. As early as the six-week mark, 18 (43%) patients who received teprotumumab had responded positively based on a number of functional and aesthetic measures, versus 2 (4%) of those in the control group.[1]

Rapid response. The drug "appears to work very quickly," said Dr. Douglas. "After two or three doses of the drug, the eye bulging and double vision improve, and patients are ecstatic

BY REBECCA TAYLOR, INTERVIEWING **ELIZABETH A. BRADLEY, MD, RAYMOND S. DOUGLAS, MD, PHD,** AND **JENNIFER A. SIVAK-CALLCOTT, MD.**

because the results are so rapid." TED leaves a trail of devastation that doesn't go away. But teprotumumab seems to not only reduce the inflammation, as steroids do, it also appears to reverse the underlying disease process, he said. "No other drug has reversed the damage this disease causes."

Length of effect? Moreover, the results appear to be long lasting, Dr. Douglas said. "If patients have to be on a drug for the rest of their lives, or it only works a short time, we all become less enthusiastic. But the data show that we're making a long-term change, with very low recurrence rates." As he noted, this raises the possibility of eliminating the need for surgery.

Unknowns and Challenges

Issues yet to be resolved include the following:

Delivery method. Teprotumumab is delivered intravenously; how well patients will accept that as a delivery method is an unknown. "Teprotumumab is delivered via IV infusion, given every three weeks, for eight infusions," said Dr. Douglas. "Maybe in the future we can do fewer infusions, but everyone would rather take a pill than [be given] an IV."

Cost. "We don't yet know the risk/benefit ratio, in terms of cost and side effects, for immunomodulatory agents," Dr. Bradley said. "We don't yet know what the cost of this therapy will be to [be able to] do a cost-effectiveness analysis. What cost is society willing to bear, and what risks and side effects are patients willing to bear?"

Side effects. In the *NEJM* study, hyperglycemia was the primary side effect associated with teprotumumab. This affected patients with diabetes and necessitated medication adjustments. Some patients also reported nausea following the first and second infusions.

"TED is not potentially life threatening, so we need more data and larger studies to determine the low-frequency, less common side effects," Dr. Bradley noted. "The surgical risks are already known and are confined to the eye socket."

Earlier intervention? The phase 2 trial was initially designed to study only patients diagnosed within the past nine months with moderate-to-severe TED. But an extension study, called OPTIC-X, is now planned to evaluate teprotumumab treatment in patients who are in the earliest stages of TED, Dr. Douglas said.

Other Research Targets

Other immunomodulatory agents that have been explored for TED include the following:

Tocilizumab (Genentech), used primarily to treat rheumatoid arthritis, "is a nice pipeline molecule, but it's many years behind the development of teprotumumab" in terms of treating TED, said Dr. Douglas. "It might be a complementary molecule at some point, helpful in reducing inflammation. It inhibits the interleukin-6 pathway, but it's unclear [at this point] whether it will reduce or reverse the damage of TED."

Tocilizumab also has the potential to engender more side effects, he said, "because it dampens down the entire immune system, rather than targeting just one immune interaction—the one specific to TED."

Rituximab (Genentech), used to treat certain autoimmune diseases and types of cancer, also has been studied for TED. To date, however, it has produced no improvement with proptosis or double vision, Dr. Douglas said.

Diagnosing TED

Drs. Bradley, Douglas, and Sivak-Callcott all agree: Comprehensive ophthalmologists are on the front line in diagnosing TED.

Early detection. TED is more common than most people realize, said Dr. Sivak-Callcott. "Patients will come in with a complaint of watering, swelling, foreign body sensation, and redness, and those complaints can [signify] many different things, but TED is the most common disease to affect the orbit," she said. Diagnosis may be missed, she said, because these symptoms are so similar to those of general dry eye.

Diagnostic clues. "Looking for early signs of restrictive myopathy is important because one of the most debilitating sequelae of this disease is double vision," Dr. Sivak-Callcott said. "The eye disease develops within about 18 months of the thyroid disease, and that 18 months can precede the [actual] diagnosis of hyperthyroidism."

"When any patient comes in with chronic irritation and redness around the eyes," Dr. Douglas advised, ask the person how they've been feeling in general. Is their heart racing? Are they losing weight? Do they have anxiety or trouble sleeping? Have they had any thyroid problems?

Four tests to run. The clinician should order tests for thyroid-stimulating hormone (TSH, the most sensitive measure to detect thyroid abnormality), free T3, and free T4.

In addition, said Dr. Sivak-Callcott, it's important to test for thyroid-stimulating immunoglobulin (TSI), a measure of autoantibodies. That's because patients may be in a euthyroid state, in which the results of their thyroid tests are normal—"but their antibodies may be up, and they have not become hyperthyroid as of yet. It may lead you to suspect the diagnosis earlier if you remember to check for the autoantibodies."

1 Smith TJ et al. *N Engl J Med.* 2017;376(18):1748-1761.

Dr. Bradley is associate professor of ophthalmology at the Mayo Clinic College of Medicine and Science in Rochester, Minn. *Financial disclosures: None.*

Dr. Douglas is professor of surgery at Cedars-Sinai Medical Center in Los Angeles. He also practices in Beverly Hills, Calif., and Shanghai. *Financial disclosures: NEI: S.*

Dr. Sivak-Callcott is an oculofacial surgery specialist with Mon Health Medical Center in Morgantown, W. Va. *Financial disclosures: None.*

See disclosure key, page 8.

Blended Vision With Multifocal Intraocular Lenses

As the tools and techniques of cataract surgery continue to advance, there is increasing impetus to improve the outcomes of this already successful procedure. Quality of life and spectacle independence are being added to the traditional measures of success: safety, improved vision, short operating times, and absence of postoperative complications.

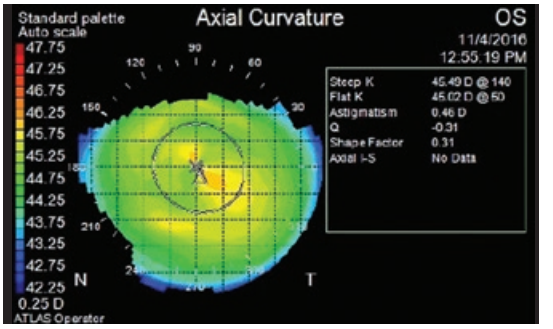
Today, numerous options for treatment and correction are available, with differing risks and benefits. More than ever, the optimal surgical techniques and intraocular lens (IOL) selection depend on the individual patient's ocular pathology, anatomy, history, and visual needs.

The surgeon's responsibility is to bring clinical experience and scientific evidence to bear on the discussion with the patient to arrive at realistic postsurgical visual goals and a clear rationale for IOL selection. Successful cataract surgery begins with agreement between the doctor and patient on these key points, well before the procedure.

Among the growing number of options that are intended to decrease spectacle dependence—including monovision, mini-monovision, accommodative IOLs, corneal inlays, and bioptic refinements—multifocal IOLs (MF-IOLs) continue to play an important role.

One approach to consider is mixing and matching different types of IOLs, including monofocal and multifocal lenses. Although such "blended vision" presents challenges, it provides an opportunity for success in selected cases.[1]

Earlier attempts at mixing and matching to achieve good blended vision were likely hampered by limited IOL options. Now, however, a wide array of designs and add powers has expanded the possibilities for refractive correction.



CORNEAL TOPOGRAPHY. *Preoperative topography shows minimal astigmatism in the left eye of the patient described in the case example.*

Patient and IOL Selection

The following considerations may help guide patient selection and IOL choice for successful refractive outcomes.

Corneal shape and power analysis. Screening for corneal irregularities using topography, tomography, or other advanced imaging is recommended in patients considering MF-IOL correction. In addition, careful attention to optical axes such as angle kappa can help decrease postoperative patient dissatisfaction.[2]

Role of eye dominance. If contemplating the use of monovision or blended vision with mixed IOLs, the surgeon should test for eye dominance. Targeting the nondominant eye for the nearer focal point should be considered.

Aberrations. Characterizing corneal aberrations is helpful when selecting IOLs. Eyes with highly aberrated corneas are not good candidates for MF-IOLs.

It is important to differentiate between aberrations related to the cornea itself and those generated by the entire optical system, including the influence of the lens and cataract. A hard contact lens trial may help determine the contribution of corneal aberrations to the patient's decreased vision, although visual disturbances are often the result of the combined effects of the lens and cornea.

Analysis of corneal aberrations may guide the decision to implant a monofocal IOL with aspheric offsets (zero or negative) to neutralize spherical aberrations. An aspheric monofocal IOL may afford the best quality for distance vision in the dominant eye. However, it may be advantageous to preserve some spherical aberration in the nondominant eye by selecting a traditional nonaspheric IOL or other design matched with the individual cornea. This combination may increase depth of focus and thereby decrease spectacle dependence for near tasks.[3]

BY **EMILY B. WORRALL, BS, BA,** AND **HOON C. JUNG, MD.** EDITED BY INGRID U. SCOTT, MD, MPH, AND SHARON FEKRAT, MD.

Hoon C. Jung, MD

Tear film. The tear film should be assessed carefully. Tear deficiency or abnormalities can affect both preoperative analysis and postoperative patient satisfaction.

Macular status. Because even subtle maculopathy can impair the visual outcome with MF-IOLs, optical coherence tomography may be used to rule out any relevant macular conditions.

Comorbidities. MF-IOLs should not be placed in eyes with significant ophthalmic comorbidities such as retinopathy, corneal disease, uveitis, and optic neuropathy. This remains a fundamental tenet of cataract surgery.

Chromophores. Introduction of chromophores into IOLs to block certain wavelengths of the electromagnetic spectrum has had variable market penetrance, and the literature continues to weigh the risks and benefits.[4]

In cases of bilateral cataract surgery, implanting IOLs with different chromophores should be strictly avoided. If one eye is treated before the other, it is important to review the surgical record or IOL card to avoid implantation of a different chromophore IOL in the second eye; otherwise, the eyes will perceive color differently.

In addition, MF-IOLs redistribute energy to different areas of the retina, and chromophores that block specific wavelengths of light reduce the total energy transmitted through the optical system. Thus, patients seeking high visual performance in low-light conditions may not be ideal candidates for MF-IOLs with chromophores.

Excimer Enhancements

Access to an excimer laser, either co-located or used in agreement with a nearby refractive center, will allow the surgeon to make bioptic refinements. This is helpful in enhancing correction for a known condition such as preoperative astigmatism and in addressing postoperative refractive ametropia. The option of possible laser correction should be discussed with the patient, and any necessary arrangements should be made, before cataract treatment.

Special Clinical Scenarios

Corneal refractive surgery. Cataract patients who have had previous corneal refractive surgery present a challenge. Given that keratorefractive procedures frequently increase corneal aberrations, the surgeon should exercise caution in using MF-IOLs in these individuals, especially those who had correction of large refractive errors.

Unilateral cataracts. Implantation of an MF-IOL for unilateral cataract has been an area of active debate.[5] Unilateral cataracts are less common than bilateral and may justify extra screening for conditions such as amblyopia (e.g., in the setting of polar cataracts) and trauma, which can damage zonules. MF-IOLs should be avoided in eyes with zonular insufficiency, as decentration of the IOL can degrade visual performance significantly. Potential acuity meter testing or pinhole-assisted methods are useful for screening if amblyopia is a concern.

The fellow eye may not require cataract surgery for years or decades. Thus, the patient should be instructed on the importance of safeguarding the IOL identification from the first surgery in case of a later procedure.

Conclusion

MF-IOLs can play an important role in decreasing spectacle dependence, although traditional contraindications remain a limiting factor. Blending of near and intermediate add powers with MF-IOLs should be considered in appropriate candidates seeking the broadest range of vision.

Blended Vision: Case Example

A 78-year-old man presented with blurry vision in his left eye. He had undergone cataract extraction 10 years earlier in his dominant right eye and received a +22.0 D SN6AD3 (Alcon) MF-IOL implant with a +4.0 D add. The patient reported general satisfaction with the right eye for distance vision; however, he was dissatisfied with intermediate and near vision in the right eye as well as the compromised vision at all ranges in the left eye. He requested cataract surgery and IOL implantation in his left eye to improve his ability to work on the computer, with the goal of achieving spectacle independence.

The patient's uncorrected distance visual acuity (UCDVA) was $20/20^{-1}$ in the right eye and $20/60^{-1}$ in the left eye, with a best-corrected distance visual acuity of 20/40, with –0.75 + 1.25 × 140 manifest refraction. There were no other relevant ocular health issues. Corneal topography (Fig. 1) and biometry were obtained in preparation for cataract surgery in the left eye.

The surgeon and patient discussed the chance that spectacles could still play a role in achieving optimal visual acuity. Together, they decided on an MF-IOL with the base sphere targeted for emmetropia at distance and a lower-power reading add (+2.5 D) than in the right eye.

Uncomplicated surgery was performed in the left eye using topical anesthesia and a superior clear corneal approach. An SV25T0 (Alcon) MF-IOL with power of +21.0 D was implanted. Seven weeks postoperatively, the patient's UCDVA was $20/15^{-2}$ with J1 vision with both eyes open at a comfortable reading distance. He achieved spectacle independence at near, intermediate, and distance vision, with improvement in activities of daily living.

1 Bilbao-Calabuig R et al. *J Refract Surg.* 2016; 32(10):659-663.

2 Tchah H et al. *Int J Ophthalmol.* 2017;10(2): 241-245.

3 Zheleznyak L et al. *Invest Ophthalmol Vis Sci.* 2013;54(5):3157-3165.

4 Brøndsted AE et al. *Acta Ophthalmol.* 2017; 95(4):344-351.

5 Hayashi K et al. *J Cataract Refract Surg.* 2013;39(6):851-858.

Ms. Worrall is a third-year medical student at University of Washington School of Medicine, Seattle Foundations Site, in Seattle. **Dr. Jung** is assistant professor of ophthalmology at the University of Washington and VA Puget Sound Health Care System, in Seattle. *Financial disclosures: None.*

A Case of Pixelated Vision

Benjamin Beauchamps,* a 65-year-old man, was experiencing an insidious onset of decreased vision in his right eye. As an engineer, he was attentive to detail. He had visited several ophthalmologists, complaining of a 10% to 15% reduction of vision in that eye. When pressed to provide more details, he said that images appeared "pixelated." At the suggestion of his primary ophthalmologist, magnetic resonance imaging (MRI) of the brain and orbits with and without contrast was ordered. It was read as normal.

We Get a Look

When Mr. Beauchamps came to our ophthalmic plastic surgery clinic, he was at his wit's end. Despite "normal exams" with multiple eye specialists, he insisted that he had decreased vision. His past ocular history was notable for ocular hypertension. To our surprise, he pulled out an Amsler grid on which he had drawn a focal area of visual decline.

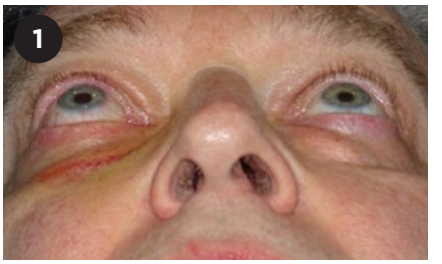
Exam. On examination, the patient's visual acuity was 20/20 in both eyes, and his intraocular pressure (IOP) with a Tonopen was 14 mm Hg bilaterally. We noted an extremely small upgaze restriction in his right eye, and Hertel exophthalmometry measured 2 mm of proptosis in the same eye (Fig. 1). Thyroid function tests, erythrocyte sedimentation rate, antinuclear antibody assay, rheumatoid factor levels, rapid plasma reagin, and complete blood count with differential were ordered. We asked Mr. Beauchamps to return with lab results and his initial MRI for us to review.

Follow-up. All lab results were within normal limits. Review of the MRI revealed an abnormal swelling in the area of the inferior rectus muscle. This might have been previously overlooked because an artifact from a tooth implant created a suboptimal image. Based on this new finding, we started the patient on an oral prednisone regimen with taper and ordered a computed tomography (CT) scan of his orbits with and without contrast.

The scan. The CT scan showed an abnormally enlarged right infraorbital nerve (ION) with an enlarged, smoothly eroded canal along its entire visualized length, from the pterygopalatine fossa to the inferior orbital foramen (Fig. 2A). In addition, we observed thickening in the posterior aspect of the right inferior rectus muscle, extending to the orbital apex and likely impinging on the optic nerve (Fig. 2B).

Differential Diagnosis

Although radiologic evidence demonstrated an orbital process likely contributing to his symptoms, which improved with steroids, we still did not have a diagnosis. The differential diagnosis included immunoglobulin (Ig)G4–related disease, reactive lymphoid hyperplasia (RLH), and lymphoma.[1]



PROPTOSIS. *Hertel exophthalmometry measured 2 mm of proptosis in the patient's right eye.*

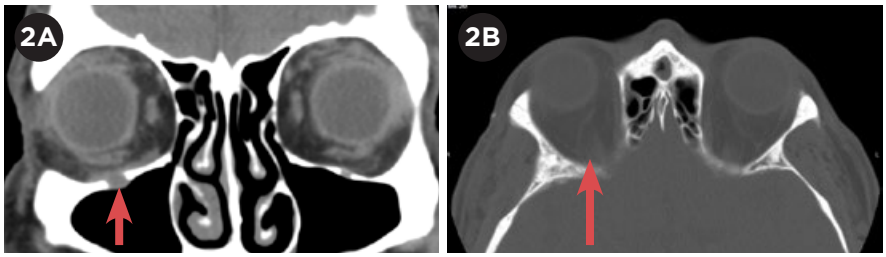
Diagnosis and Treatment

Mr. Beauchamps was then scheduled for a right anterior orbitotomy with biopsy. The biopsy with flow cytometry was consistent with a CD10-positive B-cell lymphoproliferative disorder, suggestive of low-grade follicular lymphoma. (Histology images are online with this article at aao.org/eyenet.)

We referred Mr. Beauchamps to an oncologist, who performed a bone marrow biopsy, which showed no evidence of lymphoma or leukemia. (Notably, orbital lymphoma can occur in advance of or without systemic involvement.) Analysis revealed normal cytogenetics and negative flow cytometry. Positron emission tomography (PET)/CT scan was performed; it revealed extensive fluorodeoxyglucose (FDG)-avid adenopathy from the neck through the pelvis, including the left proximal femur. It was unclear whether the adenopathy was related to lymphoma. Nonetheless, Mr. Beauchamps was treated with the National Comprehensive Cancer Network recommended therapy of bendamustine and obinutuzumab.[2]

BY **POORAV PATEL, MD, MHS, MICHAEL ANG, MD,** AND **RONA Z. SILKISS, MD, FACS.** EDITED BY STEVEN J. GEDDE, MD, MHS.

Rona Z. Silkiss, MD, FACS



CT SCAN. *(2A) Coronal CT scan shows right infraorbital nerve enlargement. (2B) Axial CT scan shows right inferior rectus impinging on the optic nerve.*

Discussion

Although follicular lymphoma was the diagnosis, the more interesting aspect of this case involved the ION enlargement. Enlargement of the ION has recently been described as strongly suggestive of IgG4 disease. However, it can also be seen in RLH and/or lymphoma.

Nomenclature. Of note, IgG4-related ophthalmic disease forms a significant portion of "idiopathic orbital inflammation" or RLH diagnoses.[3,4] The nomenclature of this disease process is evolving, as outlined by McNab et al.[3] Patients can also present with sinus disease and lacrimal gland enlargement.

ION enlargement. Hardy et al. describe ION canal enlargement in a retrospective case series of 14 patients taken from the orbital databases of Moorfields Eye Hospital and Royal Victorian Eye and Ear Hospital. All 14 patients had ION canal enlargement with biopsy-proven chronic orbital inflammation. In seven cases, the pathology was suggestive of RLH. The biopsies in the remaining seven patients were consistent with IgG4-related sclerosing inflammation. Of those, six patients had serum elevation of IgG4. One patient developed diffuse large B-cell lymphoma.[5]

RLH. RLH comprises less than 10% of periocular lymphoid lesions. Patients range in age from 23 to 80, with a mean age of 54.8, and they tend to present with an indolent, painless anterior orbital mass.[5,6] The lesion cannot be clinically or radiologically differentiated from lymphoma, necessitating a histologic diagnosis. Patients with RLH are at high risk of developing lymphoma (50% progression rate). This may be attributed to chronic, antigen-induced inflammation, which can lead to the emergence of monoclonal lymphoma as seen in other systemic diseases such as sarcoidosis.[5]

Expansion of the ION and canal is rare and is highly suggestive of IgG4 disease. However, the differential includes lymphoma, sarcoidosis, perineural or endoneural tumor invasion, aspergillosis, neurofibroma, malignant peripheral nerve sheath tumor, schwannoma, cavernous hemangioma, and traumatic neuroma.[5]

Conclusion

Fortunately, Mr. Beauchamps continued to pursue a diagnosis, despite several apparently "normal" exams. He has been doing well on treatment, with regression of the disease and improvement of symptoms.

*Patient name is fictitious.

1 Watanabe T et al. *Jpn J Radiol.* 2011;29(3):194-201.
2 www.nccn.org/patients/guidelines/nhl-follicular_lymphoma/files/assets/common/downloads/SurveyQuickGuide_waldenstroms.pdf.
3 McNab AA, McKelvie P. *Ophthalmic Plast Reconstr Surg.* 2015;31(2):83.
4 McNab AA, McKelvie P. *Ophthalmic Plast Reconstr Surg.* 2015;31(3):167.
5 Hardy TG et al. *Ophthalmology.* 2014;121(6):1297-1303.
6 Mannami T et al. *Mod Pathol.* 2001;14(7):641-649.

Dr. Patel and **Dr. Ang** are ophthalmology residents, and **Dr. Silkiss** is chief of the Division of Ophthalmic Plastic and Reconstructive Surgery. All are at the California Pacific Medical Center in San Francisco and The Eye Institute in San Francisco. *Financial disclosures: None.*

EXTRA **MORE ONLINE.** For histopathological images, see this article at aao.org/eyenet.

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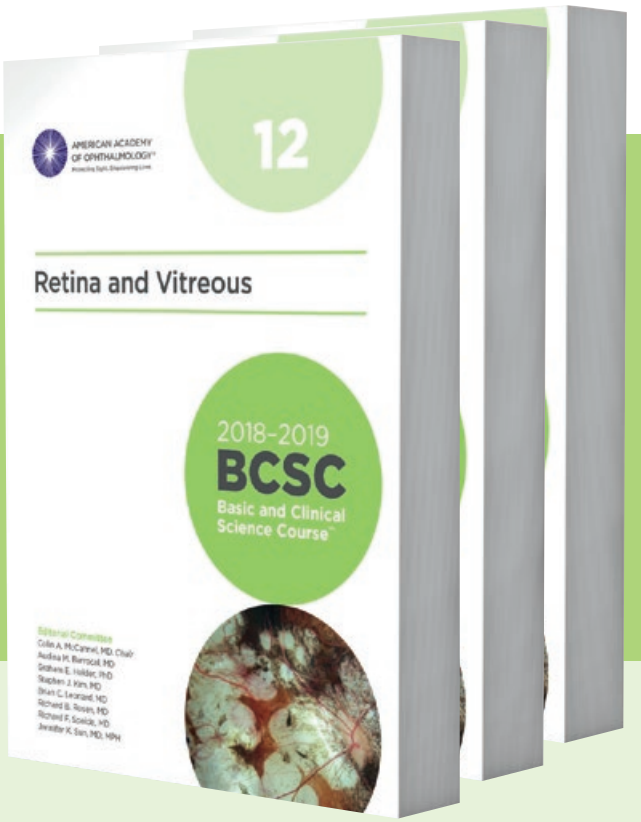

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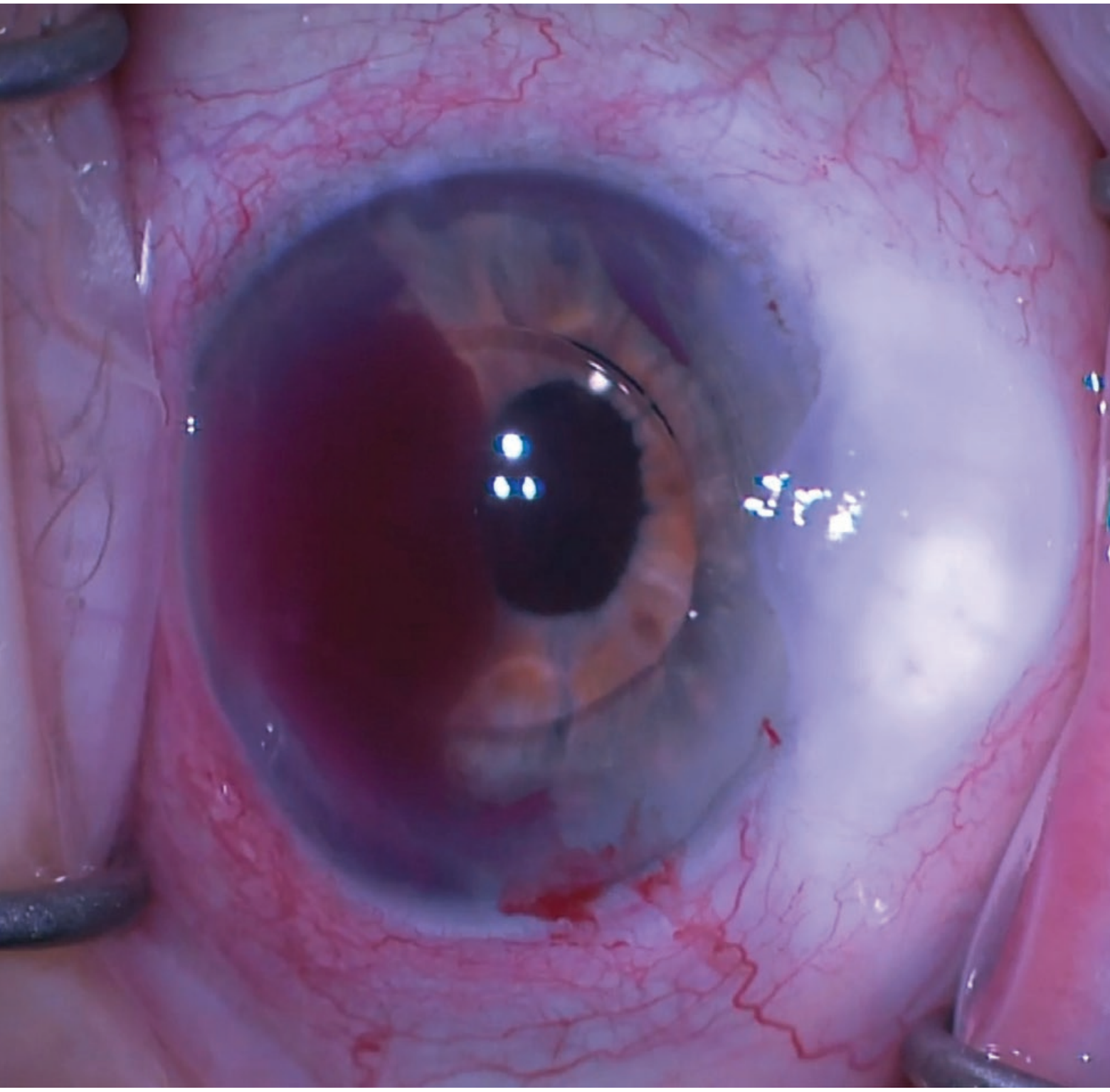


Cataract Surgical Complications

Eighteen cases cover the full spectrum of surgical complications, from the common to the rare—and from the spectacular save to the demoralizing outcome.

THIS PAST OCTOBER, THE 17TH ANNUAL SPOTLIGHT ON CATARACT SURGERY SYMposium at AAO 2018 was entitled "Pressure Cooker: Managing Nerve-racking Complications." Cochaired by Mitchell P. Weikert, MD, and myself, this four-hour case-based video symposium focused on cataract and IOL surgical complications.

Even the very best cataract surgeons suffer complications that challenge us to react, think, and operate under pressure. How and what we learn from our mistakes makes us better ophthalmologists. For this symposium, 18 cataract experts presented stressful cases in which something went wrong, with complications that tested their skills, decision-making, and nerves. What did they learn, and what would they do differently? At critical decision points during the case, the video was paused, and the attendees were asked to make clinical decisions using electronic audience response pads. Next, two discussants (who had never viewed the case) were asked to make their own management recommendations and to comment on the audience responses before the video of the outcome was shown. The audience voted for the best teaching cases and for those surgeons who displayed the most courage, both in the OR and at the podium.

Complications included anterior capsule tears (with and without posterior capsular extension), implantation of the wrong IOL, intraocular bleeding, haptic misadventures and subluxated IOLs, iris prolapse and iatrogenic iridodialysis, aqueous misdirection, suprachoroidal hemorrhage, descending nuclei and IOLs, IOL exchange complications, and capsules or zonules torn at virtually every stage of surgery. Robert J. Cionni, MD, concluded the symposium by delivering the 14th annual Academy Charles Kelman Lecture, entitled "Dealing With Damaged Zonules."

This *EyeNet* article reports the results of the audience response questions, along with written commentary from the presenters and selected panelists. Because of the anonymous nature of this polling method, the audience opinions are always honest and candid and were discussed in real time during the symposium. The entire symposium with videos can be seen at AAO Meetings on Demand (aao.org/annual-meeting/aao-on-demand).

Finally, I want to especially thank our 18 video presenters. When we are speaking in front of several thousand attendees, we would all prefer to showcase our best cases instead of our complications. We appreciate their humility and generosity in sharing these cases with us so that we might all learn important surgical lessons from them.

—David F. Chang, MD
Cataract Spotlight Program Cochairman

Kevin M. Miller, MD

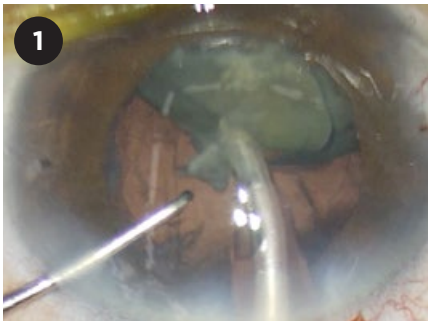
Case 1: Trampolining Makes Me Jumpy

Tetsuro Oshika presented a case of a high myope undergoing phacoemulsification of a dense cataract. As most—but not all—of the nucleus was removed, the posterior capsule was noted to be extremely floppy, and it started trampolining toward the phaco tip. Dr. Oshika stopped phaco to consider how to remove the remaining nuclear fragments.

Q1.1 What is the most likely etiology of the bulging and trampolining posterior capsule in this eye?

- Aqueous misdirection syndrome 8.8%
- Shallowing of the anterior chamber 7.9%
- Weak zonules 70.2%
- Anterior vitreous detachment 6.1%
- Other (e.g., capsular anomaly) 7.0%

Tetsuro Oshika During surgery, there was significant billowing of the posterior capsule while the anterior capsule behaved normally, showing no sign of zonular weakness. The anterior chamber was deep, without positive vitreous pressure. It seemed that the Wieger ligament was detached from the posterior capsule, and the connection between the anterior hyaloid membrane and the posterior capsule was lost. Because the latter was no longer supported by the Wieger ligament, it became significantly floppy, remarkably increasing the risk of aspirating the posterior capsule with the phaco tip. I decided to suspend phaco and implant the IOL in the bag first and then resumed phaco to remove the remaining nuclear fragment over the IOL. Before resuming phaco, I injected a dispersive ophthalmic viscoelastic device (OVD) fully into the anterior chamber in order to prevent the nuclear fragment from moving around on the IOL and damaging the corneal endothelium. Only torsional phaco was used without longitudinal power so that thermal burn of the incision could be avoided with the anterior chamber filled with dispersive OVD.



CASE 1. While the anterior capsule behaved normally, the posterior capsule became significantly floppy.

Q1.2 What would you do to prevent posterior capsular rupture with this trampolining posterior capsule while removing the last nuclear fragment?

- Insert a capsular tension ring (CTR), then phaco 16.2%
- Repeatedly inject OVD 43.0%
- Perform a pars plana anterior vitrectomy/tap, then phaco 1.7%
- Implant an IOL first, then finish phaco over the IOL 36.9%
- Manually extract the nucleus 2.2%

George Beiko Faced with this clinical observation of a trampolining posterior capsule, it is important to consider the cause. The likely cause would be either generalized zonular laxity or localized zonular loss. In either case, I would keep my phaco tip in the anterior chamber and introduce a dispersive OVD through the paracentesis in order to fill the capsular bag and manipulate the remaining nuclear fragment into the anterior chamber. The phaco tip would be removed. I would place a CTR to try to diminish the trampolining and might also place the IOL into the bag to act as a scaffold. Emulsification would be "slow motion," with lowered infusion. Dispersive OVD would be replaced as needed. The remaining cortex would be removed using a combination of dry aspiration, viscodissection, low flow/low vacuum I/A, and additional dispersive OVD. The final step would be to irrigate the anterior chamber with triamcinolone to detect any vitreous prolapse and, if present, to determine whether the capsular bag–IOL complex is stable. If it is unstable, then capsular support segments or rings would be considered. Vitreous, if present, would be removed via a posterior approach.

Case 2: A Splitting Headache

In Bill Trattler's case, a large nasal zonular dialysis became apparent during phaco as he removed the first heminucleus.

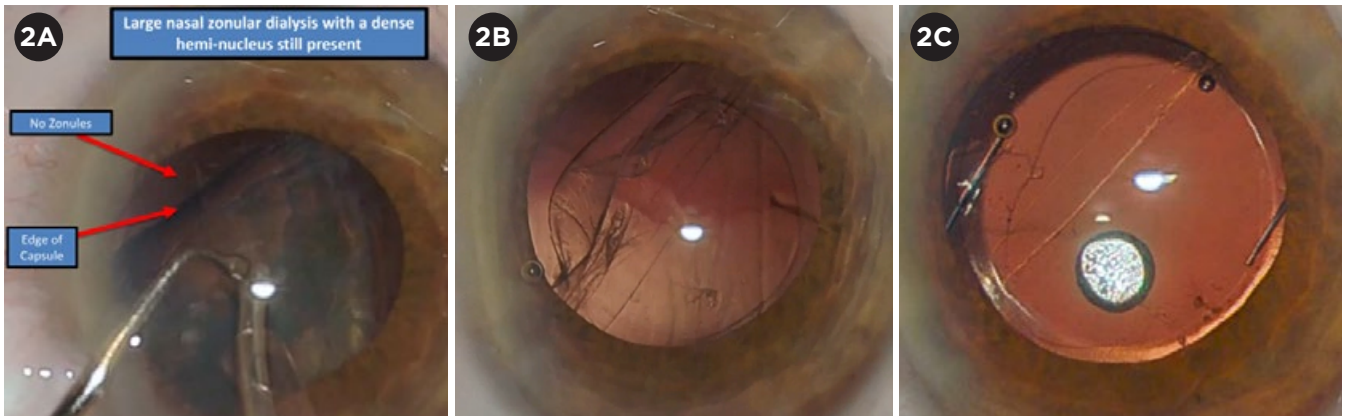
Q2.1 After discovering a large nasal zonular dialysis with a dense heminucleus still present, what would you do next?

- Fill the bag with OVD and resume slow-motion phaco in bag 15.6%
- Implant a CTR, then resume phaco in bag 37.1%
- Implant capsule retractors, then resume phaco in bag 25.3%
- Prolapse nucleus into the anterior chamber, then resume phaco in the anterior chamber 19.4%
- Convert to manual extracapsular cataract extraction (ECCE) 2.5%

Bill Trattler This case focused on the management of a patient who developed a zonular dialysis during phacoemulsification of a relatively dense cataract. After the creation of the capsulotomy, hydrodissection was performed. However, only a limited fluid wave occurred. Phacoemulsification was performed with the creation of a central groove that allowed for the nucleus to be split into halves. The first half was removed. However, when the second half was engaged with vacuum, the presence of an area of zonular dialysis became evident (Fig. 1). The vacuum was disengaged.

Audience members were relatively split on what they would recommend for the next step. The most popular recommendation was to implant a CTR to provide capsular stability.

Tetsura Oshika, MD



CASE 2. (2A) Zonular dialysis evident during phacoemulsification. (2B) Following cortical removal, the capsule is clear. The area of zonular dialysis is visible, and the surgeon must decide where to place the IOL. (2C) A three-piece IOL has been placed in the sulcus, and a 10-0 nylon suture secures the temporal corneal incision.

While this is a good option, challenges can occur when a CTR is placed early in a case. The second most popular answer was to implant capsule retractors, which is an excellent recommendation. This step would hold the capsule in place and potentially prevent further extension of the dialysis. The third most popular choice—which was what was done in this case—was to prolapse the heminucleus into the anterior chamber and then resume phacoemulsification. This was accomplished with the placement of an OVD into the capsular bag and under the heminucleus, resulting in the nuclear material shifting forward into the anterior chamber. The nucleus was removed with phaco. Following this step, the cortex was carefully removed, leaving the capsule, with the zonular dialysis evident (Fig. 2A).

Mike Snyder It's daunting when a zonular dialysis occurs during phaco, as it not only exposes the hyaloid face, which can result in vitreous loss and potential retinal sequelae, but also it can increase the chance of posterior displacement of nuclear fragments, a situation which most anterior segment surgeons loathe.

Most of the audience chose to stabilize the capsular equator. Most chose a solid restraint to the equator (some by a CTR; others by hooks), and a smaller subgroup chose to use an OVD to support the internal aspect of the capsular bag. It would be my hope that those choosing this approach would select a highly dispersive OVD. The choice to bring the remaining nucleus into the anterior chamber, selected by 19.4%, actually increases the risk of nuclear fragment loss into the vitreous cavity when compared to in-the-bag phaco in the setting of zonular dialysis. This approach does, however, minimize the risk of damage to the posterior capsule.

Conversion to a manual ECCE was the least common choice. This may reflect fading of the skills required for ECCE among the younger population of ophthalmologists.

CASE 2 CONCLUSION: The remaining nucleus was removed without a CTR or capsule retractors, and an anterior vitrectomy was performed. A large 5 clock-hour zonular dialysis was present superiorly and nasally.

Q2.2 How would you fixate an IOL with this large zonular dialysis?

Scleral suture a modified CTR (e.g., Cionni/Malyugin) plus an intracapsular posterior chamber (PC) IOL 34.6%
Scleral suture a capsular segment (e.g., Ahmed) plus an intracapsular PC IOL 20.0%
Implant a three-piece PC IOL in the sulcus 29.2%
Place a PC IOL in the sulcus and iris, or scleral suture fixation of the haptics 4.3%
Use an anterior chamber (AC) or Artisan aphakia iris-claw IOL 11.9%

Mike Snyder In the setting of a zonular dialysis, IOL fixation can be a challenge. It is telling that there was a wide diversity of opinion among the audience members on how to best manage an IOL in this case, demonstrating that there are many reasonable alternatives.

More than half of the respondents would have chosen to place the IOL in the capsular bag and to fixate the bag to the sclera using some sort of capsular fixation device. A significant percentage expressed a preference for a CTR with an integral fixation element (either a Cionni ring or a Malyugin CTR). This would have been my personal preference as well, due to the greater structural stability of the single fixation-ring unit (versus independent fixation elements). Some preferred an Ahmed segment. While this is easier to place, it does not fully expand the bag; nonetheless, it is a fully reasonable alternative for fixation of the bag to the eye wall.

Nearly 30% of all respondents chose to place a three-piece PC IOL passively in the sulcus. While this is a reasonable option, there is a chance that the IOL will eventually find its way to the zonular dialysis and subluxate, perhaps requiring a repositioning surgery. The respondents might have selected this option for a variety of reasons, including the availability (or lack thereof) of capsular fixation devices, a low percentage of experience with subluxations in similar settings, or relative familiarity with fixation alternatives. Another strategy —not included as a response option—would involve placing

William B. Trattler, MD

a three-piece PC IOL in the sulcus, then capturing the optic through the capsulorrhexis into the bag. This hybrid alternative would provide some IOL fixation without requiring transscleral or iris fixation sutures, although it might have been hard to capture the optic with such a large dialysis. The surgeon did choose passive sulcus fixation in this case, which did lead to a sustained favorable outcome.

Finally, it was interesting that nearly 12% of individuals would have chosen an AC IOL, as doing so would require significantly enlarging an existing clear corneal wound.

Case 3: Don't Cry for Me

Rosa Braga-Mele presented her case of a 63-year-old with a white and brunescent mature cataract. She aspirated cortex with a needle—but as she initiated the continuous curvilinear capsulorrhexis (CCC) under dispersive OVD, the patient coughed, and the anterior capsule split from one end to the other, creating an "Argentinian flag" sign.

Q3.1 What's your preference for anterior capsulotomy with a mature white cataract?

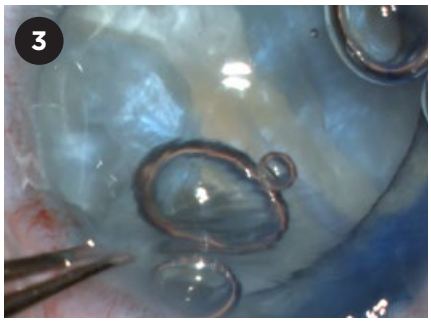
- Femto capsulotomy 16.2%
- Zepto capsulotomy 2.0%
- Manual CCC (after aspirating the cortex with a needle) 58.5%
- Manual CCC (without cortex aspiration) 21.7%
- Would refer this case 1.6%

Daniel Badoza In cases with an intumescent white cataract, my preferred technique for capsulotomy is manual CCC after aspiration of the cortex with needle. As it is important to keep the anterior chamber pressurized, when the main incision is made, the keratome should penetrate only 1 mm. Next, the chamber might be filled with a viscodispersive or viscoadaptive OVD. After the CCC is completed, the keratome is introduced completely through the initial incision in order to achieve the desired incision width. Manual CCC without cortex aspiration should be limited only to those white cataracts without an increased lens vault (noted on optical coherence tomography, ultrasound biomicroscopy, or slit-lamp exam), which is a preoperative sign of hypertension inside the bag. To date, there are few reports with Zepto capsulotomy, and there is no strong evidence that femto capsulotomy is safer than manual CCC for intumescent white cataracts.

Q3.2 What would you do now?

- Commence phaco 16.7%
- Convert to a can-opener capsulotomy, then start phaco 50.7%
- Prechop with the miLOOP, then perform phaco 4.6%
- Convert to a manual ECCE 27.7%
- Abort surgery and refer the patient 0.4%

Rosa Braga-Mele When the anterior capsule splits, as it did in this case, it is sometimes difficult to remain calm and proceed in an organized manner. In fact, the first instinct is to do the most straightforward thing . . . either abort the case and refer or convert to manual ECCE (as chosen by nearly 28% of the audience) if one does not feel comfortable proceeding with phaco.



CASE 3. *The anterior capsule split when the patient coughed.*

More than 50% of the audience would have converted to a can-opener capsulotomy and then commenced phaco. However, this could lead to more radial tears and issues with nuclear loss into the vitreous. I chose to begin phaco with the anterior capsule split as it was—but with a twist. I used a dispersive OVD throughout the case to help maintain the pressure in the eye and the structural integrity of the anterior chamber and the capsular bag, with the hope of minimizing the risk of the tear propagating posteriorly to the posterior capsule. I also removed the nucleus in its entirety from the capsular bag and used the iris as a scaffold, as I slowly phacoed the nucleus from the edge without breaking or chopping it into smaller pieces. (That way, if the bag was not intact, there would be less risk of pieces dropping posteriorly.) My most significant pearl for my colleagues is to go slow and never let the eye decompress. Maintaining a cool demeanor and a safe environment is key to getting a good outcome.

Case 4: My Bipolar Presentation

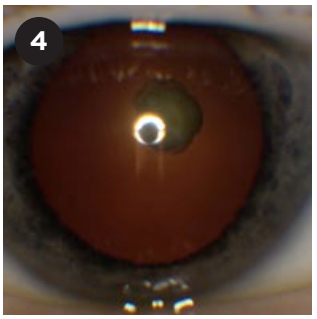
Kendall Donaldson presented her case of a posterior polar cataract. The femtosecond laser was used first to create the anterior capsulotomy and then to perform grid pattern nuclear fragmentation with a 500-µm safety zone. A large posterior capsular defect was noted nasally. The temporal subincisional heminucleus was still present.

Q4.1 What is your surgical preference for a posterior polar cataract?

- Femtosecond laser–assisted cataract surgery (FLACS) for both capsulotomy and fragmentation 12.4%
- FLACS for capsulotomy only 3.8%
- Manual phaco (I don't ever use FLACS) 70.0%
- Manual phaco (I otherwise use FLACS, but not here) 11.7%
- I refer these cases 2.1%

Bonnie Henderson I have found that not all posterior polar cataracts behave the same way. In some cases, the posterior capsule is intact but thinner and more fragile. In others, there is a frank defect in the capsule. Even in those cases with a defect, some openings are circular, with strong fibrotic borders

Rosa Braga-Mele, MD



CASE 4. *This posterior polar cataract case involved a large posterior capsular defect.*

that can often withstand the tugging/pulling associated with lens removal. In these cases, the defect does not extend into a tear.

However, it is prudent to prepare for every posterior polar cataract case as if a capsular tear can occur. I recommend avoiding hydrodissection and proceeding with hydrodelination to mobilize and remove the inner nuclear core before carefully removing the epinucleus and cortex. Using a dispersive OVD to "plug" the hole in the posterior capsule is also useful to keep the vitreous in a posterior position.

The management of a posterior polar cataract can be challenging because of this unpredictability of the posterior capsule. Because the use of a femtosecond laser creates air bubbles that can build up pressure in a closed eye, I agree with 81.7% of the audience that a manual approach in this case would have been better. Although some surgeons may argue that the use of the femtosecond laser can ensure a continuous anterior capsulotomy and successful lens fragmentation, the difficulty in managing a posterior polar cataract does not lie in these steps. Instead, the difficulty is removing the lens in the face of a capsular defect, which is not made safer using a laser.

Q4.2 How would you remove the remaining heminucleus in the presence of this large posterior capsular defect?

- Cautiously resume phaco in the bag 5.5%
- Attempt to use the I/A tip to aspirate the remaining nucleus 1.7%
- Elevate the nucleus into the anterior chamber, then perform phaco 50.0%
- Elevate the nucleus into the anterior chamber and phaco over an IOL scaffold 41.1%
- Convert to manual extraction of the nucleus 1.7%

Kendall Donaldson In the case of a posterior polar cataract, the lens is generally not very dense aside from the central posterior core, so the remainder of the lens should require very little phaco energy to remove in its entirety. In this case, the vitreous had not yet prolapsed, so dispersive OVD was used as a tool to prevent the vitreous from shifting forward. I turned to the audience's preferred strategy (the third choice), and I used a Drysdale spatula to gently lift the remaining lens material into the anterior chamber. Low bottle height, high vacuum, and full occlusion of the nuclear material with the phaco tip was maintained at all times. Despite my best efforts, vitreous prolapse did occur, and I had to do an anterior vitrectomy. Ideally, the vitrectomy should be done through the pars plana or through a new wound after suturing the primary wound with 10-0 nylon. I also like the idea of an IOL scaffold (the fourth option). I would still try to remove more of the lens material before placing the IOL, so as not to capture lens material in the eye. With so little of the capsular bag intact, reverse optic capture (ROC) would be difficult, especially if the capsulotomy is on the larger side (larger than the optic).

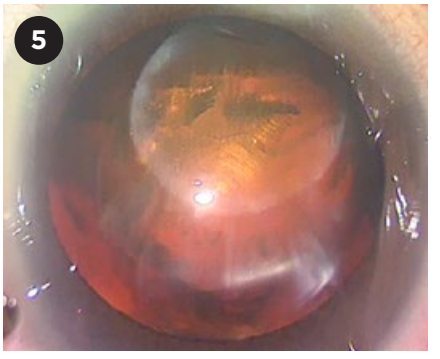
Case 5: Battle Royale: Femto Versus Nucleus

Soon-Phaik Chee's case involved an 80-year-old patient with an ultrabrunescent rock-hard cataract with a 5.9-mm lens thickness. The femtosecond laser was first used to successfully complete a 5.5-mm anterior capsulotomy. The patient moved during the femtosecond laser nuclear fragmentation, causing the laser firing to abort. When the patient was finally positioned beneath the operating microscope, one-half of the nucleus could be seen prolapsing through the pupil.

Q5.1 What would you do now that the lens is prolapsing into the anterior chamber?

- Phaco after repositing the nucleus into the bag 32.9%
- Phaco after prolapsing the nucleus into the anterior chamber 45.9%
- Manual ECCE (large incision) 12.0%
- Small-incision manual ECCE (e.g., with miLOOP) 7.1%
- Abort and refer 2.1%

Soon-Phaik Chee One pole of this thick brunescent nucleus prolapsed into the anterior chamber following excessive gas formation, lifting the partially fragmented nucleus against an incomplete femto capsulotomy and leading to an anterior capsular rip. This was certainly a challenging situation, and it is no surprise that 2.1% of respondents voted to abort surgery and refer the case on. The largest percentage of the audience voted to phaco after prolapsing the nucleus into the anterior chamber. Bearing in mind the nuclear density and thickness, this would have been technically difficult due to the limited space available in the anterior chamber for manipulating this huge rock, inevitably resulting in significant endothelial cell loss. The option to convert from phaco to large- or small-incision ECCE was the choice of almost 20% of attendees. This option avoids the risk of a dropped nucleus



CASE 5. *One pole of the nucleus prolapsed into the anterior chamber.*

Soon-Phaik Chee, MD; Kendall E. Donaldson, MD

and is perhaps associated with a smaller risk of posterior capsular rupture, but it requires a larger incision.

I decided to proceed with phaco after repositing the nucleus into the capsular bag, which was the choice of a third of the attendees. Faced with the unforeseen, I stained the capsule with capsular dye from the side port to visualize the capsulotomy. The nucleus was gently reposited into the capsular bag using the viscoelastic cannula, releasing the trapped gas bubbles from behind the tilted nucleus. After the anterior capsular rip was identified, phacoemulsification without hydrodissection was started with reduced parameters, using an in-situ chop technique. The lateral separation of nuclear fragments was performed at a location away from the anterior capsular rip to avoid extending the tear posteriorly. It was tedious and difficult to completely separate the fragments, despite the partial femto-fragmentation, as the nucleus was thick and leathery. Rotation of the nucleus was executed carefully about its central axis in order to minimize its lateral movement. The nucleus wobbled during the procedure, suggesting a lack of posterior support, but the fragments continued to swirl around normally.

Finally, an intact thin cushion of cortex covering the posterior capsule was bared. This defined layer was likely to be a result of the 500-µm PC femtosecond laser offset. The anterior chamber was maintained by injecting dispersive OVD before removing instruments from the eye. Coaxial irrigation and aspiration of cortical material was initiated, exposing a wide capsular rip that extended from the anterior capsular tear across the posterior capsule, leaving the anterior vitreous face intact.

CASE 5 CONCLUSION: After the prolapsed nucleus was displaced posteriorly, a radial anterior capsulotomy tear could be seen extending to the equator. The nucleus was manually chopped and removed with phaco—and at this point, the radial anterior capsular tear could be seen extending into a large tear across the entire posterior capsule. Cortex was removed without vitreous prolapse or any need to perform an anterior vitrectomy.

Q5.2 What IOL would you implant at this point?

- An iris-claw or AC IOL 5.9%
- A three-piece PC IOL in the sulcus (no suture) 84.4%
- An iris- or scleral-sutured three-piece PC IOL 7.5%
- Glued intrascleral haptic fixation (ISHF) of a PC IOL 0.6%
- Yamane ISHF of a PC IOL 1.7%

Edward Holland In the situation of an anterior capsular tear extending into the posterior capsule, the surgeon must assess the stability of the anterior capsule. If there is adequate anterior capsular support, a three-piece PC IOL in the sulcus is definitely the procedure of choice. This technique was far and away the one favored by the audience. With an adequate anterior capsule, there is no need for the more complex fixation procedures listed above.

If, however, the anterior and posterior capsular tears are extensive and the IOL needs fixation, then the surgeon should be equipped to perform additional steps to secure the IOL. The most common choice would be an iris- or scleral-sutured three-piece PC IOL, and that was the second choice favored by the audience. The sutured three-piece PC IOL is the favored fixation method utilized, and it has excellent results. Newer techniques, such as the glued ISHF and the Yamane ISHF, are innovative and avoid fixation sutures. However, most surgeons do not have experience with these methods.

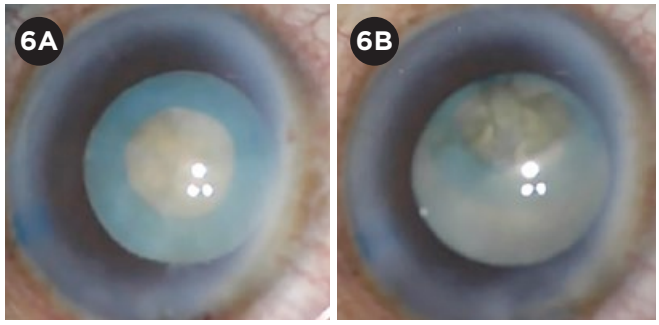
Case 6: I Could Use More Support

Sumitra Khandelwal presented a case of a 52-year-old uveitis patient with a unilateral white cataract. This eye had previously undergone two pars plana vitrectomies and had a history of cystoid macular edema (CME). After trypan blue staining, a small-diameter capsulorrhexis was completed. In the course of divide-and-conquer phaco, the capsular bag became increasingly mobile. After Dr. Khandelwal withdrew the phaco tip for inspection, the entire subincisional pole of the lens prolapsed into the anterior chamber due to severe zonulopathy.

Q6.1 Now that the subincisional lens has prolapsed into the anterior chamber because of severe zonulopathy, what would you do next?

- Reposit the lens posteriorly with OVD, then resume phaco 23.8%
- Insert a lens scaffold (e.g., IOL) and resume phaco 3.6%
- Convert to a manual ECCE (by extending the corneal incision) 33.9%
- Convert to a manual ECCE (via a separate new incision) 31.8%
- Abort the surgery and refer the patient 6.9%

Sumitra Khandelwal This was a tough situation because the whole capsular bag–IOL complex prolapsed into the anterior chamber, risking the lens falling to the back with typical approaches. Much of the audience response reflects individual comfort levels, as this is not an ideal case in which to try something new. I resumed phaco, taking care to prevent



CASE 6. *In this case of a unilateral white cataract (6A), the capsular bag–IOL complex prolapsed into the anterior chamber (6B).*

Sumitra S. Khandelwal, MD

the lens from falling posteriorly. The scaffold technique would only really work if there was a posterior capsule or the surgeon chose scleral fixation, but likely this is not the best choice at this time. Conversion to an ECCE—or, in this case, an intracapsular cataract extraction (ICCE)—would likely be the best option for anyone who is unfamiliar with using capsule retractors. The downside would be a large incision and the risk of retinal detachment; however, the risk of detachment reported with ICCE is based on normal zonules requiring cryotherapy to break them and vitreous prolapse. This patient is postvitrectomy, so the latter is not an issue.

CASE 6 CONCLUSION: After Dr. Khandelwal reposited the capsular bag posteriorly with OVD, she supported the capsular bag with nylon iris retractors (capsule retractors were not available). However, the capsulorrhexis tore when the phaco tip was inserted. She successfully removed the nucleus without any posterior capsular rupture.

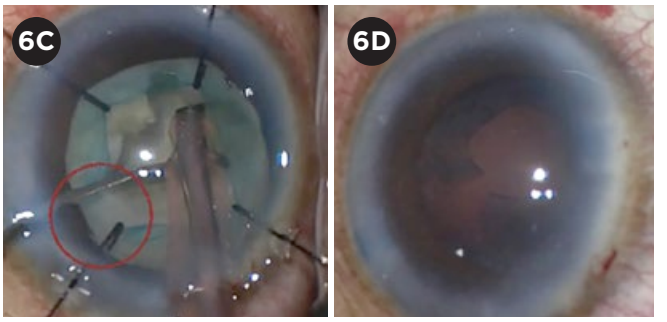
Q6.2 What IOL fixation method would you use with a radially torn anterior capsule, a possible posterior capsular tear, and severe zonulopathy in this post-vitrectomized eye with a history of CME?

- An iris-claw or AC IOL..... 16.2%
- A three-piece PC IOL in the sulcus (no suture)..50.0%
- Iris- or scleral-sutured PC IOL..... 20.3%
- Glued ISHF of a PC IOL.....4.9%
- Yamane ISHF of a PC IOL 8.6%

Rob Weinstock The audience response to this question is very telling. Half the respondents felt comfortable placing a three-piece lens in the sulcus space despite the zonular instability and the tear in the anterior and posterior capsules. This is a bit surprising since the audience clearly saw at least half of the capsule tilted up and floating in the anterior chamber at the start of the case. The fact that the inferior zonules seem to be intact may be the reason these surgeons felt confident that a lens would be stable in the sulcus. My concern would be that the entire capsule and zonules are not supportive enough, and the IOL could decenter or even dislocate into the vitreous with time.

The other half of respondents chose to do some type of more stable IOL fixation, which would be my preference as well. Surprisingly, most chose either an AC IOL or an iris- or scleral-sutured IOL, while only 9% chose the Yamane technique. This may represent the fact that many surgeons have not been trained or are not comfortable yet with this elegant but novel IOL fixation method and, therefore, prefer a more traditional and practiced technique.

Sumitra Khandelwal In a case with greater than 4 clock-hours of poor zonules, the surgeon can utilize CTRs and segments, but we are unable to do that in the case of an anterior capsular tear. It's best for the surgeon to do what is most comfortable for him or her. It is surprising that 50% of the audience picked a PC IOL in the sulcus without a suture. Given the combination of diffuse zonules and the anterior



CASE 6. *Although the capsular bag was supported by iris retractors (6C), the capsulorrhexis tore when the phaco tip was inserted (6D).*

capsular tear, the sulcus is not a stable place for the IOL. The IOL will likely fall to the vitreous, if not during surgery then shortly postoperatively. If the surgeon is not comfortable with iris or scleral fixation, then an AC IOL or aphakia is the best option, as a posterior dislocation of the IOL will require retinal surgery and involve possible additional complications.

An iris- or a scleral-fixated lens could be an excellent option. Again, the choice of technique depends on the surgeon's comfort level. In general, I avoid iris fixation in the setting of history of vitrectomy because of the risk of pseudophacodonesis. However, in this case, there is some posterior capsular support. I also avoid it in cases with a history of uveitis because iritis often occurs, so perhaps scleral fixation is best. Surgeons can choose the option that is best in their hands.

A well-sized AC IOL is always a great choice; several studies have found good outcomes in complex cases, and even in eyes with uveitis. The relatively young age of the patient is concerning for long-term complications, but an endothelial cell count and an IOL exchange can always be performed later. Again, scleral fixation is likely the best option assuming the surgeon is comfortable with this technique, which is why we made that choice.

Case 7: Getting Shot Down

In this case presented by Daniel Terveen, Tom Oetting started what he thought would be a routine cataract surgery. The patient had been treated for age-related macular degeneration (AMD) with a series of intravitreal injections over several years. After an uneventful capsulorrhexis and hydrodissection of the lens, the nucleus became excessively mobile during phaco. As the nucleus was rotated, it started to descend posteriorly through a posterior capsular defect (Fig. 7).

Q7.1 What would you do next once the nucleus starts to sink posteriorly?

- Try posterior assisted levitation (PAL) to levitate it anteriorly..... 26.9%
- Urgently summon a vitreoretinal colleague to the OR.....18.0%
- Leave the nucleus and leave the eye aphakic.....8.2%

Sumitra S. Khandelwal, MD

Leave the nucleus and implant a three-piece PC IOL in the sulcus 40.1%
Leave the nucleus and implant a one-piece PC IOL in the sulcus using ROC..... 6.8%

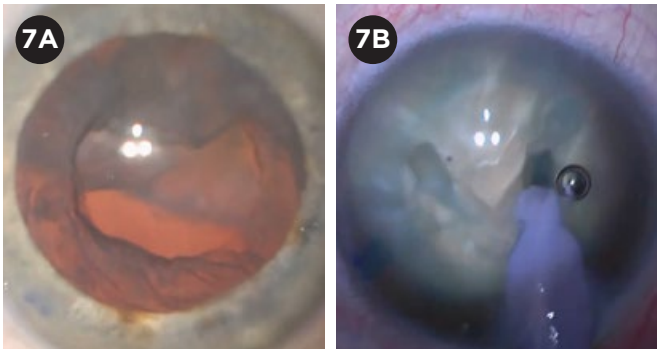
Roger Zaldivar These cases represent a real challenge to a surgeon's ego, and the most difficult decision involves setting limits in order to avoid compromising the patient's safety. Once the nucleus starts to sink posteriorly, we like to keep things simple by removing residual cortical material, performing an anterior vitrectomy, and placing a three-piece PC IOL in the sulcus. Performing a pars plana vitrectomy to remove the fallen nucleus can take place in a second attempt, usually two days later.

Daniel Terveen Dr. Oetting did as the audience suggested by removing residual cortical material and performing an anterior vitrectomy aided by preservative-free triamcinolone. We placed an MA50 IOL (Alcon) initially in the sulcus and then positioned just the optic into the bag, which is a very stable configuration. A few days later the patient had a pars plana vitrectomy to remove the fallen nucleus.[1]

Q7.2 What do you think was the most likely cause of the early posterior capsular tear in this case?

Capsular block with hydrodissection 40.1%
Chopping too aggressively 17.0%
Rotating the nucleus too aggressively 17.4%
Postocclusion surge 4.3%
Occult posterior capsular defect 21.3%

Daniel Terveen Several interesting studies have reported that patients who have a history of intravitreal injections are two to three times more likely to experience posterior capsular rupture during cataract surgery. These studies suggest that iatrogenic trauma from the injections may have increased both the risk of loss of lens material into the posterior chamber and the risk of a capsular tear. A V-groove nucleofractis technique can be used when you do not want to do hydrodissection or lens rotation, as in cases of posterior polar cataract, or when you suspect posterior capsular injury—e.g., after pars plana vitrectomy[2] or, as in this case, following intravitreal injections (Fig. 7B).



CASE 7. *(7A) The lens fell early in the case. (7B) A V-groove nucleofractis technique was used to eliminate the need for hydrodissection.*

1 www.facebook.com/cataract.surgery/videos/10154988848396868/. Accessed Dec. 5, 2018.
2 webeye.ophth.uiowa.edu/eyeforum/cases/239-post-vit-cataract-surgery.htm. Accessed Dec. 5, 2018.

Case 8: Nothing Wrong With LRIs

Elizabeth Yeu's case involved a 72-year-old patient with axial myopia and 2.5 D of with-the-rule astigmatism. A toric IOL was planned; after a femtosecond laser capsulotomy and nuclear fragmentation, the nucleus was removed. However, during cortical cleanup, a large posterior capsular rent was created by the I/A tip. Vitreous prolapse was avoided.

Q8.1 What IOL would you implant in this case?

A three-piece spherical PC IOL in the sulcus (manage astigmatism with LASIK) 39.0%
A three-piece spherical PC IOL, plus astigmatic keratotomy (AK)..... 30.5%
Place a one-piece toric IOL in the sulcus with CCC/optic capture..... 12.5%
Place a one-piece toric IOL in the bag with ROC 17.4%
Leave aphakic and refer the patient..... 0.7%

Eric Donnenfeld This patient has 2.5 D of preoperative astigmatism and is a candidate for a toric IOL—and now has a large posterior capsular tear. Although there are several alternatives to consider for managing this complication, the overriding goal should be to choose the procedure that provides the safest outcome for the patient, and that procedure is very surgeon-dependent. Because all toric IOLs in the United States require placement in the capsular bag, if the surgeon feels comfortable with this approach, a toric IOL with primary or reverse optic capture can be considered. It does, however, entail some risk.

The audience overwhelmingly suggested a three-piece PC IOL in the sulcus followed by either LASIK or AK. I agree that this is the safest approach. I would perform LASIK, which is more precise and is less likely to result in irregular astigmatism.

Elizabeth Yeu My video demonstrated the option of carefully aligning the toric IOL that is tucked into the capsular bag in a controlled posterior capsular rent with ROC (in which the haptics are in the capsular bag and the optic is prolapsed anteriorly to sit in front of the anterior capsulotomy). Understandably, however, this is not the choice of the audience majority.

Anecdotally, I have found this to work nicely, but I will consider it only in axial myopes who have a well-centered approximately 5-mm capsulotomy without any complications that would necessitate further surgery (i.e., lens fragment in vitreous). The IOL should be calculated for sulcus placement if ROC is performed.

I do agree that a conservative approach of a three-piece IOL injected into the sulcus, ideally combined with optic

Thomas A. Oetting, MD

capture to prevent any iris chafing and recurrent iritis, is an excellent approach any time the posterior capsule is compromised. The corneal astigmatism can be reduced intraoperatively with AK or postoperatively with excimer laser, AK, or spectacles. Modern one-piece IOLs should never be placed into the sulcus, as a form of uveitis-glaucoma-hyphema (UGH) syndrome will result from the chafing of the haptics themselves against the posterior iris, even if the optic is captured.

Case 9: Shifting Fortunes

Bill Wiley's patient was an ophthalmologist with pseudoexfoliation, a small pupil, and primary open-angle glaucoma (POAG). After Dr. Wiley inserted a Malyugin ring, the capsulorrhexis and hydrodissection were completed. Zonulopathy was noted during divide-and-conquer phaco, and Dr. Wiley paused to insert capsule retractors. The cortex was successfully removed despite severe circumferential zonulopathy, but an anterior capsular tear was noted in the region of one of the capsule retractors.

Q9.1 At this point, what IOL fixation method would you employ?

- Place a three-piece PC IOL in the sulcus 55.2%
- Place a one-piece PC IOL in the bag 26.9%
- Scleral fixate the haptics of a three-piece PC IOL 11.1%
- Iris suture the haptics of a three-piece PC IOL 3.7%
- Use an AC or iris-claw IOL 3.1%

Bill Wiley During the extraction of the complicated cataract, an anterior capsular rent developed, which further complicated the surgery. I believe the rent was caused by the capsule support hook, which might have caused undue stress on the anterior capsule during the insertion of the I/A tip or the phase fusion. (It's important to note that the tension of the hooks should be adjusted after the anterior chamber is manually filled with balanced salt solution [BSS].)

This anterior capsular rent in a bag with loose zonules presented me with a critical decision: Where should the lens be placed? The audience chose a three-piece IOL in the sulcus. In general, I believe this is a good decision, and it is ultimately what I chose to do. However, in addition to placing the lens in the sulcus, I decided to further support the capsule-bag complex by placing a CTR in the bag. This maneuver can cause stress on the bag, and it introduces the risk of further expanding the anterior capsular tear. To help prevent that, I used a suture in the CTR to help with insertion and to give an option to remove the ring if I felt that it was not providing support.

After I inserted the CTR into the bag, I noted that the anterior capsular tear was stable and had not extended, and the ring seemed to give the needed support. At that point I considered placing a lens in the now-stabilized bag, but I opted for sulcus placement instead. At the conclusion of the case, the lens appeared secure; it was centered and stable in the sulcus on top of the bag and CTR. Unfortunately, the next day, the lens was subluxated inferiorly even though the bag appeared stable. I believe the lens slipped past an area of absent zonules, resulting in the malpositioned optic.

CASE 9 CONCLUSION: After Dr. Wiley implanted a CTR in the bag, he implanted a three-piece PC IOL in the sulcus without any supplemental haptic suture or scleral fixation. On postoperative day 1, however, there was a major "sunset" inferior subluxation of the PC IOL.

Q9.2 How would you manage this IOL, which is already subluxated one day after surgery?

- Iris suture the existing PC IOL 18.2%
- Scleral fixate the existing PC IOL 40.2%
- Perform an IOL exchange with an AC or iris-claw IOL 7.4%
- Exchange for an Akreos IOL (Bausch + Lomb) with Gore-Tex scleral fixation 4.4%
- Refer the patient 29.7%

Alan Crandall Since the CTR is still in the eye, that device should be removed. Looking at the possibilities, the first (iris fixation using the IOL) would be feasible, as the retina associate is doing a vitrectomy.

I prefer not to use iris fixation, as there can be significant pseudophacodonesis (which can lead to UGH and recurrent inflammation), but if an anterior vitrectomy is all that is needed, it would be a reasonable choice.

With regard to an IOL exchange with an AC IOL or the iris-claw IOL, I prefer not to use AC IOLs in patients this young because of potential downstream problems (glaucoma, peripheral anterior synechiae, and/or ovalization of iris). The iris-claw lens would be a reasonable choice; however, it is not yet FDA approved. As for an IOL exchange with the Akreos, using four-point scleral fixation with Gore-Tex sutures: This can be an elegant procedure, and it is one I have used and like. My one caveat is that the lens is made of a hydrophilic acrylic material. Some of these complicated eyes may need a DSAEK procedure—and the air bubble could cause the anterior IOL surface to opacify. (Bausch + Lomb is planning to develop a version with a hydrophobic acrylic material, which would not opacify with air.)

Finally, the option of scleral fixation with the existing lens would be my choice in this setting. One could use the Yamane technique or any version of a glued IOL.[1-3]

Bill Wiley Nearly one-third of the audience recommended referral. I took this path, and I referred the patient to a retina specialist. My colleague performed a vitrectomy with a lens exchange, using an Akreos IOL (Bausch + Lomb), which allowed for four-point fixation with Gore-Tex sutures. This created a very stable fixation and—because of the patient's underlying POAG—was preferable to the choice of iris fixation or an AC IOL.

1 Yamane S et al. *Ophthalmology.* 2017;124(8):1136-1142.

2 Gabor SC, Pavilidis MM. *J Cataract Refract Surg.* 2007;33(11):1851-1854.

3 Agarwal A et al. *J Cataract Refract Surg.* 2008;34(9):1433-1438.

Case 10: When Routine Becomes Not-so-Routine

Kerry Solomon presented his case of a 29-year-old patient who had been continuously unhappy with her uncorrected near vision following previous implantation of a distance monofocal acrylic IOL in her right eye. Both eyes were very blurry with 20/70 best-corrected visual acuity (BCVA) in her right eye due to a secondary membrane and 20/50 BCVA in her left eye (due to cataract). She wanted to be spectacle independent, if possible.

Q10.1 What would you recommend for this patient?

- YAG the right eye, then implant a monofocal IOL (mini or full monovision) in the left eye..... 36.5%
- YAG the right eye, then implant an extended depth of focus (EDOF) or monofocal IOL in the left eye 23.6%
- Implant an EDOF or a monofocal IOL in the left eye, then address the right eye..... 22.4%
- Implant a monofocal IOL (mini or full monovision) in the left eye, then address the right eye..... 5.7%
- Exchange the monofocal IOL in the right eye for an EDOF or a monofocal IOL in that eye..... 8.7%
- Refer this patient elsewhere 3.0%

Thomas Kohnen Young adult cataract patients have often been excluded from receiving multifocal IOLs. However, these patients can now benefit from new IOL technology and modern IOL power estimations, as outcomes are now so much better. As this patient is unhappy with the near visual acuity after monofocal IOL implantation, this should be best addressed with an IOL exchange or IOL addition (add-on technology).

The question of which eye should be treated first and which IOL should be chosen is not an easy one to answer. If we assume the right eye is the dominant one, one option would be to perform an exchange with an EDOF IOL in the right eye and a trifocal IOL for near vision in the left eye. The second option could be to use panfocal (tri-/quadrifocal) IOLs in both eyes. With the progress we have made over the last five years with these IOLs, I would feel comfortable exchanging the monofocal IOL for a tri-/quadrifocal IOL. The secondary cataract can be addressed intraoperatively with a posterior capsular opening, which would provide the patient with a clear view directly after the intervention. However, the latter treatment, when performed with an Nd:YAG laser, would enable an easier IOL exchange in the future.

A third option would be to implant a trifocal add-on IOL, which leaves the monofocal IOL in place. In addition, the procedure is reversible. Posterior capsular opacification in this case can be treated later with a Nd:YAG laser. If the patient is happy with the outcome of the right eye, the left eye could be treated immediately after with a tri-/quadrifocal IOL. Overall, in our experience, patients who have received these IOLs are happier with near visual acuity than are those who have received EDOF IOLs with a very similar optical phenomena effect. As a result, I prefer tri-/quadrifocal IOLs for those patients who really want to be spectacle independent.

My final thought is on IOL calculation. As we know the outcome of the first eye, we would take the IOL power of the right eye implant into consideration in case of an IOL exchange. Add-on IOL power calculation is based on the postoperative refractive outcome; for the second eye, we would choose one of the modern IOL calculation formulas, such as Barrett Universal II or Hill-RBF.

CASE 10 CONCLUSION: Dr. Solomon did cataract surgery first in the left eye and implanted an EDOF IOL. The patient was extremely happy with the uncorrected vision and requested that the monofocal IOL in her right eye be explanted and exchanged for an EDOF IOL. She still wanted better uncorrected near vision, and Dr. Solomon planned an IOL exchange with a multifocal IOL. The single-piece acrylic IOL was dissected free from the capsular bag and then was bisected with an IOL cutter prior to removal. As the posterior capsule was vacuumed with the I/A tip, a large posterior capsular tear was discovered.

Q10.2 What IOL would you implant, given the presence of this large posterior capsular tear?

- Place a one-piece multifocal IOL in the bag 8.5%
- Place a one-piece multifocal IOL using ROC 10.5%
- Place a three-piece multifocal IOL in the sulcus with CCC/optic capture 50.8%
- Place a three-piece monofocal IOL in the sulcus 29.8%
- Abort the surgery and refer the patient 0.4%

Kerry Solomon This 29-year-old woman with posterior subcapsular cataracts had a hyperopic outcome after having a monofocal IOL implanted three years earlier in her first eye. She was interested in spectacle independence for both distance and near vision, and she had not tolerated monovision in the past. In addition to her BCVA, she had visually significant posterior capsule opacification (PCO) in her previously operated eye and a posterior subcapsular cataract in her fellow eye. She underwent uneventful cataract surgery with an EDOF IOL in the fellow eye. While her distance vision was excellent (20/20), she still wanted better near vision. Subsequently, I performed an IOL exchange of her single-piece acrylic IOL—and discovered an open capsule.

At this point, most of the attendees (51%) chose a three-piece multifocal IOL for sulcus placement and CCC optic capture. This is a very reasonable response, and this strategy would achieve the patient's goal of improved reading vision with a stronger reading add in a multifocal compared to an EDOF lens. The next largest response (30%) was for a monofocal IOL placed in the sulcus. While this is also a reasonable response, the patient would likely need to continue to use reading glasses. If she were older, this might not be an issue, but at age 29, this would likely be of greater concern. Finally, 19% of attendees would choose a single-piece multifocal.

I chose a single-piece multifocal IOL with ROC. Although the lens centered very well in the capsule without optic capture, capturing the optic may provide a little more security in the short term for centration. The patient has been and will need to be followed for pigment dispersion. To date (eight months postoperatively), none has been detected.

Case 11: Why Don't You Stay?

In Rich Hoffman's case, following routine surgery, the intracapsular single-piece acrylic monofocal IOL was discovered to be decentered on postoperative day 1.

Q11.1 What would you do for this asymptomatic patient at this point?

- No intervention unless or until the patient becomes symptomatic....65.4%
- Try a miotic to see whether the edge is still exposed....6.3%
- Return to the OR to surgically reposition the IOL....20.3%
- Perform an IOL exchange with a three-piece PC IOL in either the bag or the sulcus....7.7%
- Refer the patient....0.3%

John Hovanesian As this implant decentration was not discovered until the day after surgery, it is reasonable to wait to assess the patient's symptoms before deciding on further surgical steps, as 65% of the audience members recommended. However, the significant degree of decentration in this case suggested that the patient would experience symptoms, which did indeed occur. Simply returning to the OR to "reposition" the implant, as suggested by 20% of the audience, is not likely to be a viable option; a single-piece implant with significant decentration usually signals either a peripherally torn capsule with haptic extrusion into the vitreous or a damaged haptic. In this case, with a damaged haptic, the only viable option was to replace the lens.

CASE 11 CONCLUSION: The patient was promptly brought back to the OR to surgically reposition the IOL. However, each time the IOL optic was manually centered, it kept migrating within the capsular bag to the same decentered position that it started in.

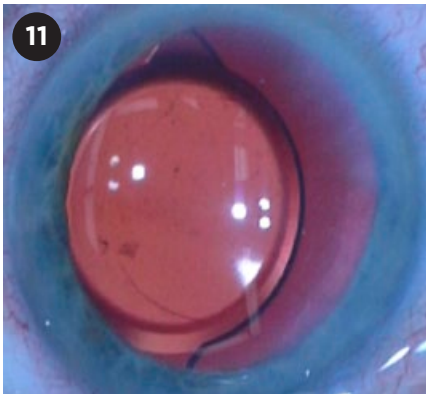
Q11.2 What would you do next?

- Leave it alone....18.1%
- Insert a CTR....21.3%
- Fixate it with ROC through the CCC....47.7%
- Exchange it for a three-piece PC IOL in the bag..4.2%
- Exchange it for a three-piece PC IOL in the sulcus....8.7%

Rich Hoffman This single-piece IOL would not center. After several attempts at simple recentration with a Sinskey hook, I decided that there was probably something abnormal about the capsular bag equator that was causing the decentration. At this point, I decided to rotate the IOL 90 degrees, thinking that placing the haptics in a new location within the bag should eliminate the tendency of the IOL to drift nasally. To my surprise, half of one of the haptics was missing, and this was the cause for the perpetual decentration.

Before I discovered the missing haptic, "leaving the IOL alone" was an option, but it's always difficult leaving a lens in the eye in a suboptimal position. Most of the audience thought that centering and fixating the IOL with ROC was the best choice—and, in general, I think this is a good option other than the small refractive change and eventual onset of PCO. Once the damaged haptic was discovered, I elected to remove it and replace it with a three-piece IOL in the bag. Another single-piece IOL could also have been placed in the bag.

Whenever possible, I believe it is best to try to determine the cause of the decentration. It can result from occult vitreous prolapse, a kinked haptic, or, as in this case, a torn haptic. Once I discovered that the haptic was missing, it was very important to determine if the torn haptic fragment was still in the eye. The last video clip in this presentation demonstrated an old case of corneal decompensation that required a penetrating keratoplasty (before the days of DSAEK and DMEK) several months after a routine IOL exchange. Apparently, after bisecting the IOL to be exchanged, the surgeon left a small sliver of IOL in the eye, and this was ultimately responsible for the endothelial decompensation. If my decentered IOL case had just been "left alone" and a haptic fragment remained in the eye, a catastrophic complication could have occurred. Luckily, the fragment was never injected into the eye; this was confirmed by reviewing the original video and documenting that the IOL was injected without the haptic fragment.



CASE 11. *Each time the IOL optic was manually centered, it migrated.*

Case 12: Fool Me Once . . .

Luis Izquierdo presented the case of a 58-year-old patient who has always worn contacts for a large degree of congenital anisometropia. Her goal was to have balanced refraction so that contacts would no longer be necessary. After cataract surgery in her more myopic left eye, she immediately complained that she was unable to see anything on postoperative day 1. A review of the chart revealed that she had received the wrong IOL power—one that would have been correct for her right eye. She required a low-power +4.0 D IOL for her left eye. Dr.

Richard S. Hoffman, MD

Izquierdo explained what had happened and took her back to the OR for an IOL exchange in that eye.

Q12.1 What is your preferred method for explanting a single-piece acrylic IOL for an IOL exchange?

- Bisect the lens with an IOL cutter 49.5%
- Cut 90% across the IOL to leave it hinged, and remove it as one piece 24.8%
- Use the "Pac-Man" method: Excise one quadrant with scissors, then rotate the IOL out 18.2%
- Use forceps to refold the acrylic IOL inside the eye 5.3%
- Use another method 2.3%

Natalie Afshari My preferred method of explanting a single-piece acrylic IOL is to cut the lens with an IOL cutter while supporting it with retinal forceps and then removing it. This could be performed by cutting through 90% of the IOL and then removing it as one piece through the incision (my technique of choice) or bisecting it fully into two pieces and removing each half separately. I agree with the majority of the audience. Folding the IOL inside the eye can be tricky, but it is a nice maneuver if the surgeon has experience with that technique, and it eliminates the risks that come with having a sharp instrument in the eye.

While no major studies have demonstrated the superiority of one technique over another—and there are no studies that directly assess endothelial cell loss with each technique—I feel that cutting the IOL into multiple small pieces or folding the IOL may induce more endothelial damage, as these strategies involve more maneuvering in the anterior chamber. (In these cases, the use of an OVD in the anterior chamber is crucial for endothelial cell protection.) Therefore, although removing the IOL as one piece or bisecting it may be more technically demanding and require the main incision to be enlarged, it could be more endothelial cell–friendly. In the presence of a deep enough anterior chamber, I would also consider inserting the new IOL before explanting the old one so that it could serve as a scaffold and protect the posterior capsule.

CASE 12 CONCLUSION: Dr. Izquierdo explanted the single-piece IOL by first refolding it inside the eye with forceps. When the low-power three-piece IOL was implanted into the capsular bag, the haptic was bent during injection. This resulted in poor intracapsular centration of the IOL, and a posterior capsular tear was also noted. Because of the unusual low power, no backup IOL was available.

Q12.2 At this point, what would you do?

- Leave the IOL in the bag 17.3%
- Leave the IOL but implant a CTR in the bag 3.8%
- Position the IOL in the sulcus and suture the haptic to the iris 17.3%
- Explant the IOL and leave the eye aphakic 43.8%
- Use another method 17.8%

Luis Izquierdo At this point, my options included leaving the IOL in place to see if some decentration could be tolerated—or explanting it and leaving the patient aphakic. With the low-powered IOL, the patient might have a tolerable amount of hyperopia, or a secondary IOL could be performed later after a replacement IOL was ordered. In this particular case, the patient was already very unhappy that she required a second surgery to exchange the wrong power IOL. As I hated to leave her with anything but a perfect result, I tried a novel approach. Even though the IOL had already unfolded within the eye, what if I could just replace the bent haptic and keep the same optic? I pulled the bent haptic out of the optic while the IOL was still in the eye. I then pulled a haptic off a brand-new IOL (one with a different power), and I was able to dock this into the vacant haptic tunnel within the intraocular optic. The docking was secure, and the IOL was then rotated into the capsular bag with beautiful centration!

Case 13: When Push Comes to Shove

Bob Osher presented a case in which, following routine phaco and cortical cleanup, the single-piece acrylic toric monofocal IOL was inserted upside down. The IOL was flipped within the eye to the proper orientation, but there was some posterior pressure during this maneuver. As the OVD was removed with the I/A tip, the globe became firm and the anterior chamber shallowed due to massive positive pressure. It was difficult to even remove the I/A tip due to flattening of the chamber despite continuing irrigation.

Q13.1 What would be your next step?

- Add more retentive OVD via the side port 33.2%
- Start intravenous (IV) mannitol, then add more OVD 29.8%
- Perform a vitreous tap (e.g., via the pars plana) 14.1%
- Insert IOL before resuming phaco 1%
- Abort the surgery in case of a suprachoroidal hemorrhage concern 22.0%

Bob Osher There are a number of useful steps to prevent unexpected chamber shallowing, especially if it is related to fluid misdirection, which occurs as the infusion during the phaco and I/A follow gravity through the zonules, thus expanding the contents of the vitreous cavity.

I always recommend hydrating the incision before introducing the I/A tip to remove the OVD. After the OVD has been removed and before I withdraw the phaco tip, I will place a cannula on a syringe filled with either BSS or Miochol-E (Bausch + Lomb) through the side port. Then I will kick off the continuous irrigation on my footswitch and simply observe the behavior of the chamber. If it remains deep, I will inject fluid and withdraw the I/A tip before hydrating the incision once again. However, if the lens moves forward and the chamber begins to collapse, I will inject fluid through the side port and keep the I/A tip in place

(allowing it to act like a "finger in the dike") as I depress the footswitch, thus activating irrigation to forcefully deepen the chamber. Mild positive pressure can be managed by injecting fluid with the left hand, withdrawing the I/A tip, and immediately hydrating the incision again. But if the positive pressure appears to be significant, the I/A tip should remain in the incision while the second cannula is exchanged for another syringe containing air.

The injection of air will deepen the chamber and allow the surgeon to withdraw the I/A tip and forcefully hydrate the main incision. The air bubble is both highly effective and cost-efficient. Air has mild endothelial toxicity, so it can be exchanged for either BSS or Miochol-E in small aliquots. But it is difficult to remove air from the corneal dome with a conventional cannula because the distortion of the incision results in loss of fluid. Therefore, I designed a curved cannula with Bausch + Lomb (I receive no royalties), which allows access to the corneal dome, where some of the air is aspirated. The cannula is withdrawn, and fluid is injected through the stab incision. This sequence is repeated several times until most or all the air is removed and replaced with fluid, thus maintaining a deep chamber.

A plurality of surgeons responded that they would add a retentive OVD; however, this does not solve the problem and still has to be removed. Another group recommended starting mannitol, but it takes too long to have any meaningful effect. Performing a vitreous tap will certainly work, although it is unnecessary. The last answer, aborting the case if a suprachoroidal hemorrhage is present, is reasonable, but the surgeon should be able to view the fundus, which can easily be accomplished with the Osher fundus lens (Ocular Instruments; again, no royalties). The urgent use of air is an excellent surgical technique for managing the shallow anterior chamber in fluid misdirection syndrome.

Q13.2 Have you ever experienced anterior chamber shallowing with aqueous misdirection syndrome?

- Never 7.3%
- Possibly, but I didn't recognize the etiology 26.4%
- Once or twice 35.3%
- Approximately three to five times 18.5%
- More than five times 12.5%

Marjan Farid Aqueous misdirection—or, more accurately, infusion misdirection—can occur during or at the end of a routine cataract surgery, and it is common enough that most busy cataract surgeons will experience this phenomenon a few times during the course of their career. The audience response supports this, in that approximately 65% of attendees stated that this has happened to them one or more times.

It is important to identify infusion misdirection when it occurs, ensure that the positive posterior pressure and firmness of the globe are not related to a suprachoroidal hemorrhage, and have a directed plan of action for its management. In mild cases, it is possible to reposit any prolapsing iris with a small amount of dense, cohesive OVD, put a suture through the wound, and recheck the pressure in an hour to make sure that it is normalizing. Dr. Osher demonstrated an excellent technique that involved placing an air bubble into the anterior chamber and securing the wound while allowing time for the pressure to normalize, the vitreous to contract, and the eye to stabilize in the postoperative area.

KELMAN LECTURE. *Robert J. Cionni, MD, was the 2018 Charles D. Kelman lecturer. He is shown here with Drs. Chang (left) and Weikert (right).*

In more severe instances, in which the globe is very dense and the anterior chamber is flat, it is quite reasonable to cut a small-port sclerotomy about 3 mm posterior to the limbus, create a vitrectomy port, and perform a small amount of posterior vitrectomy with no irrigation to break up the anterior hyaloid and deepen the anterior chamber. This requires only one to two seconds of vitrectomy to break the posterior pressure. Of course, it is very important to confirm that the vitrector is in the center of the eye and well visualized behind the IOL before starting the vitrectomy. This technique is very effective at breaking the infusion misdirection, softening the globe, and deepening the anterior chamber.

Case 14: Getting Squeezed

In Nicole Fram's case of a 72-year-old patient with Parkinson disease, the globe became very firm following uncomplicated femtosecond laser capsulotomy, phaco, and cortical cleanup. The anterior chamber was shallowing during I/A, so Dr. Fram switched to bimanual I/A for some remaining subincisional cortex, but the anterior chamber became increasingly shallow. The eye was firm, but the patient reported no pain, and there was no fundus shadow evident against the red reflex. A cohesive OVD was injected in order to implant the IOL, resulting in some partial prolapse of the subincisional iris.

Q14.1 What would you do next?

- Start IV mannitol and attempt IOL implantation 35.4%

MedMeeting Images, Todd Buchanan

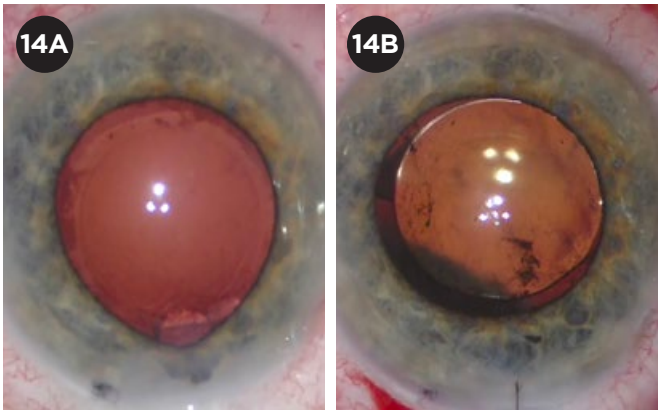
Perform a pars plana vitreous tap, then implant the IOL 37.5%
Stop surgery, have the patient rest for an hour, then attempt IOL insertion 16.5%
Reposit the iris and abort surgery, leaving the eye aphakic 9.1%
Leave the iris prolapsed and abort surgery, leaving the eye aphakic 1.4%

Dick Lindstrom Unexpected shallowing of the anterior chamber with significant positive posterior pressure occurs during cataract surgery in 1% to 2% of procedures. The differential diagnosis includes fluid misdirection syndrome (in which the infusion fluid passes through the zonules and pushes the posterior capsule and iris forward) and the more serious choroidal hemorrhage.

Fluid misdirection syndrome can result in the so-called rock-hard eye syndrome. This can be relieved by removing fluid from the vitreous, as recommended by 37.5% of the audience, using needle aspiration with a 23-gauge needle or pars plana vitreous cutter. I prefer a vitreous cutter but have had success with simple needle vitreous aspiration. It is important to rule out a choroidal hemorrhage before vitreous aspiration, as this maneuver can increase choroidal bleeding and possibly result in direct damage to the retina in the face of a choroidal detachment.

Patients with a choroidal hemorrhage usually have significant pain and loss of red reflex, and the hemorrhage can be seen with intraoperative visualization of the retina. I no longer personally use IV mannitol, but many in the audience have found this useful. It is usually necessary to soften the eye some to be able to reposit prolapsed iris, and a high-molecular-weight cohesive OVD can be helpful along with a miotic applied directly to the prolapsed iris. I never excise prolapsed iris in cataract surgery, but a small peripheral iridotomy can be helpful in some cases. In a difficult case, I do not hesitate to close the wound with sutures and abort the case. I can then check the intraocular pressure (IOP) and examine the patient with the slit lamp and indirect ophthalmoscope 60 minutes later.

In the case of fluid misdirection syndrome, the positive pressure almost always spontaneously resolves, and the patient can be returned to the OR later the same day or the next day for completion of the procedure. In the face of a choroidal hemorrhage, the diagnosis becomes clear, and the patient can be counseled and managed appropriately, usually in collaboration with a retina specialist.



CASE 14. *Unexpected shallowing of the anterior chamber (14A) was followed by a suprachoroidal hemorrhage (14B).*

CASE 14 CONCLUSION: A suprachoroidal hemorrhage was diagnosed postoperatively. It eventually resolved without further surgery with an excellent visual outcome (20/20) by one month. The patient was pleased and was eager to undergo surgery in the second eye.

Q14.2 The patient was happy with the first outcome and requested surgery on the second eye. What would you recommend?

Advise that he delay or avoid the second surgery due to high risk 2.8%
Refer him elsewhere for the second surgery 5.6%
Do phaco under topical anesthesia 24.8%
Do phaco with retrobulbar block or general anesthesia 60.4%
Do phaco (either the third or fourth choice), but with FLACS 6.4%

Nicole Fram Significant risk factors for suprachoroidal hemorrhage during cataract surgery include advanced age, hypertension, anticoagulation, glaucoma filtering procedures, penetrating keratoplasty, high myopia, large-incision surgery, and/or a Valsalva maneuver. The pathophysiological mechanism of suprachoroidal hemorrhage involves abrupt hypotony or trauma causing shearing of the short or long posterior ciliary blood arteries or vortex veins in the potential space between the deep sclera and the choroid.

The surgeon who is considering cataract surgery in a patient who has demonstrated the potential for a suprachoroidal hemorrhage in the first eye should take precautions in the second eye. Interestingly, this particular patient had no obvious risk factors. Nonetheless, I avoided all conceivable triggers of IOP fluctuation that might cause hypotony pre-, peri-, and postoperatively. Preoperatively, general anesthesia with paralysis was administered to avoid any potential for squeezing intraoperatively. A retrobulbar block was excluded due to the potential for high and then low surrounding ocular pressure. In addition, FLACS was excluded to avoid any potential for abrupt IOP fluctuations during suction release. Intraoperatively, careful attention was made to ensure that the anterior chamber was stable throughout the procedure by filling with BSS or viscoelastic each time an instrument was removed. This allowed for minimal IOP fluctuation and maximum stability with a normotensive IOP at the conclusion of the case. Postoperatively, special precautions were taken to avoid excessive coughing or Valsalva maneuvers while the patient was waking up from general anesthesia. Fortunately, the patient had an uneventful manual small-incision phacoemulsification and no complications.

If a suprachoroidal hemorrhage had occurred in the sec-

Nicole R. Fram, MD

ond eye and the patient had classic signs of pain and anterior chamber shallowing with a decreased red reflex, the best course of action would have been to close the eye, evaluate the patient postoperatively with a retina colleague to assess the extent of the hemorrhage, and maintain normotensive IOP control to tamponade the hemorrhage. Mannitol or acetazolamide should be given only in the setting of high postoperative IOP, as hypotony is undesirable in the immediate management of suprachoroidal hemorrhages.

Case 15: My Turn to Turn Red

Kevin Miller's case involved an 85-year-old patient with bilateral ReSTOR multifocal IOLs and a trabeculectomy in the left eye. The bag-IOL complex in the left eye became dislocated following a car accident. There was a history of pseudoexfoliation, and no CTR was implanted.

Q15.1 How would you address this late bag–multifocal IOL dislocation?

- IOL exchange with a scleral-fixated three-piece multifocal ReSTOR 23.9%
- IOL exchange with an iris- or a scleral-sutured monofocal PC IOL 23.5%
- IOL exchange with ISHF monofocal PC IOL (glued or Yamane) 18.2%
- IOL exchange with an AC or iris-claw IOL 13.0%
- Refer this patient 21.5%

Kevin Miller It's interesting to note that there was absolutely no audience consensus on the best way to proceed with this bag–multifocal IOL dislocation. Achieving perfect pupil centration when securing a lens to the sclera is difficult. If the entire central ring of a diffractive optic is not completely within the pupil, quality of vision suffers. About a fifth of respondents would refer the patient, which is always a reasonable choice. There was an almost even split between iris or scleral suture fixation of a monofocal lens and intrascleral haptic fixation. Both of these approaches would normally place the patient at higher risk of bleeding than the approach I took, which was to exchange the ReSTOR for an AC IOL. I have found that AC IOL implantation is quick and easy and, if sized appropriately, safe for the corneal endothelium, especially in an older patient.

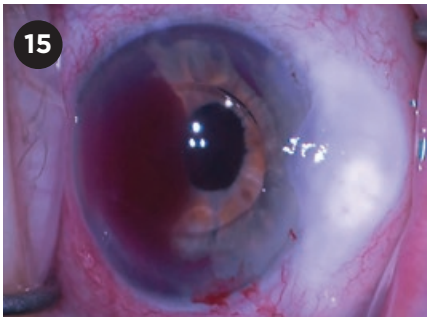
An additional benefit of AC lenses is that they do not dislocate. There are no sutures to break and no haptics to wiggle their way out of scleral tunnels. Unfortunately, the quest to perfectly position the haptics led to an inadvertent iris root tear and pesky intraoperative bleeding. Maybe the audience was right!

CASE 15 CONCLUSION: An IOL exchange was performed, during which the bag-IOL complex was explanted and an anterior limbal vitrectomy was performed. An AC IOL was implanted. While Dr. Miller was maneuvering the IOL away from the incision, significant bleeding commenced from the iris root adjacent to the rotated haptic.

Q15.2 Would you stop blood thinners prior to performing a vitrectomy and an IOL exchange?

- Would not stop any blood thinners 28.7%
- Aspirin would be okay, but I would stop warfarin 17.0%
- Would stop all blood thinners, including aspirin 33.6%
- Yes for an AC IOL; no for a PC IOL 9.8%
- Would refer these patients 10.9%

Sam Masket In general terms, I am comfortable leaving patients on anticoagulant therapy for routine cataract surgery, as this is, or should be, an avascular procedure. That said, surgery is not truly "routine" until it is completed. With warfarin therapy I prefer that the INR (international normalized ratio) be no higher than 3.2.



CASE 15. *An iris root hemorrhage occurred while an AC IOL was being dialed into final position.*

However, in consideration of the more involved surgery for IOL exchange, including multiple pars plana entries, vitrectomy, and potential scleral fixation of the IOL, my comfort zone changes. In this instance, I prefer that the patient discontinue use of all anticoagulant agents, as the procedure invades vascular tissue and there is a potential for hypotony early after surgery. The latter increases the risk for significant ocular hemorrhage.

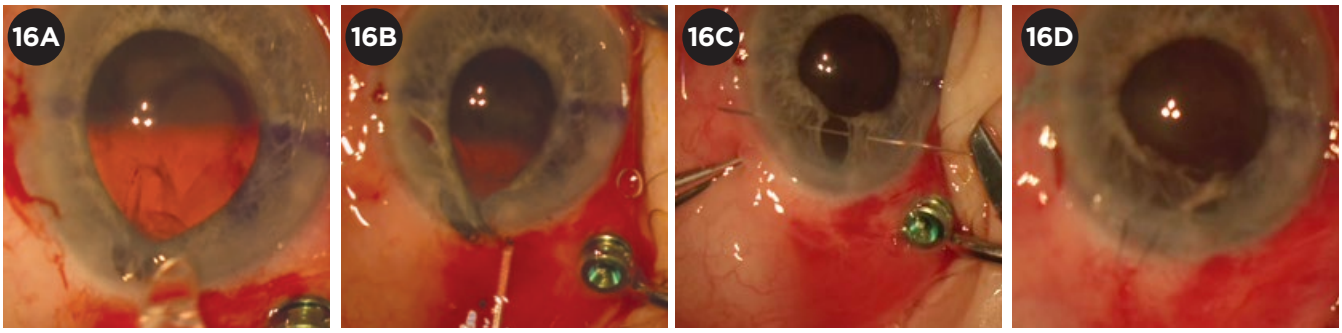
It is prudent to be in contact with the patient's general physician and coordinate plans for stopping and starting anticoagulants, as some cases will require use of heparin or similar agents in the perioperative period, while others may be safe off medication for prolonged periods, varying with the underlying indication for anticoagulant therapy.

Interestingly, the audience response showed no clear trend, as 29% would not—and 34% would—stop blood thinners for the complex case at hand.

Case 16: Who Knows What Evil Lurks?

Cathleen McCabe presented her case of a patient with Parkinson disease, hypertension, and a subluxated multifocal IOL. He was also on tamsulosin. During the IOL exchange, a bimanual pars plana anterior vitrectomy was performed with a pars plana infusion cannula. The IOL was successfully bisected and explanted. A three-piece monofocal IOL was to be inserted for ISHF using the Yamane technique; however, as the incision was manipulated with the IOL injector tip, the iris started to prolapse. A dark fundus shadow could be seen nasally.

Kevin M. Miller, MD



Q16.1 The anterior chamber formed, but there is a peripheral fundus shadow in this aphakic eye. What now?

- Proceed with a scleral-supported foldable PC IOL 1.9%
- Proceed with an iris-supported foldable PC IOL 1.5%
- Place an AC IOL to avoid transscleral needles 1.1%
- Stop; try to resume surgery after the patient rests in the recovery room 21.2%
- Abort the surgery and leave the patient aphakic 74.2%

Lihteh Wu The clinical picture of the dark fundus shadow and the iris prolapsing strongly suggests the presence of a suprachoroidal hemorrhage. Large fluctuations in IOP and fluid dynamics are some of the most important risk factors in the development of a suprachoroidal hemorrhage. I noticed that Dr. McCabe used a pars plana infusion, yet I did not see her check for verification of the position of the cannula inside the vitreous cavity. Inadvertent infusion into the suprachoroidal space could potentially occur.

I agree with the choice of the majority of the respondents to abort surgery and leave the patient aphakic. The most important step is to immediately close the wound to prevent the extrusion of intraocular contents. Once the wound is tightly closed, one can check the status of the posterior segment with an indirect ophthalmoscope. Don't yield to the temptation of trying to drain the suprachoroidal hemorrhage immediately, as the blood very often clots rather fast. Refer the patient to a vitreoretinal colleague, who should follow these patients closely with serial echography. Drainage of the hemorrhage should be planned when the clot liquefies. At times one needs to intervene sooner, as with kissing choroidals, the presence of a retinal detachment, or the combination of uncontrolled elevated IOP and pain.

During the drainage procedure, it's very important to place an anterior chamber infusion to control the IOP. Create a sclerotomy and let the blood drain. If there is difficulty in draining the blood because the clot has not liquefied enough, one may inject tissue plasminogen activator (tPA) into the suprachoroidal space. (Of note, the surgeon needs to let the tPA sit for 30 to 45 minutes before the clot liquefies.) Once the clot is drained enough, the surgeon can place a long (6 mm) infusion canula into the vitreous cavity and proceed with a pars plana vitrectomy and other additional vitreoretinal maneuvers, as needed.

CASE 16. *(16A) The first appearance of the shadow indicating a suprachoroidal hemorrhage during lens implantation. (16B) Iris incarceration in the incision after iris fixation of the three-piece IOL. (16C) Passing a 10-0 Prolene suture to close the iris defect. (16D) The appearance at the end of the surgery after closing the incision with 10-0 nylon sutures.*

CASE 16 CONCLUSION: Dr. McCabe elected to insert the three-piece monofocal IOL into the posterior chamber and to then trap the optic with a Miochol-E–constricted pupil for ISHF. This was successfully done for both haptics. In the course of the surgical manipulation, a defect occurred in the temporal subincisional iris, which was also partially prolapsed.

Q16.2 How would you address the iris defect and incarceration in the incision?

- Quit: Leave it incarcerated and don't suture the incision 2.1%
- Leave the iris incarcerated but suture the incision 4.3%
- Excise the prolapsed iris, then suture the incision 14.6%
- Reposit the iris without suturing the iris defect 54.6%
- Reposit the iris, then suture the iris defect 24.3%

Cathleen McCabe Iris prolapse during cataract surgery or IOL exchange can result from increased IOP posterior to the iris, as in this case of a suprachoroidal hemorrhage. Excessive viscoelastic in the eye, a floppy iris, and iris trauma with the vitrector were contributing factors and exacerbated the prolapse. In general, surgical management of iris prolapse consists of decompressing the anterior chamber through a paracentesis and then gently repositing the iris into the anterior chamber. A dispersive OVD can be used to, first, gently ease the tissue back into the eye with the cannula through a paracentesis. Next, push the tissue away from the incision by coating the anterior surface of the iris with a thin layer of viscoelastic, being careful not to overinflate the eye. In this case, the posterior pressure remained high due to the suprachoroidal hemorrhage, and this led to multiple episodes of iris prolapse.

The majority of the audience voted to reposit the iris without suturing the iris defect. I decided to attempt to suture the iris despite the looming suprachoroidal hemorrhage

Cathleen M. McCabe, MD

with increasing vitreous pressure. A 10-0 Prolene suture on a long straight needle was passed through the iris without difficulty, but the iris continued to prolapse repeatedly through the main incision. I continued to struggle with repositing the iris while trying to complete tying of the suture. The iris became increasingly traumatized during this procedure. Eventually, I was able to tie the suture, reposit the iris, and close the main incision with 10-0 nylon sutures. In retrospect, leaving the iris defect and coming back another day to repair the defect would have prevented additional trauma to the iris, resulting in a better ultimate surgical outcome.

Case 17: Haptic Misadventures

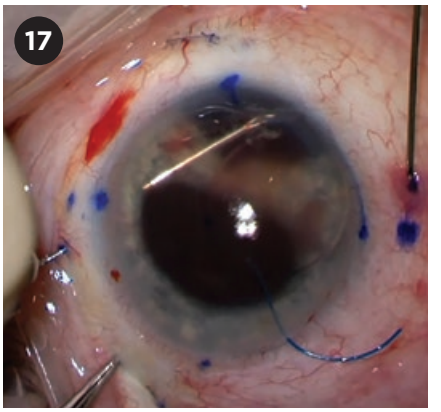
Terry Kim presented a case of a 67-year-old pseudophakic patient who had undergone a pseudophakic vitrectomy for floaters and, later, another vitrectomy and scleral buckle to repair a retinal detachment. The patient presented 10 years after the original cataract surgery with a dislocated single-piece monofocal IOL. The dislocated IOL was removed, and a three-piece acrylic monofocal IOL was implanted using the Yamane ISHF technique. While Dr. Kim attempted to dock the trailing haptic, the leading haptic and optic remained in the anterior chamber. With globe movement, it disinserted the iris with a 4 clock-hour nasal iridodialysis.

Q17.1 How would you proceed following this large iatrogenic iridodialysis?

- Complete the Yamane PC IOL fixation and leave the iris alone 11.1%
- Complete the Yamane PC IOL fixation, then repair the iridodialysis 82.4%
- Remove the IOL, repair the iridodialysis, and implant an AC IOL 4.1%
- Leave the eye aphakic and repair the iridodialysis 1.6%
- Leave the eye aphakic and leave the iris alone 0.8%

Terry Kim At this particular juncture of this complicated case (see Fig. 17), the majority of the audience voted to complete the Yamane PC IOL fixation and proceed with repairing the iridodialysis. I think this is a very reasonable option, and after PC IOL fixation, I proceeded to repair the iridodialysis using a 10-0 Prolene double-armed suture with a CTC-6 needle on each end.

First, I made a conjunctival peritomy in the same quadrant of the nasal iridodialysis and then used a Supersharp blade to create a 2-mm partial-thickness (~50% deep) scleral groove about 2 mm posterior and parallel to the limbus. Next, I grasped one edge of the torn iris with an MST forceps through a paracentesis incision and passed the first CTC-6 needle end of the 10-0 Prolene double-armed suture first through the main corneal incision and then through this first edge of the torn iris, exiting out one side of the scleral groove. I repeated this step by grasping the second edge of the torn iris with the second CTC-6 needle and exited through the opposite side of the scleral groove. Care should be taken to ensure that each needle of the 10-0 Prolene suture does not catch any portion of the corneal incision so that the suture can be pulled freely into the anterior chamber. Finally, both CTC-6 needles were carefully pulled simultaneously so that the 10-0 Prolene suture apposed the torn iris edge to the sclera, and then a 3-1-1 throw was used to tie down the suture, which was nicely buried within the scleral groove along with the knot. An irrigation port inserted by the retina service helped to clear the hemorrhage created by the iridodialysis.



CASE 17. *An inadvertent iridodialysis occurred during this Yamane ISHF case.*

The main teaching point of this Yamane ISHF case is that after docking the first haptic, the surgeon should place the TSK needle and the leading haptic and optic behind the iris in order to avoid an inadvertent iridodialysis, which can occur during globe movement while the trailing haptic is docked. Fortunately, this patient did extremely well and was very happy with his corrected VA of 20/40 (which was limited by his history of a retinal detachment). Anatomically, the procedure was successful with a round pupil, normal iris architecture, and a PC IOL with good position and centration.

Case 18: Another Longest Day

In Amar Agarwal's case, the patient had a small pupil and brunescent nucleus. A pupil expansion ring was placed. A radial anterior capsular tear developed, which then extended posteriorly during phaco. This only became apparent when the nucleus suddenly descended posteriorly.

Q18.1 What is your next step now that the nucleus has dropped posteriorly, but cortex is floating in the center of the pupil?

- Attempt the PAL technique 3.3%
- Attempt to remove cortex before it descends 17.0%
- Perform a limbal anterior vitrectomy 24.5%
- Perform a pars plana anterior vitrectomy 16.7%
- Call a vitreoretinal surgeon to the OR 38.6%

Doug Koch There is an interesting spread in the responses, but most agree on a fundamental concept: Don't reach into the vitreous cavity with the phaco probe to try to engage a dropped nuclear fragment; the standard protocol is to remove vitreous in the anterior segment and aspirate remaining cortex.

There has been much debate over the years as to whether

Terry Kim, MD

the vitrectomy should be performed via an anterior limbal incision or through a pars plana incision, using anterior irrigation in either approach.

In my view, either is acceptable as long as the surgeon avoids anterior vitreous traction by placing the vitrectomy probe posterior to the capsular plane to pull prolapsed vitreous posteriorly. And, of course, surgical sponge vitrectomies are strictly off limits.

If one is lucky enough to have the nuclear piece float up to the capsular plane, it can be captured by inserting an instrument or injecting an OVD behind it. As tempting as it might be, mechanical levitation alone, as with the phaco tip, carries the risk of creating vitreous traction. Once a fragment is brought into the anterior chamber, one helpful pearl is to insert the IOL into the anterior chamber beneath the nuclear fragment, creating a barrier to minimize the risk of the nucleus falling posteriorly once again.

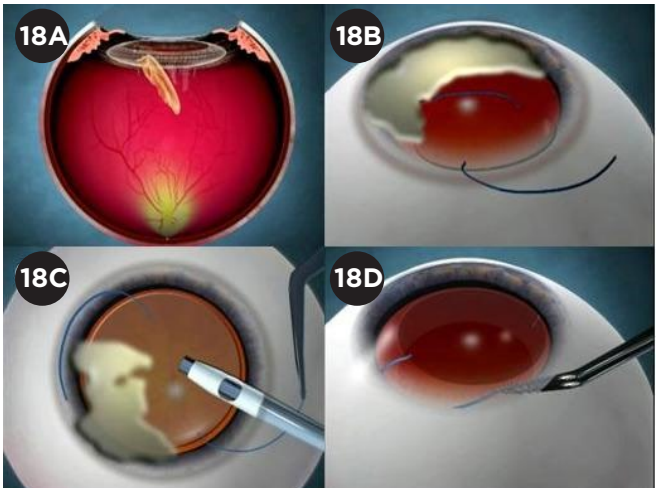
CASE 18 CONCLUSION: During the anterior vitrectomy, the nuclear fragment was fortuitously drawn up to the vitrectomy port located just behind the iris. A second instrument was placed behind it to levitate it into the anterior chamber.

Q18.2 What would you do once the remaining nuclear fragment is levitated into the anterior chamber?

- Extract it manually with a lens loop 14.3%
- Resume phaco in the anterior chamber 22.4%
- Remove the pupil ring, then phaco the fragment in the anterior chamber 2.7%
- Insert a three-piece IOL beneath the fragment and phaco over the IOL scaffold 52.9%
- Remove the pupil ring, then proceed as in the previous option 7.7%

Boris Malyugin Resuming phaco in the anterior chamber, as suggested by 22.4% of respondents, is very risky because of the high chance for the vitreous gel to be aspirated by the phaco needle. Traction resulting from the aspiration force will significantly increase the chance for retinal tear. Most of the audience (52.9%) suggests placing the three-piece IOL behind the nuclear fragment located in the anterior chamber. I fully agree with that option, as I am personally in favor of what Dr. Agarwal calls the "IOL scaffold" maneuver. However, 7.7% of respondents supported the best available option, in my opinion: They opted to remove the pupil expansion ring prior to proceeding with IOL scaffolding.

Having nucleus fragments, an IOL, and a pupil expansion ring in the anterior chamber at the same time is not a good idea given the limited anterior chamber depth and the necessity of introducing one more device—i.e., the phaco tip—to remove the nucleus fragments. At some time point, the anterior chamber might be too crowded with all four devices located in there. Prior to inserting the IOL, I would suggest cutting the ring with Vannas scissors, grasping one of the cut ends with the forceps and removing it from the anterior chamber. After the pupil expander is removed, the pupil will most likely constrict, which is very good at that point. Pupil constriction will reduce the chance of the nucleus fragments dislocating backward during emulsification in the anterior chamber at a later step of the procedure.



CASE 18. *(18A) The natural lens is falling from the bag during cataract surgery. (18B) In the IOL scaffold maneuver, the remaining lens is held in the anterior part of the eye, and an IOL is inserted behind it. (18C) Cataract pieces are lying on top of the IOL. The phaco handpiece can now be used to remove the cataract without the fear of the cataract pieces falling down, as the IOL is acting as a scaffold. (18D) The IOL is centered at the end of surgery.*

Then, I would sequester the nucleus fragments in the anterior chamber with dispersive OVD, which can also be used to push the vitreous back from the anterior chamber. Limited "dry" vitrectomy with a 23-gauge needle may also help to clean the strands located in the anterior chamber.

A three-piece IOL should then be inserted and positioned on top of the anterior iris surface. Special caution should be paid not to touch the IOL optic with the vibrating phaco tip, as it will easily cause scratches on the lens surface. After successful nucleus fragment removal with phaco, iris hooks can be used to enlarge the pupil again and to facilitate IOL implantation and fixation utilizing residual capsular bag remnants.

Amar Agarwal More than half of the audience members (52.9%) feel that if there is a posterior capsular rupture with nuclear fragments one of the better ways to manage the case is to use the IOL scaffold technique (Fig. 18). In this technique, a foldable IOL is used to prevent the nucleus fragment from descending into the vitreous in the case of a posterior capsular rupture. After removing the vitreous in the anterior chamber by anterior vitrectomy, a three-piece foldable IOL is injected via the existing corneal incision with one haptic above the iris and the other haptic extending outside the incision. The IOL can be placed into the sulcus—or, if the iris is not floppy, both haptics can be implanted above the iris. The nucleus is emulsified with the phaco probe above the IOL optic.

It is always better to perform the entire surgery with a

Amar Agarwal, MD

trocar anterior chamber maintainer so that fluid is always in the eye. Cortical cleaning is done and the IOL is then placed over the remnants of the capsule in the ciliary sulcus. This can be performed in eyes with moderate to soft cataracts. It avoids corneal incision extension and thereby limits induced astigmatism.

Posterior capsular rupture in association with nonemulsified nuclear fragments and absent sulcus support is a challenging scenario for the anterior segment surgeon. Under such circumstances, the glued IOL scaffold technique helps to overcome all the limitations, although it calls for a definite surgical skill set. Preplacement and prefixation of an IOL via the glued IOL scaffold method effectively compartmentalizes the anterior and posterior chambers, and the preplaced IOL acts as an artificial posterior capsule and allows safe emulsification of the nuclear fragments subsequently.

Another option for a sinking nucleus in the absence of capsular support is to use a triumvirate of techniques: modified PAL plus the IOL scaffold technique and then ending the case with a glued IOL. PAL helps to retrieve and levitate the sinking nucleus in the anterior chamber. Once the nucleus is levitated in the anterior chamber, the IOL scaffold procedure helps the surgeon emulsify the nuclear remnants with the phacoemulsification probe.

EXTRA **MORE ONLINE.** For audience recognition of the most hair-raising cases, view this article at aao.org/eyenet.

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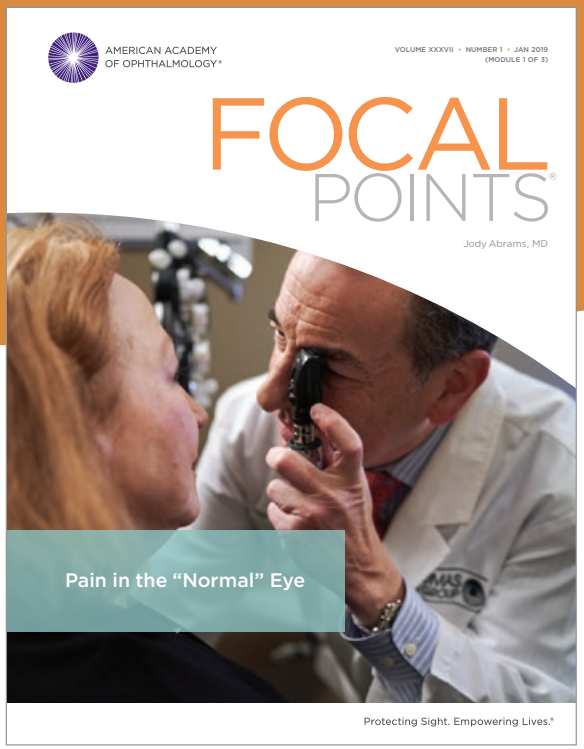

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The CPT and HCPCS Changes That Impact Coding in Ophthalmology

Each year, the American Medical Association updates its Current Procedural Terminology (CPT). In 2019, the most significant changes for ophthalmology include new codes for electroretinography and biopsies, plus (see "More Online") a new HCPCS code for corneal cross-linking and new Category III codes. In the 2019 listings, a red dot (●) is used to flag new codes.

The following changes impact all your payers, not solely Medicare Part B.

ERG Testing

To distinguish between the different types of electroretinography (ERG) testing that are now in use, CPT code 92275 *ERG* was deleted and replaced with two Category I, Level I codes (92273 and 92274) and one Category III code (0509T).

● CPT code 92273 *ERG with interpretation and report; full field (i.e., ffERG, flash ERG, Ganzfeld ERG)*. The RVS Update Committee (RUC) had determined that this new code should be assigned a work Relative Value Unit (wRVU) of 0.80, but CMS disagreed and assigned it a wRVU of 0.69. The typical allowable is $138. The technical component (–TC) requires general supervision. The National Correct Coding Initiative (CCI) bundles five codes with 92273: 99211, 99446, 99447, 99448, and 99449.

● CPT code 92274 *ERG with interpretation and report; multifocal (mfERG)*. CMS assigned 92274 a wRVU of 0.61, despite the RUC recommending a wRVU of 0.72. The typical allowable is $93. The technical component requires general supervision. CCI bundling for this code is the same as for CPT code 92273.

Note: New testing services might not be immediately recognized by commercial payers. (For example, some commercial payers implement updates at the start of their fiscal year instead of at the start of a calendar year.)

● 0509T *ERG with interpretation and report, pattern (PERG)*. This Category III code was created specifically for appropriate reporting of this technology, and it has significant differences from the historical ERG code. CCI bundling is the same as for CPT code 92273. (See this article online for Category III code payment policies.)

Biopsies

CPT codes 11100 *Biopsy of skin; single lesion* and the add-on code +11101 for each separate/additional lesion have been deleted. They have been replaced with a new family of biopsy codes that are defined by technique:

- Tangential biopsy (e.g., shave, scoop, saucerize, and curette)
- Punch biopsy involves use of a punch tool to get a full-thickness cylindrical sample of skin, and it includes simple closure.
- Incisional biopsy involves use of a sharp blade to obtain a full-thickness sample of tissue via a vertical incision or wedge, and it includes simple closure.

The three new primary codes each have an add-on code. The add-on code should be listed separately, in addition to the code for the primary procedure.

● CPT code 11102 *Tangential biopsy of skin; single lesion.*

● +11103 *each separate/additional lesion.* This is 11102's add-on code.

● CPT code 11104 *Punch biopsy of skin; single lesion.*

● +11105 *each separate/additional lesion.* This is 11104's add-on code.

● CPT code 11106 *Incisional biopsy of skin; single lesion.*

● +11107 *each separate/additional lesion.* This is 11106's add-on code.

Example. If the physician performs a punch biopsy and two tangential biopsies, the claim submission includes three codes—11104, 11102, and +11103—and each would have a 1 in the unit field. It is enough to indicate the number of units; you don't need to append –RT, –LT, –E1, or –E4.

Note: When the biopsy is more than superficial, report CPT code 67810 *Incisional biopsy of eyelid skin, including eyelid margin.*

BY **CHERIE MCNETT,** ACADEMY DIRECTOR OF HEALTH POLICY, **MICHAEL X. REPKA, MD, MBA,** ACADEMY MEDICAL DIRECTOR OF GOVERNMENT AFFAIRS, AND **SUE VICCHRILLI, COT, OCS,** ACADEMY DIRECTOR OF CODING AND REIMBURSEMENT.

EXTRA **MORE ONLINE.** For three more Category III codes and a HCPCS J code for Photrexa, see this article at aao.org/eyenet.

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MIPS—What's New for 2019, Part 2: Quality, Improvement Activities, and Cost

How will changes to the Merit-Based Incentive Payment System (MIPS) impact ophthalmology practices? Part 1 of this two-part series reviewed changes to payment adjustments, eligibility criteria, and how your MIPS final score is calculated. It also summarized the revamped promoting interoperability (PI) performance category. Part 2 reviews what's new with the other three performance categories.

Why MIPS matters. If you don't take part in MIPS in 2019, your payments for Medicare Part B services in 2021 could suffer a –7% penalty.

Use the IRIS Registry. It is free for Academy members; it focuses exclusively on ophthalmology; and—as a qualified clinical data registry (QCDR)—it can develop subspecialty-specific quality measures. You can use it to manually report quality measures, improvement activities, and PI measures. Furthermore, if you integrate your electronic health record (EHR) system with the IRIS Registry, you can use an automated process to extract the data that are needed for quality reporting, get credit for PI's Clinical Data Registry Reporting measure, and perform the QCDR-related improvement activities.

Learn more about the IRIS Registry and MIPS at aao.org/iris-registry and aao.org/medicare.

What's New With Quality

Claims-based reporting: Expanded access for small practices; not an option for large practices. In 2019, clinicians in large practices can no longer report quality measures via Medicare Part B claims. However, clinicians in small practices can continue to do so and—new this year—can do so when reporting as a group, not just when reporting as individuals. Warning: Many claims-based quality measures are topped out at a low decile, which hinders your ability to get a high score for quality with claims-based reporting.

Facility-based scoring for hospital-based clinicians. Facility-based scoring will be available to you only if you provide at least 75% of your covered professional service—based on claims submitted between Oct. 1, 2017, and Sept. 30, 2018—at an inpatient hospital (place of service [POS] code: 21), on-campus outpatient hospital (POS code: 22), or emergency room (POS code: 23), with at least one service at an inpatient hospital or emergency room.

Bonus points for opioid-related measures. In response to the opioid epidemic, CMS now considers opioid-related quality measures to be high priority. The IRIS Registry developed an opioid-related QCDR measure for oculoplastic surgeons (see IRIS37, listed on the next page).

Bonus for electronic reporting now requires 2015-edition CEHRT. Like last year, you can earn bonus points if you report quality measures using a certified EHR technology (CEHRT) for end-to-end reporting, but in 2019 you will get this bonus only if you are using the 2015-edition CEHRT.

Some topped out measures may be retired early. CMS considers a measure to be topped out when a lot of clinicians are attaining, or almost attaining, maximum performance for that measure (e.g., the average performance rate is 95% or higher). CMS had previously established a four-year life cycle for such measures—if they are topped out for at least two years, they would be subject to a seven-point cap; topped out for three consecutive performance years, they would be eliminated in the fourth year. Now CMS is accelerating that process in some cases: If a measure is *extremely topped out* (e.g., the average performance rate is 98% or higher), it can be removed from MIPS in the following year, even if it hasn't been topped out for three consecutive years. (Note: Topped out QCDR measures also are on an accelerated timetable for removal, even if they aren't extremely topped out.)

In rare cases, a measure might be "suppressed." During the course of 2019, changes in clinical guidelines may mean that continued adherence to a measure could result in patient harm and/or provide misleading results as to good quality care. In the unlikely event that this happens with one of ophthalmology's measures, CMS could

BY **REBECCA HANCOCK,** DIRECTOR, IRIS REGISTRY, **CHRIS MCDONAGH,** SENIOR EDITOR, *EYENET*, **MOLLY PELTZMAN,** MANAGER, IRIS REGISTRY, AND **JESSICA PETERSON,** MD, MPH, ACADEMY MANAGER OF QUALITY AND HIT POLICY.

suppress that measure. This means that if you submitted data on the measure before it was suppressed—because, for example, you were reporting by claims—1) you wouldn't score points for that measure and 2) when CMS calculates your quality score it would reduce your denominator by 10 points (so you wouldn't be penalized for reporting the measure).

Small practice bonus is moved to quality. For 2019, CMS will no longer apply a 5-point small practice bonus when calculating the MIPS final score; instead, when calculating your quality score, it will apply a 6-point bonus to your numerator for that performance category—but only if you report data on at least one quality measure.

New QCDR measures available via the IRIS Registry. The Academy, working with subspecialty societies, has developed six new QCDR measures:

- IRIS35: Improvement of Macular Edema in Patients With Uveitis
- IRIS36: Visual Acuity Improvement Following Cataract Surgery Combined With a Trabeculectomy or an Aqueous Shunt Procedure
- IRIS37: Postoperative Opioid Management Following Oculoplastic Surgery
- IRIS38: Endothelial Keratoplasty: Dislocation Requiring Surgical Intervention
- IRIS39: Intraocular Pressure Reduction Following Trabeculectomy or an Aqueous Shunt Procedure
- IRIS48: Adult Surgical Esotropia: Postoperative Alignment

IRIS Registry adds three MIPS CQMs for manual reporting. In addition to the new QCDR measures, three additional MIPS clinical quality measures (MIPS CQMs) are available if you report manually via the IRIS Registry:

- Measure 154: Falls: Risk Assessment
- Measure 236: Controlling High Blood Pressure
- Measure 474: Zoster (Shingles) Vaccination

CMS removed some MIPS CQMs. The eliminated measures include three MIPS CQMs that had been useful for Academy subspecialists:

- Measure 18: Diabetic Retinopathy: Documentation of Presence or Absence of Macular Edema and Level of Severity of Retinopathy
- Measure 140: AMD: Counselling on Antioxidant Supplement
- Measure 224: Melanoma: Avoidance of Overutilization of Imaging Studies

Eight QCDR measures removed. These 2018 QCDR measures are not available in 2019:

- IRIS9: Diabetic Retinopathy: Documentation of the Presence or Absence of Macular Edema and the Level of Severity of Retinopathy
- IRIS11: Nonexudative AMD: Loss of Visual Acuity
- IRIS17: Acute Anterior Uveitis: Post-Treatment Grade 0 Anterior Chamber Cells
- IRIS20: Idiopathic Intracranial Hypertension: No Worsening or Improvement of Mean Deviation
- IRIS25: Adenoviral Conjunctivitis: Avoidance of Antibiotics
- IRIS26: Avoidance of Routine Antibiotic Use in Patients Before or After Intravitreal Injections
- IRIS31: Avoidance of Genetic Testing for AMD
- IRIS34: AMD: Disease Progression.

What if you use multiple collection types? Suppose, for example, you report six measures by Medicare Part B claims and you report the same six measures manually via the IRIS Registry portal. If you did that during the 2018 performance year, CMS would 1) assess your score for the six claims-based submissions, 2) assess your score for the six IRIS Registry–based submissions, and 3) assign you the higher of those two scores (i.e., your score would be based on either the six measures reported by claims or the six measures reported via the IRIS Registry portal). During the 2019 performance year, CMS will make that comparison for individual measures—so your final quality score could, for example, be based on five measures that were reported via the IRIS Registry and one reported via claims.

What's New With Improvement Activities

The improvement activities performance category remains largely the same as in 2018—though 10 additional activities are available to report via the IRIS Registry, including one for eye exams.

An improvement activities score of 100% is no longer enough to avoid the payment penalty. As in 2018, if your 2019 improvement activities score is 100%, you will earn 15 points toward your MIPS final score. In 2018, that would have been enough to avoid a future MIPS payment penalty, but not in 2019. Because the threshold for avoiding a penalty has increased to a MIPS final score of 30 points, you should also try to score points for quality measures and/or PI measures.

Improvement activities no longer contribute to your PI score. In 2018, certain improvement activities would earn you a PI bonus if CEHRT was used to help you perform those activities. This is no longer the case in 2019.

Ten improvement activities have been added to the IRIS Registry. When you report activities manually via the IRIS Registry, you can choose from 34 activities (up from 24 in 2018).

Two of the additions are high-weighted improvement activities:

- Provide education opportunities for new clinicians (IA_AHE_6)
- Participation in population health research (IA_PM_17)

Eight of the additions are medium-weighted improvement activities:

- Leveraging a QCDR for use of standard questionnaires (IA_AHE_4)
- Evidence-based techniques to promote self-management into usual care (IA_BE_16)
- Improved practices that disseminate appropriate self-management materials (IA_BE_21)
- Improved practices that engage

QCDR Copyright

patients pre-visit (IA_BE_22)
- Use of telehealth services that expand practice access (IA_EPA_2)
- Participation in user testing of the Quality Payment Program website: https://qpp.cms.gov (IA_EPA_5)
- Participation in private payer clinical practice improvement activities (IA_PSPA_12)
- Comprehensive eye exam (IA_AHE_7).

Performing the eye exam activity (IA_AHE_7). According to CMS, this medium-weight activity is intended for "1) nonophthalmologist/optometrists who refer patients to ophthalmologists/optometrists, 2) ophthalmologists/optometrists caring for underserved populations at no cost [participating in EyeCare America may help you fulfill this activity; aao.org/volunteer], or 3) any clinician providing literature and/or resources on this topic." CMS also states that this "activity must be targeted at underserved and/or high-risk populations that would benefit from engagement regarding their eye health with the aim of improving their access to comprehensive eye exams."

What's New With Cost

New cataract measure. In 2019, CMS will start scoring ophthalmologists on a new episode-based measure: Routine Cataract Surgery With Intraocular Lens (IOL) Implantation (0-10 points).

Attribution. An episode of cataract surgery will be attributed to the clinician who performed the procedure, as identified by HCPCS codes or CPT codes.

Case minimum. This cataract measure has a case minimum of 10 episodes, which means that it will contribute to your cost score only if at least 10 episodes of cataract surgery are attributed to you.

What costs are included? The measure takes into account only the cost of items and services that are related to the cataract procedure (unlike the Total Per Capita Cost measure, which includes all services provided to a patient over a given time frame). Your costs for the measure will undergo payment standardization and risk adjustment, in an attempt to account for cost variations that are beyond your control, such as geographic variations in wage levels and patient characteristics that might lead to increased spending.

Other cost measures. As in 2018, you get a score for the Total Per Capita Cost measure (0-10 points) only if at least 20 patients are attributed to you. Patients are attributed to you if they were not seen by a primary care clinician and you billed the majority of their primary care services, which can include evaluation and management (E&M) service codes but not Eye visit codes. There also is a Medicare Spending Per Beneficiary measure (MSPB; 0-10 points), but it rarely will apply to ophthalmologists.

Calculating your cost performance category score. Like last year, your cost performance category score = cost achievement points ÷ available cost points, and is reported as a percentage.

Example. Suppose CMS scored you as follows:
- 5 points for the Total Per Capita Cost measure (out of 10 available points);
- 7 points for the cataract episode-based measure (out of 10 available points)

Your cost achievement points would be 12 (5 + 7) and your available cost points would be 20 (because you were only scored on two cost measures). So your cost score would be cost achievement points (12) ÷ available points (20) = 0.6, or 60%.

Cost can contribute up to 15 points to your 2019 MIPS final score; a cost score of 60% would therefore contribute 9 points (60% of 15 points) to your MIPS final score.

New Terminology

In 2018, CMS used "submission mechanism" as a term that, depending on the context, could refer to 1) the entity that submits the data to CMS (e.g., the IRIS Registry), 2) the method of submitting the data (e.g., via claims or via attestation), and 3) certain types of measures (e.g., electronic clinical quality measures). CMS has said that in 2019, instead of referring to submission mechanism, it will start using the three distinct terms below.

Submitter type. This refers to the individual or organization that submits the MIPS data to CMS, and it includes MIPS eligible clinicians, groups, and virtual groups, as well as any third parties (e.g., the IRIS Registry) that submit data on their behalf.

Submission type. This refers to the mechanism that a submitter type uses to submit data to CMS. Examples include direct, log in and upload, log in and attest, and Medicare Part B claims.

Collection type. This refers to types of quality measure that have comparable specifications. Examples include:
- eCQMs: electronic clinical quality measures
- MIPS CQMs: MIPS clinical quality measures (reported manually)
- QCDR measures
- Medicare Part B claims measures

Example. The Diabetes Eye Exam quality measure exists in three different collection types: If you report via IRIS Registry–EHR integration or via your EHR vendor, you would use the eCQM version; if you report via manual entry into the IRIS Registry web portal, you would use the MIPS CQM version; and if you report via Medicare Part B claims, you would use the claims version. These three versions of the Diabetes Eye Exam measure each have their own specifications and their own benchmark.

What about QCDR measures? QCDRs, such as the IRIS Registry, can develop subspecialty-specific measures. Most of the IRIS Registry's QCDR measures have two different versions—one for manual reporting and the other for reporting via IRIS Registry–EHR integration.

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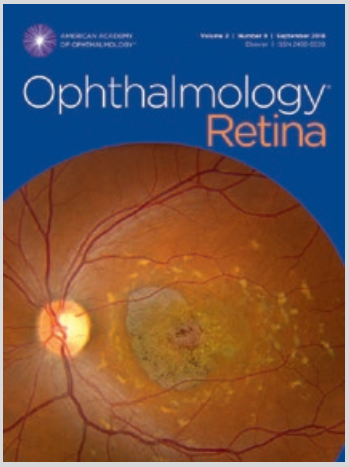

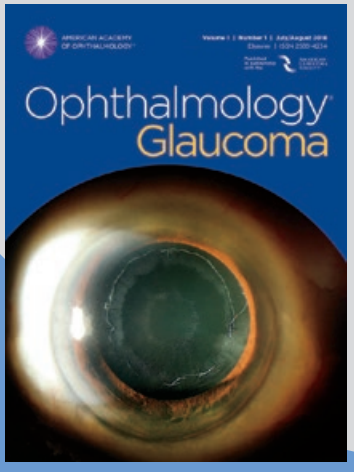

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Academy Notebook

NEWS • TIPS • RESOURCES

FROM ONE SCHOLAR TO ANOTHER. *During Student Engagement Weekend, Keith D. Carter, MD, FACS, who was serving as Academy President, delivered an empowering speech to MOM students. Dr. Carter, who was himself a National Medical Fellowship (NMF) scholarship recipient, has said of this distinction, "The NMF scholarship was very important and inspirational because of the effort of an organization offering to assist me with my training expense. I have always been grateful for this generosity."*

WHAT'S HAPPENING

Minority Medical Students Awarded Scholarships

In December, two Minority Ophthalmology Mentoring (MOM) program participants were awarded the 2018 National Medical Fellowship (NMF) Scholarship in Ophthalmology. They are **Ja'Qualane Scales** of Howard University College of Medicine in Washington, D.C., and **Joshua Chazaro** of Loyola Stritch School of Medicine in Maywood, Illinois. The second-year medical students were chosen based on scholastic and leadership achievement and active participation in the MOM program, a partnership between the Academy and Association of University Professors of Ophthalmology.

Ja'Qualane Scales

Joshua Chazaro

Minority Ophthalmology Mentoring. The scholarship recipients were two of 22 medical and MD/PhD students selected by the Academy to join the MOM program for its inaugural year. This program was designed to attract underrepresented minorities (African Americans, Hispanics, and Native Americans) in medicine to a career in ophthalmology and help prepare them to be competitive residency applicants. After being paired with ophthalmologist mentors in August 2018, the participating students were invited to Student Engagement Weekend at AAO 2018, where they had the opportunity to meet their mentors in person, as well as to explore the many facets of ophthalmology.

National Medical Fellowship Scholarship in Ophthalmology. Just prior to the annual meeting, NMF, which shares the MOM program's mission of providing more opportunities to underrepresented minority students pursuing medical careers, generously offered to provide two $5,000 scholarships to MOM students who clearly displayed leadership qualities through their research, academic performance, and extracurricular activities.

The impact. By supporting the education of these two students, the NMF scholarships uphold the greater mission of MOM and NMF to support diversity in and accessibility of health care. According to NMF, the shortage of health care professionals in communities of color is estimated to be between 46,000 and 90,000 physicians by 2025. Ms. Scales and Mr. Chazaro, in their applications to the MOM program, stressed the value they placed in pursuing a medical education, not only to pave the way for minority students interested in becoming ophthalmologists, but also to provide better care to patients in underserved communities.

TAKE NOTICE

Academy Year in Review

Academy leadership, staff, and countless volunteers work hard to provide you with the best member experience. Find out what the Academy achieved in the last year on all fronts, including advocacy, education, and public service. The *2018 Year in Review* highlights some of the Academy's greatest achievements, including the following:

- establishing a permanent research

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fund to advance the practice of pediatric ophthalmology;
- launching a campaign to build a new Museum of Vision in San Francisco;
- lobbying for ophthalmology's best interests in state and federal government affairs; and
- developing an award-winning public education campaign.

Learn more at aao.org/yearinreview.

A Request From *EyeNet*

This month and next, some of you will be asked to participate in a magazine readership survey conducted by Kantar Media. If you are a fan of *EyeNet* and the work we do, please participate to help keep our scores high. Being ranked among the most widely and thoroughly read ophthalmic publications enables us to secure funding for projects that help you in the clinical realm and in your practice, like the MIPS manual.

Attend the Cochrane Systematic Review Workshop

Join Cochrane Eyes and Vision U.S. Satellite and learn to more effectively review and conduct research. During this two-day intensive workshop, participants will attend lectures by experienced reviewers, then have the opportunity to apply these insights in hands-on exercises designed to reinforce the latest Cochrane methodology. Mark your calendars now for March 28-29 in Stanford, California.

Apply to attend at https://eyes.cochrane.org/March28. The deadline is March 1.

Visit the Academy at APAO Congress

From March 6-9, the Academy will exhibit at the 34th Asia-Pacific Academy of Ophthalmology Congress in Bangkok. If you plan to attend this conference on "The Sciences and Arts of Ophthalmology," visit the Academy's booth for the latest information on Academy resources and products.

PROTECTING SIGHT, EMPOWERING LIVES. *The cover of the Academy's* 2018 Year in Review *report reflects a continued effort by the Academy and its members to uphold its mission to enrich patients' lives. Diagnosed with Leber congenital amaurosis, Creed Pettit had been slowly going blind since birth and was unable to see except in bright light. During an experimental treatment, Audina M. Berrocal, MD, pediatric retina surgeon at the Bascom Palmer Eye Institute in Miami, delivered healthy genes to Creed's eyes. Within a month after gene therapy, Creed was able to see details of the world he had never seen before.*

MEMBERS AT LARGE

Suzanne Véronneau-Troutman Award

The Suzanne Véronneau-Troutman Award, established by Suzanne Véronneau-Troutman, MD, FRCS(C), FACS, and awarded annually by the Women in Ophthalmology board of directors, recognizes the woman who did the most during the previous year to advance and enhance the position of women in the field.

Last fall during AAO 2018, the award was presented to **Nancy M. Holekamp, MD,** Professor of Clinical Ophthalmology and Visual Sciences at the Washington University School of Medicine in St. Louis, Missouri. Dr. Holekamp has been a champion for women in the profession through her outstanding body of clinical work as well as through her support of mentorship within the American Society of Retina Specialists' Women in Retina (WinR), of which she is Board Chair.

Nancy M. Holekamp, MD

Dr. Holekamp said, "I was so incredibly honored to receive the Suzanne Véronneau-Troutman award, joining a long list of impressive women leaders in ophthalmology. I think receiving this award is a nod to the great work being done by WinR. Of course, it takes many people to create meaningful programs that support women ophthalmologists, so I have to thank my colleagues at WinR."

ACADEMY RESOURCES

Attend the Ophthalmology Business Summit

Creating value for your practice while effectively serving patients is more challenging than ever. Join the Academy's business-focused "boot camp" and uncover actionable strategies that can immediately impact your practice's revenue and growth. Physician leaders and senior administrators can attend the Ophthalmology Business Summit individually or as a team to benefit from an intensive two-track program developed by notable business experts and Academy leaders. Attend March 23-24 in Chicago and position your practice for success.

Find the complete curriculum at aao.org/business-summit.

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MEETING MATTERS

Get Ready for AAO 2019 in San Francisco

Mark your calendar: AAO 2019 takes place Oct. 12-15 at Moscone Center in San Francisco. At the meeting, you will become well-versed in recent advancements of clinical care, learn the latest surgical techniques, and hear faculty share evidence-based recommendations. Following your educational sessions, find more inspiration as you cruise around the bay, take in the San Francisco Museum of Modern Art, visit the entertaining colonies of sea lions, shop in Chinatown, or sample California cuisine in the city of its origin.

Learn more at aao.org/2019.

Be Part of AAO 2019

Want to contribute to the world's most comprehensive ophthalmology meeting? Prepare a paper, poster, or video abstract for AAO 2019. The online abstract submitter opens March 7 and closes April 9.

Find more information at aao.org/presentercentral.

D.C. REPORT

Be Heard! Attend Mid-Year Forum 2019

The Mid-Year Forum (MYF) is one of the Academy's most significant yearly meetings, bringing the ophthalmology community together to implement the highest quality of care for patients through politics, policy, and practice management. MYF 2019 takes place April 10-13 in Washington, D.C., and is an ideal opportunity to directly advocate for your profession, learn about health care policy changes impacting your practice, and develop strategies to implement new programs in your patient-care approach.

Congressional Advocacy Day: Meet legislators at their place of business. On April 11, from 8:00 a.m. to 3:00 p.m., attend Academy-facilitated meetings with your members of Congress and their staff. With 111 new lawmakers between the U.S. House and Senate, the Academy can use every bit of help to build lasting relationships quickly. The Academy will provide talking points during a dinner briefing on April 10.

Politics. Policy. Practice management. On April 11 and 12, attend sessions on efforts to rein in drug spending; how to create an inclusive practice; social media—why we need it and how to do it right; understanding private equity and its impact on ophthalmology; what's new with the IRIS Registry; and emergency planning and disaster preparedness.

Academy Council meeting. From the afternoon of April 12 and continuing through the next day, unite with your colleagues from ophthalmic subspecialty and state societies to discuss issues facing our profession. This is also an opportunity to advise the Board of Trustees on what you view as the highest priorities for the organization. Make your voice heard.

Register. MYF 2019 is open to all Academy members. Preregistration is available through March 25 at aao.org/myf_registration. The registration fee is $225 through March 6 and $325 as of March 7 and onsite; the fee includes MYF materials and meals. There is an option to register to participate only in Congressional Advocacy Day for free.

PEOPLE

Passages

James E. Standefer, MD, ophthalmologist, professor, and international volunteer, passed away on Dec. 28, 2018. He was 83.

Although Dr. Standefer spent much of his career as an adjunct professor at the University of Minnesota and as the founder of Associated Eye Physicians and Surgeons in Stillwater, Minnesota (1970-1993), he left private practice in 1995 to serve as a full-time international volunteer. He was best known for teaching two-week glaucoma workshops in developing nations using the "Train the Trainers" principle; in each workshop, he taught five post-residency ophthalmologists from five different training centers so that the students could then return to their center and share what they had learned with a separate group of doctors.

Dr. Standefer also volunteered his medical expertise by treating glaucoma and cataract patients in developing areas, particularly in Central America and the Solomon Islands in the South Pacific. In addition, he donated much of his time practicing at Mercy Hospital in Abak, Nigeria. Between teaching workshops and volunteering treatment, his service spanned more than 31 developing countries.

A dedicated member of the Academy for nearly 50 years, Dr. Standefer served as Chairman of the Academy's International Educational Development Committee (now referred to as the Global Education and Outreach Committee) from 2000 to 2007. Dr. Standefer was influential in establishing the International Forum at the annual meeting (now referred to as the Global Forum), which offers insightful lectures and panel discussions on global issues in ophthalmology. In addition, over the years, he shared his knowledge about volunteerism with his peers by teaching courses and participating in sessions at the annual meeting.

Dr. Standefer

During his lifetime, the Academy honored his acts of service with the 2015 International Blindness Prevention Award, the 2001 Academy Foundation's International Public Service Award, and the 1998 Outstanding Humanitarian Service Award.

In remembrance of his friend and colleague, Bruce E. Spivey, MD, FACS, said, "Jim was a person who toiled outside of the spotlight, but whose commitment was deeper and larger than most. He was a great person with a huge heart and dedication."

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"When it comes to giving, the decision really comes down to supporting an organization that is most prominent in what we do on a day-to-day basis — and that's the American Academy of Ophthalmology. It's investing in the future of ophthalmology; this is the way we can pay it forward."

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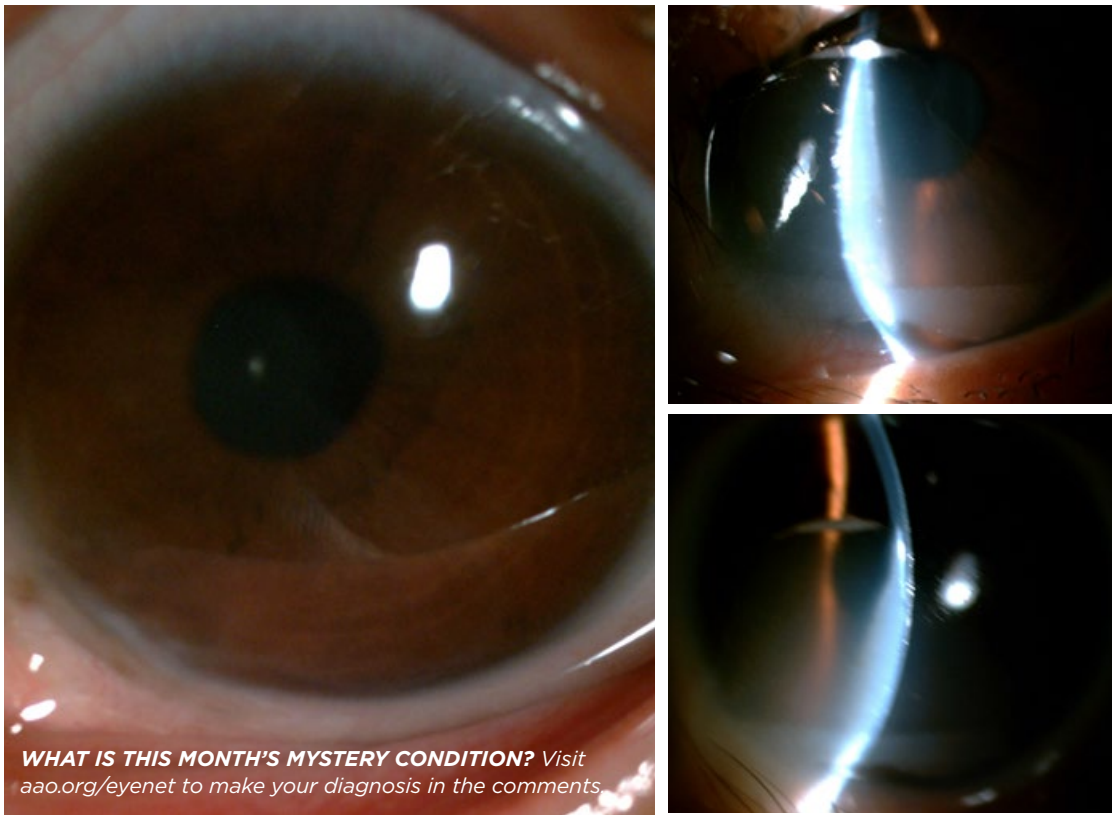
MYSTERY IMAGE

BLINK



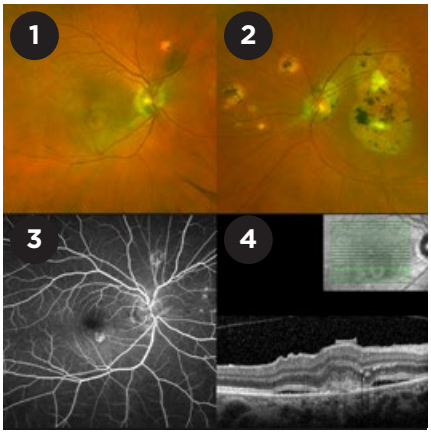
WHAT IS THIS MONTH'S MYSTERY CONDITION? *Visit aao.org/eyenet to make your diagnosis in the comments.*

Kenneth L. Cohen, MD

LAST MONTH'S BLINK

Presumed Ocular Histoplasmosis Syndrome

A 62-year-old woman presented with blurry vision in her right eye, which had started 3 weeks prior to her visit. Her ocular history was significant for long-standing poor vision in the left eye from presumed ocular histoplasmosis syndrome (POHS). On exam, the best-corrected visual acuity was 20/60 in her right eye and count fingers at 1 foot in her left. Intraocular pressure was normal in both eyes.



Dilated funduscopic exam of the right eye (Fig. 1) showed a 1/4 disc–diameter gray lesion in the inferior macula with subretinal fluid and associated small hemorrhage. Both eyes had peripapillary atrophy with punched-out lesions in the midperiphery. In the left eye, disciform macular scarring was present (Fig. 2). Fluorescein angiography of the right eye (Fig. 3) illustrated early staining with late leakage in the inferior macula consistent with a choroidal neovascular membrane (CNVM). Optical coherence tomography of the right eye (Fig. 4) confirmed ellipsoid zone disruption from a subretinal lesion with associated fluid.

Intravitreal bevacizumab treatment was initiated in the right eye only, with involution of the CNVM and complete resolution of subretinal fluid after 3 treatments. Vision in this eye improved to 20/20.

POHS may develop a CNVM with an annual incidence of 1.8%.[1] These lesions are very responsive to anti-VEGF as in this case.

1 Macular Photocoagulation Study Group. *Arch Ophthalmol.* 1996;114(6):677-688.

WRITTEN BY **PHILIP L. AMES, MD, KATHLEEN A. REGAN, MD,** AND **SIVA S. RADHAKRISHNAN IYER, MD.** PHOTOS BY DR. IYER, UNIVERSITY OF FLORIDA COLLEGE OF MEDICINE, GAINESVILLE, FLA.

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1 INDICATIONS AND USAGE
LUCENTIS is indicated for the treatment of patients with:

1.1 Neovascular (Wet) Age-Related Macular Degeneration (AMD)

1.2 Macular Edema Following Retinal Vein Occlusion (RVO)

1.3 Diabetic Macular Edema (DME)

1.4 Diabetic Retinopathy (DR)

1.5 Myopic Choroidal Neovascularization (mCNV)

4 CONTRAINDICATIONS

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

4.2 Hypersensitivity
LUCENTIS is contraindicated in patients with known hypersensitivity to ranibizumab or any of the excipients in LUCENTIS. Hypersensitivity reactions may manifest as severe intraocular inflammation.

5 WARNINGS AND PRECAUTIONS

5.1 Endophthalmitis and Retinal Detachments
Intravitreal injections, including those with LUCENTIS, have been associated with endophthalmitis and retinal detachments. Proper aseptic injection technique should always be used when administering LUCENTIS. In addition, patients should be monitored following the injection to permit early treatment should an infection occur *[see Dosage and Administration (2.6, 2.7) in the full prescribing information and Patient Counseling Information (17)]*.

5.2 Increases in Intraocular Pressure
Increases in intraocular pressure have been noted both pre-injection and post-injection (at 60 minutes) while being treated with LUCENTIS. Monitor intraocular pressure prior to and following intravitreal injection with LUCENTIS and manage appropriately *[see Dosage and Administration (2.7 in the full prescribing information)]*.

5.3 Thromboembolic Events
Although there was a low rate of arterial thromboembolic events (ATEs) observed in the LUCENTIS clinical trials, there is a potential risk of ATEs following intravitreal use of VEGF inhibitors. ATEs are defined as nonfatal stroke, nonfatal myocardial infarction, or vascular death (including deaths of unknown cause).

Neovascular (Wet) Age-Related Macular Degeneration
The ATE rate in the three controlled neovascular AMD studies (AMD-1, AMD-2, AMD-3) during the first year was 1.9% (17 of 874) in the combined group of patients treated with 0.3 mg or 0.5 mg LUCENTIS compared with 1.1% (5 of 441) in patients from the control arms *[see Clinical Studies (14.1 in the full prescribing information)]*. In the second year of Studies AMD-1 and AMD-2, the ATE rate was 2.6% (19 of 721) in the combined group of LUCENTIS-treated patients compared with 2.9% (10 of 344) in patients from the control arms. In Study AMD-4, the ATE rates observed in the 0.5 mg arms during the first and second year were similar to rates observed in Studies AMD-1, AMD-2, and AMD-3.

In a pooled analysis of 2-year controlled studies (AMD-1, AMD-2, and a study of LUCENTIS used adjunctively with verteporfin photodynamic therapy), the stroke rate (including both ischemic and hemorrhagic stroke) was 2.7% (13 of 484) in patients treated with 0.5 mg LUCENTIS compared to 1.1% (5 of 435) in patients in the control arms (odds ratio 2.2 (95% confidence interval (0.8-7.1))).

Macular Edema Following Retinal Vein Occlusion
The ATE rate in the two controlled RVO studies during the first 6 months was 0.8% in both the LUCENTIS and control arms of the studies (4 of 525 in the combined group of patients treated with 0.3 mg or 0.5 mg LUCENTIS and 2 of 260 in the control arms) *[see Clinical Studies (14.2 in the full prescribing information)]*. The stroke rate was 0.2% (1 of 525) in the combined group of LUCENTIS-treated patients compared to 0.4% (1 of 260) in the control arms.

Diabetic Macular Edema and Diabetic Retinopathy
Safety data are derived from studies D-1 and D-2. All enrolled patients had DME and DR at baseline *[see Clinical Studies (14.3, 14.4 in the full prescribing information)]*.

In a pooled analysis of Studies D-1 and D-2 *[see Clinical Studies (14.3 in the full prescribing information)]*, the ATE rate at 2 years was 7.2% (18 of 250) with 0.5 mg LUCENTIS, 5.6% (14 of 250) with 0.3 mg LUCENTIS, and 5.2% (13 of 250) with control. The stroke rate at 2 years was 3.2% (8 of 250) with 0.5 mg LUCENTIS, 1.2% (3 of 250) with 0.3 mg LUCENTIS, and 1.6% (4 of 250) with control. At 3 years, the ATE rate was 10.4% (26 of 249) with 0.5 mg LUCENTIS and 10.8% (27 of 250) with 0.3 mg LUCENTIS; the stroke rate was 4.8% (12 of 249) with 0.5 mg LUCENTIS and 2.0% (5 of 250) with 0.3 mg LUCENTIS.

5.4 Fatal Events in Patients with DME and DR at baseline
Diabetic Macular Edema and Diabetic Retinopathy
Safety data are derived from studies D-1 and D-2. All enrolled patients had DME and DR at baseline *[see Clinical Studies (14.3, 14.4 in the full prescribing information)]*.

A pooled analysis of Studies D-1 and D-2 *[see Clinical Studies (14.3 in the full prescribing information)]*, showed that fatalities in the first 2 years occurred in 4.4% (11 of 250) of patients treated with 0.5 mg LUCENTIS, in 2.8% (7 of 250) of patients treated with 0.3 mg LUCENTIS, and in 1.2% (3 of 250) of control patients. Over 3 years, fatalities occurred in 6.4% (16 of 249) of patients treated with 0.5 mg LUCENTIS and in 4.4% (11 of 250) of patients treated with 0.3 mg LUCENTIS. Although the rate of fatal events was low and included causes of death typical of patients with advanced diabetic complications, a potential relationship between these events and intravitreal use of VEGF inhibitors cannot be excluded.

6 ADVERSE REACTIONS
The following adverse reactions are discussed in greater detail in other sections of the label:
- Endophthalmitis and Retinal Detachments *[see Warnings and Precautions (5.1)]*
- Increases in Intraocular Pressure *[see Warnings and Precautions (5.2)]*
- Thromboembolic Events *[see Warnings and Precautions (5.3)]*
- Fatal Events in patients with DME and DR at baseline *[see Warnings and Precautions (5.4)]*

6.1 Injection Procedure
Serious adverse reactions related to the injection procedure have occurred in < 0.1% of intravitreal injections, including endophthalmitis *[see Warnings and Precautions (5.1)]*, rhegmatogenous retinal detachment, and iatrogenic traumatic cataract.

6.2 Clinical Studies Experience
Because clinical trials are conducted under widely varying conditions, adverse reaction rates observed in one clinical trial of a drug cannot be directly compared with rates in the clinical trials of the same or another drug and may not reflect the rates observed in practice.

The data below reflect exposure to 0.5 mg LUCENTIS in 440 patients with neovascular AMD in Studies AMD-1, AMD-2, and AMD-3; in 259 patients with macular edema following RVO. The data also reflect exposure to 0.3 mg LUCENTIS in 250 patients with DME and DR at baseline *[see Clinical Studies (14 in the full prescribing information)]*.

Safety data observed in Study AMD-4, D-3, and in 224 patients with mCNV were consistent with these results. On average, the rates and types of adverse reactions in patients were not significantly affected by dosing regimen.

Ocular Reactions
Table 1 shows frequently reported ocular adverse reactions in LUCENTIS-treated patients compared with the control group.

Table 1 Ocular Reactions in the DME and DR, AMD, and RVO Studies

	DME and DR 2-year		AMD 2-year		AMD 1-year		RVO 6-month	
Adverse Reaction	LUCENTIS 0.3 mg n=250	Control n=250	LUCENTIS 0.5 mg n=379	Control n=379	LUCENTIS 0.5 mg n=440	Control n=441	LUCENTIS 0.5 mg n=259	Control n=260
Conjunctival hemorrhage	47%	32%	74%	60%	64%	50%	48%	37%
Eye pain	17%	13%	35%	30%	26%	20%	17%	12%
Vitreous floaters	10%	4%	27%	8%	19%	5%	7%	2%
Intraocular pressure increased	18%	7%	24%	7%	17%	5%	7%	2%
Vitreous detachment	11%	15%	21%	19%	15%	15%	4%	2%
Intraocular inflammation	4%	3%	18%	8%	13%	7%	1%	3%
Cataract	28%	32%	17%	14%	11%	9%	2%	2%
Foreign body sensation in eyes	10%	5%	16%	14%	13%	10%	7%	5%
Eye irritation	8%	5%	15%	15%	13%	12%	7%	6%
Lacrimation increased	5%	4%	14%	12%	8%	8%	2%	3%
Blepharitis	3%	2%	12%	8%	8%	5%	0%	1%
Dry eye	5%	3%	12%	7%	7%	7%	3%	3%
Visual disturbance or vision blurred	8%	4%	18%	15%	13%	10%	5%	3%
Eye pruritus	4%	4%	12%	11%	9%	7%	1%	2%
Ocular hyperemia	9%	9%	11%	8%	7%	4%	5%	3%
Retinal disorder	2%	2%	10%	7%	8%	4%	2%	1%
Maculopathy	5%	7%	9%	9%	6%	6%	11%	7%
Retinal degeneration	1%	0%	8%	6%	5%	3%	1%	0%
Ocular discomfort	2%	1%	7%	4%	5%	2%	2%	2%
Conjunctival hyperemia	1%	2%	7%	6%	5%	4%	0%	0%
Posterior capsule opacification	4%	3%	7%	4%	2%	2%	0%	1%
Injection site hemorrhage	1%	0%	5%	2%	3%	1%	0%	0%

Non-Ocular Reactions
Non-ocular adverse reactions with an incidence of ≥ 5% in patients receiving LUCENTIS for DR, DME, AMD, and/or RVO and which occurred at a ≥ 1% higher frequency in patients treated with LUCENTIS compared to control are shown in Table 2. Though less common, wound healing complications were also observed in some studies.

Table 2 Non-Ocular Reactions in the DME and DR, AMD, and RVO Studies

	DME and DR 2-year		AMD 2-year		AMD 1-year		RVO 6-month	
Adverse Reaction	LUCENTIS 0.3 mg n=250	Control n=250	LUCENTIS 0.5 mg n=379	Control n=379	LUCENTIS 0.5 mg n=440	Control n=441	LUCENTIS 0.5 mg n=259	Control n=260
Nasopharyngitis	12%	6%	16%	13%	8%	9%	5%	4%
Anemia	11%	10%	8%	7%	4%	3%	1%	1%
Nausea	10%	9%	9%	6%	5%	5%	1%	2%
Cough	9%	4%	9%	8%	5%	4%	1%	2%
Constipation	8%	4%	5%	7%	3%	4%	0%	1%
Seasonal allergy	8%	4%	4%	4%	2%	2%	0%	2%
Hypercholesterolemia	7%	5%	5%	5%	3%	2%	1%	1%
Influenza	7%	3%	7%	5%	3%	2%	3%	2%
Renal failure	7%	6%	1%	1%	0%	0%	0%	0%
Upper respiratory tract infection	7%	7%	9%	8%	5%	5%	2%	2%
Gastroesophageal reflux disease	6%	4%	4%	6%	3%	4%	1%	0%
Headache	6%	8%	12%	9%	6%	5%	3%	3%
Edema peripheral	6%	4%	3%	5%	2%	3%	0%	1%
Renal failure chronic	6%	2%	0%	1%	0%	0%	0%	0%
Neuropathy peripheral	5%	3%	1%	1%	1%	0%	0%	0%
Sinusitis	5%	8%	8%	7%	5%	5%	3%	2%
Bronchitis	4%	4%	11%	9%	6%	5%	0%	2%
Atrial fibrillation	3%	3%	5%	4%	2%	2%	1%	0%
Arthralgia	3%	3%	11%	9%	5%	5%	2%	1%
Chronic obstructive pulmonary disease	1%	1%	6%	3%	3%	1%	0%	0%
Wound healing complications	1%	0%	1%	1%	1%	0%	0%	0%

6.3 Immunogenicity
As with all therapeutic proteins, there is the potential for an immune response in patients treated with LUCENTIS. The immunogenicity data reflect the percentage of patients whose test results were considered positive for antibodies to LUCENTIS in immunoassays and are highly dependent on the sensitivity and specificity of the assays.

The pre-treatment incidence of immunoreactivity to LUCENTIS was 0%-5% across treatment groups. After monthly dosing with LUCENTIS for 6 to 24 months, antibodies to LUCENTIS were detected in approximately 1%-9% of patients.

The clinical significance of immunoreactivity to LUCENTIS is unclear at this time. Among neovascular AMD patients with the highest levels of immunoreactivity, some were noted to have iritis or vitritis. Intraocular inflammation was not observed in patients with DME and DR at baseline, or RVO patients with the highest levels of immunoreactivity.

6.4 Postmarketing Experience
The following adverse reaction has been identified during post-approval use of LUCENTIS. Because this reaction was reported voluntarily from a population of uncertain size, it is not always possible to reliably estimate the frequency or establish a causal relationship to drug exposure.
- Ocular: Tear of retinal pigment epithelium among patients with neovascular AMD

7 DRUG INTERACTIONS
Drug interaction studies have not been conducted with LUCENTIS.

LUCENTIS intravitreal injection has been used adjunctively with verteporfin photodynamic therapy (PDT). Twelve (12) of 105 (11%) patients with neovascular AMD developed serious intraocular inflammation; in 10 of the 12 patients, this occurred when LUCENTIS was administered 7 days (± 2 days) after verteporfin PDT.

8 USE IN SPECIFIC POPULATIONS

8.1 Pregnancy
Risk Summary
There are no adequate and well-controlled studies of LUCENTIS administration in pregnant women.

Administration of ranibizumab to pregnant monkeys throughout the period of organogenesis resulted in a low incidence of skeletal abnormalities at intravitreal doses 13-times the predicted human exposure (based on maximal serum trough levels [C_{max}]) after a single eye treatment at the recommended clinical dose. No skeletal abnormalities were observed at serum trough levels equivalent to the predicted human exposure after a single eye treatment at the recommended clinical dose *[see Animal Data]*.

Animal reproduction studies are not always predictive of human response, and it is not known whether ranibizumab can cause fetal harm when administered to a pregnant woman. Based on the anti-VEGF mechanism of action for ranibizumab *[see Clinical Pharmacology (12.1 in the full prescribing information)]*, treatment with LUCENTIS may pose a risk to human embryofetal development.

LUCENTIS should be given to a pregnant woman only if clearly needed.

Data
Animal Data
An embryo-fetal developmental toxicity study was performed on pregnant cynomolgus monkeys. Pregnant animals received intravitreal injections of ranibizumab every 14 days starting on Day 20 of gestation, until Day 62 at doses of 0, 0.125, and 1 mg/eye. Skeletal abnormalities including incomplete and/or irregular ossification of bones in the skull, vertebral column, and hindlimbs and shortened supernumerary ribs were seen at a low incidence in fetuses from animals treated with 1 mg/eye of ranibizumab. The 1 mg/eye dose resulted in trough serum ranibizumab levels up to 13 times higher than predicted C_{max} levels with single eye treatment in humans. No skeletal abnormalities were seen at the lower dose of 0.125 mg/eye, a dose which resulted in trough exposures equivalent to single eye treatment in humans. No effect on the weight or structure of the placenta, maternal toxicity, or embryotoxicity was observed.

8.2 Lactation
Risk Summary
There are no data available on the presence of ranibizumab in human milk, the effects of ranibizumab on the breastfed infant or the effects of ranibizumab on milk production/excretion.

Because many drugs are excreted in human milk, and because the potential for absorption and harm to infant growth and development exists, caution should be exercised when LUCENTIS is administered to a nursing woman.

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

8.3 Females and Males of Reproductive Potential
Infertility
No studies on the effects of ranibizumab on fertility have been conducted. and it is not known whether ranibizumab can affect reproduction capacity. Based on the anti-VEGF mechanism of action for ranibizumab, treatment with LUCENTIS may pose a risk to reproductive capacity.

8.4 Pediatric Use
The safety and effectiveness of LUCENTIS in pediatric patients have not been established.

8.5 Geriatric Use
In the clinical studies, approximately 76% (2449 of 3227) of patients randomized to treatment with LUCENTIS were ≥ 65 years of age and approximately 51% (1644 of 3227) were ≥ 75 years of age *[see Clinical Studies (14 in the full prescribing information)]*. No notable differences in efficacy or safety were seen with increasing age in these studies. Age did not have a significant effect on systemic exposure.

10 OVERDOSAGE
More concentrated doses as high as 2 mg ranibizumab in 0.05 mL have been administered to patients. No additional unexpected adverse reactions were seen.

17 PATIENT COUNSELING INFORMATION
Advise patients that in the days following LUCENTIS administration, patients are at risk of developing endophthalmitis. If the eye becomes red, sensitive to light, painful, or develops a change in vision, advise the patient to seek immediate care from an ophthalmologist *[see Warnings and Precautions (5.1)]*.

LUCENTIS®
[ranibizumab injection]
Manufactured by:
Genentech, Inc.
A Member of the Roche Group
1 DNA Way
South San Francisco, CA
94080-4990

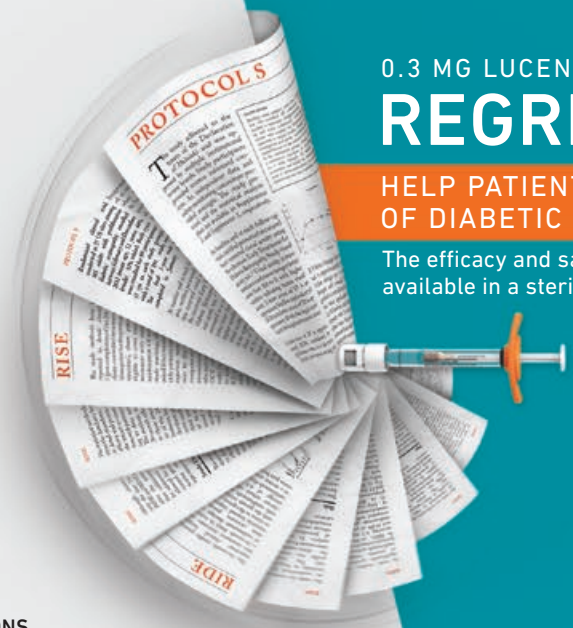
Initial US Approval: June 2006
Revision Date: LUC/021815/0050(4) 2017

0.3 MG LUCENTIS PREFILLED SYRINGE

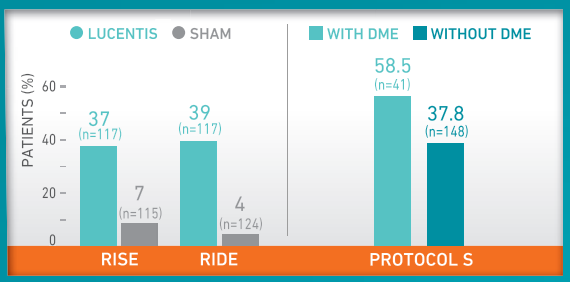
REGRESSION DELIVERED[1]

HELP PATIENTS TURN BACK TO AN EARLIER STAGE OF DIABETIC RETINOPATHY (DR)[1]

The efficacy and safety of LUCENTIS in DR, studied in 3 clinical trials, available in a sterile glass prefilled syringe.[1]



≥2-STEP IMPROVEMENTS AT 2 YEARS[1]*



≥3-STEP IMPROVEMENTS AT 2 YEARS[1]:

RISE AND RIDE
- LUCENTIS 0.3 mg: 9% (n=117) and 17% (n=117), respectively
- Sham arms: 0% (n=115) and 2% (n=124), respectively

PROTOCOL S
- Patients without DME: 28.4% (n=148)
- Patients with DME: 31.7% (n=41)

Confidence intervals (95%): ≥2-step—RISE: 31% (21%, 40%); RIDE: 35% (26%, 44%). Protocol S (DR with DME): 58.5% (43.5%, 73.6%); (DR without DME): 37.8% (30%, 45.7%). ≥3-step—RISE: 9% (4%, 14%); RIDE: 15% (7%, 22%). Protocol S (DR with DME): 31.7% (17.5%, 46%); (DR without DME): 28.4% (21.1%, 35.6%).[1]

INDICATIONS

LUCENTIS® (ranibizumab injection) is indicated for the treatment of patients with:
- Diabetic retinopathy (DR)
- Diabetic macular edema (DME)

IMPORTANT SAFETY INFORMATION

CONTRAINDICATIONS

- LUCENTIS is contraindicated in patients with ocular or periocular infections or known hypersensitivity to ranibizumab or any of the excipients in LUCENTIS. Hypersensitivity reactions may manifest as severe intraocular inflammation

WARNINGS AND PRECAUTIONS

- Intravitreal injections, including those with LUCENTIS, have been associated with endophthalmitis, retinal detachment, and iatrogenic traumatic cataract. Proper aseptic injection technique should always be utilized when administering LUCENTIS. Patients should be monitored following the injection to permit early treatment, should an infection occur
- Increases in intraocular pressure (IOP) have been noted both pre-injection and post-injection (at 60 minutes) with LUCENTIS. Monitor intraocular pressure prior to and following intravitreal injection with LUCENTIS and manage appropriately
- Although there was a low rate of arterial thromboembolic events (ATEs) observed in the LUCENTIS clinical trials, there is a potential risk of ATEs following intravitreal use of VEGF inhibitors. ATEs are defined as nonfatal stroke, nonfatal myocardial infarction, or vascular death (including deaths of unknown cause)
- In a pooled analysis of Studies DME-1 and DME-2, the ATE rate at 2 years was 7.2% (18 of 250) with 0.5 mg LUCENTIS, 5.6% (14 of 250) with 0.3 mg LUCENTIS, and 5.2% (13 of 250) with control. The stroke rate at 2 years was 3.2% (8 of 250) with 0.5 mg LUCENTIS, 1.2% (3 of 250) with 0.3 mg LUCENTIS, and 1.6% (4 of 250) with control. At 3 years, the ATE rate was 10.4% (26 of 249) with 0.5 mg LUCENTIS and 10.8% (27 of 250) with 0.3 mg LUCENTIS; the stroke rate was 4.8% (12 of 249) with 0.5 mg LUCENTIS and 2.0% (5 of 250) with 0.3 mg LUCENTIS
- Fatal events occurred more frequently in patients with DME and DR at baseline treated monthly with LUCENTIS compared with control. A pooled analysis of Studies D-1 and D-2, showed that fatalities in the first 2 years occurred in 4.4% (11 of 250) of patients treated with 0.5 mg LUCENTIS, in 2.8% (7 of 250) of patients treated with 0.3 mg LUCENTIS, and in 1.2% (3 of 250) of control patients. Over 3 years, fatalities occurred in 6.4% (16 of 249) of patients treated with 0.5 mg LUCENTIS and in 4.4% (11 of 250) of patients treated with 0.3 mg LUCENTIS. Although the rate of fatal events was low and included causes of death typical of patients with advanced diabetic complications, a potential relationship between these events and intravitreal use of VEGF inhibitors cannot be excluded

ADVERSE EVENTS

- Serious adverse events related to the injection procedure that occurred in <0.1% of intravitreal injections included endophthalmitis, rhegmatogenous retinal detachment, and iatrogenic traumatic cataract
- In the LUCENTIS Phase III clinical trials, the most common ocular side effects included conjunctival hemorrhage, eye pain, vitreous floaters, and increased intraocular pressure. The most common non-ocular side effects included nasopharyngitis, anemia, nausea, and cough
- As with all therapeutic proteins, there is the potential for an immune response in patients treated with LUCENTIS. The clinical significance of immunoreactivity to LUCENTIS is unclear at this time

Please see Brief Summary of LUCENTIS full Prescribing Information on following page.

*The following clinical trials were conducted for the **DR & DME** indications: ***RISE & RIDE***—Two methodologically identical, randomized, double-masked, sham injection–controlled, Phase III pivotal trials (N=759) that studied the efficacy and safety of LUCENTIS 0.3 mg and 0.5 mg administered monthly to patients with DR and DME at baseline. The primary outcome was the proportion of patients gaining ≥15 letters at 2 years. ***Protocol S***—A randomized, active-controlled study that evaluated LUCENTIS 0.5 mg vs panretinal photocoagulation in DR patients with and without DME. All eyes in the LUCENTIS group (n=191) received a baseline 0.5 mg intravitreal injection followed by 3 monthly injections. Further treatments were guided by prespecified retreatment criteria. FDA approval was based on an analysis of the LUCENTIS arm of Protocol S. The primary outcome was mean change in visual acuity from baseline to 2 years.[2-3]

LUCENTIS 0.3 mg is recommended to be administered by intravitreal injection once a month (approximately 28 days).[1]

DME, diabetic macular edema.

REFERENCES: 1. LUCENTIS [package insert]. South San Francisco, CA: Genentech, Inc; 2018. **2.** Brown DM, et al; RISE and RIDE Research Group. *Ophthalmology*. 2013;120:2013-2022. **3.** Gross JG, et al; Writing Committee for the Diabetic Retinopathy Clinical Research Network. *JAMA*. 2015;314:2137-2146.

Genentech
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LUCENTIS®
RANIBIZUMAB INJECTION