

# News in Review

COMMENTARY AND PERSPECTIVE

## Surgery May Reverse Glaucoma Damage

**CONVENTIONAL WISDOM HOLDS** that glaucoma treatment may preserve vision but cannot reverse damage. Now, researchers at the Jules Stein Eye Institute (JSEI) at UCLA report that damage may be reversible, at least for some patients following trabeculectomy.<sup>1</sup> They found that filtering surgery not only slowed the rate of perimetric decay from glaucoma but also provided evidence of sustained, long-term improvement of visual function.

The implications for clinical treatment are profound. Rather than simply treating glaucoma patients to maintain stability, doctors should understand that long-term improvement of visual function is possible, said Joseph Caprioli, MD, professor of ophthalmology at JSEI. He said that clinicians should begin to “evaluate visual fields in a different way, and not always dismiss apparent improvement as an artifact.”

**Study design.** The retrospective, comparative, longitudinal cohort study involved 2 groups. In the surgery (“Trab”) group, 74 eyes of 64 patients underwent trabeculectomy with mitomycin-C. The comparison group included 71 eyes of 65 patients with open-angle glaucoma who did not have surgery. Baseline damage, number of visual field (VF) tests, and follow-up were similar in both groups.

Patients were followed for about 5 years before and 5 years after surgery.

To mitigate “noise” effects, VF tests were acquired at multiple time points before and after surgery.

**Key results.** “The finding that surprised me the most was that improvement was a fairly common event, if you look for it properly,” said Dr. Caprioli.

Among the findings:

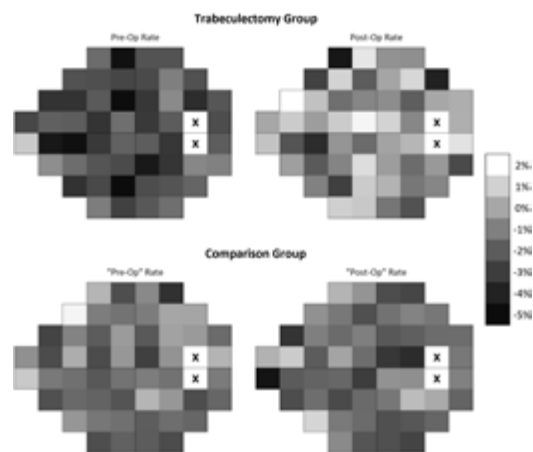
- The magnitude of IOP reduction correlated with the number of VF locations that exhibited long-term improvement postoperatively.

- 80% of Trab eyes improved at 5 or more test locations in the VF.
- More than half of the Trab eyes (57%) showed improvement at 10 or more VF test locations.

**Possible mechanism.** While medical therapy might also yield VF improvement, “a more dramatic effect can be seen with the kind of robust pressure reduction that one can achieve with trabeculectomy,” Dr. Caprioli said. (Mean IOP fell 32%, from an average of 15 mm Hg preoperatively.)

To explain their findings, the researchers theorize that retinal ganglion cells that are damaged, but not dead, contribute to decreased perimetric sensitivity. Reduction of IOP-related stress after surgery may restore function in these damaged cells. This insight could lead to an approach called neurorescue—novel treatments to revive dying nerve cells.

The researchers will follow these patients to monitor duration of effect.



**VF CHANGE.** Distribution of the average rate of change at each location for the 2 groups, comparing the first study period (“pre-op”) and the post-op follow-up. The scale shows change in percentage/year; positive numbers indicate improvement.

They are also planning studies to help predict which patients would achieve visual gains from treatment.

**Clinical implications.** In the meantime, Dr. Caprioli has modified his therapeutic approach. “In patients who are not too elderly, do not have too much visual damage, and who have relatively high pressures, I am becoming more aggressive about lowering eye pressure to a level at which some reversal of visual loss occurs.”

He encouraged others to be mindful of the study’s findings. “I would like those physicians who care for glaucoma patients to simply have a mind-set that allows them to believe that sustained improvement of visual function after treatment can occur.” —Miriam Karmel

1 Caprioli J et al. *Ophthalmology*. 2016;123(1):117-128.

**Relevant financial disclosures**—Dr. Caprioli: Allergan: S; Alcon: S; National Eye Institute: S; New World Medical: S; Research to Prevent Blindness: S.

## Anti-VEGF Tx as Effective as Laser

**ONCE AGAIN, IT'S LOOKING LIKE** anti-VEGF injection therapy can preserve the vision of patients with a retinal disease—and this time, the good news is about proliferative diabetic retinopathy (PDR).

**Noninferiority proved.** The positive results came from the 2-year outcomes of a large randomized multicenter trial comparing the long-standard treatment, panretinal photocoagulation (PRP), against intravitreal (IVT) injections with ranibizumab (Lucentis). The study in 394 eyes with PDR found that IVT anti-VEGF therapy was as effective as laser treatment and that there were fewer side effects in the IVT group.<sup>1</sup> It's important to note that the trial was designed to assess the noninferiority of visual outcomes with ranibizumab versus PRP.

Mean improvement in visual acuity at 2 years was no worse in the ranibizumab group (+2.8 letters) than the PRP group. The study also found that patients in the ranibizumab group had less visual field loss, had a lower rate of vitrectomy (4% vs. 15%), and were less likely to develop diabetic macular edema (DME; 9% vs. 28%) compared with the PRP group.

**Expanded treatment options for PDR.** When researchers from the Diabetic Retinopathy Clinical Research Network (DRCR.net) announced their findings at AAO 2015 in Las Vegas, the reaction was swift and enthusiastic.

"I think that was because this is the first really major advance offering a treatment alternative to PRP for proliferative diabetic retinopathy in about 40 years," said Jeffrey G. Gross, MD, who chaired the trial for DRCR.net. "It gives physicians another option, another tool in their toolbox, to treat proliferative diabetic retinopathy." Dr. Gross is the founder and managing partner at Carolina Retina Center, in Columbia, S.C.

"Our study also showed that over the course of 2 years—not just at 2 years— injection therapy was more ef-

fective than panretinal photocoagulation for vision," he said, adding that patients will be followed for a total of 5 years to assess long-term results.

**Choosing between PRP and ranibizumab.** Because IVT ranibizumab already is approved for treating DME, clinicians who want to apply these study results to their practice might consider the presence or absence of DME in deciding between ranibizumab and laser therapy.

The study stated: "When DME is present for which ranibizumab treatment is planned, PRP may be unnecessary because ranibizumab, already being given for the treatment of DME, will also treat the PDR."

The likelihood of patient compliance with all necessary follow-up visits also is an important factor to consider, Dr. Gross said. "This was a structured protocol of injections, which mandated a structured schedule of follow-up," Dr. Gross said. "In clinical usage it should also be effective, but it's important that



**PRP.** The primacy of laser therapy for PDR may be challenged by recent findings.

the patient can adhere to this type of structure." He added that if patients are not able to adhere to a regular follow-up regimen, "it's unknown whether the same results will be obtained."

—Linda Roach

<sup>1</sup> Writing Committee for the Diabetic Retinopathy Clinical Research Network. *JAMA*. 2015;314(20):2137-2146.

**Relevant financial disclosures**—Dr. Gross: Regeneron: S.

### PHARMACEUTICAL COMPOUNDING

## Bevacizumab Use Falls After Regulatory Changes in Ohio

**ONE YEAR AFTER OHIO MANDATED** patient-specific prescriptions (PSPs) for off-label compounded medications, bevacizumab use decreased by nearly 33% in one retina specialty practice.<sup>1</sup> A survey of its 9 physicians found that 89% made the switch to ranibizumab or aflibercept because of the burdens of PSPs, rather than concerns about the efficacy or safety of bevacizumab.

**Impact of tighter controls on compounded drugs.** The Ohio Board of Pharmacy had tightened its regulation of off-label medications after a 2012 outbreak of fungal meningitis linked with drugs from a single compounding pharmacy in New England. The new requirements for labels with individual patient names and dates on preloaded syringes precluded bulk purchases and resulted in extra patient visits and practice expenses, said coauthor David G. Miller, MD, at Retina Associates of Cleveland.

"At the end of the month, we would end up with dozens of unused syringes containing names of patients who never came back to use them." For these reasons, the move to on-label medications was expected, he said. However, he was surprised by the magnitude of the shift in such a short time, which added a significant burden to the health care system. Between the 2 study periods, the mean cost per injection increased from

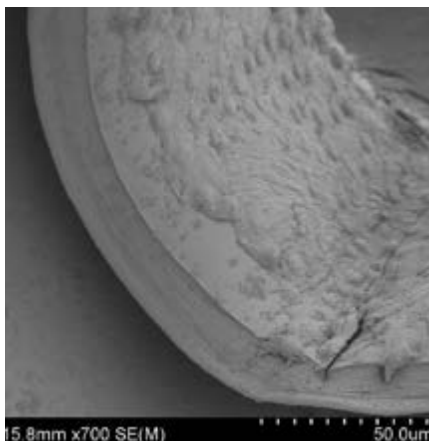
## Femtosecond Cataract Surgery Put to the Test

### ALTHOUGH IT ENTERED THE MARKET

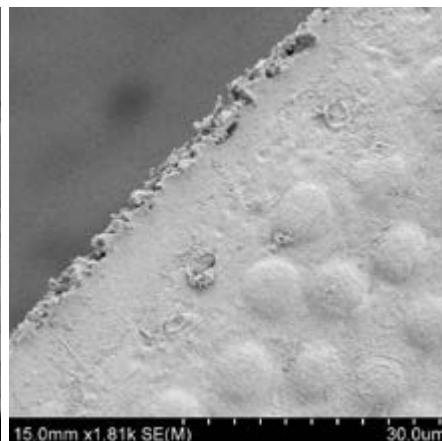
a few years ago amidst high expectations, femtosecond laser–assisted cataract surgery (LCS) did not prove superior to phacoemulsification cataract surgery (PCS) in an Australian prospective multicenter comparative case series.<sup>1</sup> The study evaluated postoperative visual and refractive outcomes in a total of 1,876 eyes 6 months after femtosecond LCS or PCS.

**Mixed outcomes.** The letter gain in best-corrected visual acuity (BCVA) was lower in LCS cases than in PCS cases, although mean BCVA was slightly better in the LCS cohort, a finding that the authors attributed to baseline differences between groups. In comparison with LCS eyes, a higher percentage of PCS eyes were within 0.5 D of the preoperative refractive goal (LCS, 72.2%; PCS, 82.6%).

Complications such as capsular



**PCS VS. LCS.** Left, smooth edge of manual capsulorhexis. Right, laser capsulotomy shows jagged edge, with pits and tags.



tears, perioperative corneal haze, epithelial defect, Descemet membrane trauma, ocular hypertension, and corneal and cystoid macular edema were all higher with LCS.

**Cost-effectiveness.** “Without a significant visual benefit over PCS and with complication rates at similar levels or worse for LCS, there is little benefit in using LCS for most cataract patients,” said coauthor Brendan J. Vote, FRANZCO, clinical associate professor at the University of Tasmania, who was an early adopter of LCS. “Our cost-effectiveness analysis<sup>2</sup> revealed that LCS does not reach internationally accepted thresholds to be considered a cost-effective intervention.”

**LCS benefits some patients.** Although statistically significant evidence is currently lacking, he said, certain complex cases—accounting for less than 5% to 10% of all cataract surgeries—may achieve benefit from LCS. These include eyes with low endothelial cell counts or markedly brunescant cataracts, especially with zonular compromise. These are the only subsets of patients in which Dr. Vote now performs LCS.

—Annie Stuart

1 Ewe YP et al. *Ophthalmology*. 2016;123(1):178-182.

2 Abell RA et al. *Ophthalmology*. 2014;121(1):10-16.

Relevant financial disclosures—Dr. Vote: None.

\$808 to \$1,365.

**Stay tuned for future developments.** Passage of the federal Drug Quality and Security Act of 2013 now supersedes state laws like those in Ohio. Although the FDA requires PSPs for compounded medications nationwide, certified outsourcing facilities regulated by the FDA are now allowed to repackage bevacizumab without PSPs, thus easing its use. But perhaps not for long: The FDA is considering a proposal to add 72-hour expiration dates on bevacizumab labels.

—Annie Stuart

1 Holfinger S et al. *JAMA Ophthalmol*. Published online Nov. 5, 2015. doi:10.1001/jamaophthalmol.2015.4331.

Relevant financial disclosures—Dr. Miller: None.

### NEW ONLINE TOOLS

## Innovative Pediatric Resource Center

**LATE LAST YEAR, THE ACADEMY** launched a center dedicated solely to children’s ocular diseases and disorders: The Knights Templar Eye Foundation Pediatric Ophthalmology Education Center. Funded by a Knights Templar Eye Foundation grant, the online center is part of the Academy’s ONE Network and enables ophthalmologists to better serve the 19 million children worldwide who are visually impaired. Its features include:

- Reference guides on diagnostic and treatment criteria in critical and emergency situations
- More than 80 video demonstrations on symptomatology, diagnostic approaches, and surgical techniques
- Interactive simulators and virtual patient cases demonstrating, for example, strabismus evaluation

Dale Fajardo, EdD, MBA, Academy Vice President for Education, said, “The new Pediatric Ophthalmology Education Center equips eye physicians and surgeons with the specialized tools and information they need to fight the growing threat of visual impairment in children.”

For more information, visit [www.aao.org/pediatric-ophthalmology-education-center](http://www.aao.org/pediatric-ophthalmology-education-center).

For the financial disclosure key, see page 10. For full disclosures, including category descriptions, view this News in Review at [www.eyenet.org](http://www.eyenet.org).