

# News in Review

COMMENTARY AND PERSPECTIVE

## Prior Intravitreal Injections Raise Risk of PCR

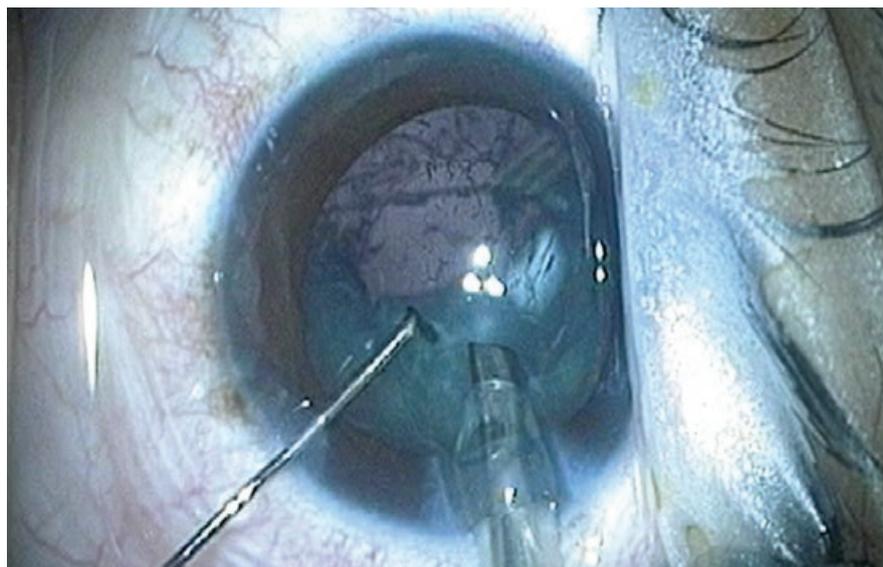
**EVIDENCE IS BUILDING THAT THERE** is a new patient risk factor for cataract surgeons to consider during preoperative planning: prior intravitreal injections.

Even a single intravitreal injection at some point in the past significantly raises the risk of posterior capsular rupture (PCR) during a later cataract surgery, British researchers have found.<sup>1</sup>

**More patients at risk.** At a time when intravitreal injections are being performed to treat a wide variety of retinal problems, this risk could affect a significant segment of the cataract surgery population, the authors warned. They found that intravitreal injections were associated with a 66% rise in risk for PCR during cataract surgery.

“Given the increased risk, surgery should be performed by cataract surgeons able to amend their surgical technique according to need,” the researchers wrote. They further advised that preoperative biometry “should provide lens powers for sulcus 3-piece intraocular lens options, and anterior vitrectomy with triamcinolone should be available if required.”

**EHR review.** The London researchers gleaned their evidence for this new risk factor from a retrospective review of the electronic health records (EHRs) of 62,994 cataract procedures performed at Moorfields Eye Hospital in London. Capsular rupture occurred in 1.04% of



**RUPTURE RISK.** In the latest study, previous intravitreal injections were associated with a 66% increase in the risk of posterior capsular rupture (shown here).

the eyes in the total cohort. However, among the 1,035 eyes with an intravitreal injection history, the PCR rate was 1.88%, they reported.

“These eyes are certainly not routine eyes,” said coauthor Zaid Shalchi, FRCOphth, MRCP, MSc. “This is important when counseling patients for surgery, as well as when deciding on the seniority of the surgeon undertaking the surgery.”

**Building on earlier reports.** The group’s findings were similar to those reported by 3 groups of U.S. and U.K. researchers during 2016. One U.S. group analyzed Medicare data and found that patients with prior intravitreal injections had a significantly increased risk of requiring removal of retained lens fragments within 28 days of surgery.<sup>2</sup> In another U.S. study, researchers found a higher risk of PCR among 197 previously injected eyes than in matched controls.<sup>3</sup>

The third study also combed thousands of EHR records to uncover a direct association between intravitreal injections and the risk of PCR.<sup>4</sup>

**Question of dose response.** In the third study, researchers concluded that the risk of PCR increased by 4% with each additional injection an eye had received, Dr. Shalchi noted. In contrast, Dr. Shalchi said that his group could not find any difference in risk between eyes that had a single injection and those that received 10 or more.

“We did not find a dose response,” he said. “It is a reminder that we still do not understand what leads to PCR in these eyes. Further work is necessary to consider potential hypotheses, such as weakness of the capsule due to previous trauma from injections.”

—Linda Roach

1 Shalchi Z et al. *Am J Ophthalmol.* 2017;177:77-80.

2 Hahn P et al. *Ophthalmology.* 2016;123(2):309-315.

3 Hahn P et al. *Eye (Lond).* 2016;30(8):1101-1109.

4 Lee AY et al. *Ophthalmology.* 2016;123(6):1252-1256.

Relevant financial disclosures—Dr. Shalchi: None.

## Researchers Able to Observe Retinal Cell Death

**USING A NEW IMAGING TECHNIQUE**, researchers for the first time have visualized retinal cell death in human subjects.<sup>1</sup> Their proof-of-concept study involved glaucomatous eyes, but the technique, known as DARC (detection of apoptosing retinal cells), has implications for observing cell death in other neurodegenerative diseases and may eventually play a role in predicting early neurodegenerative activity.

“It is a novel technique for looking at ‘sick’ single nerve cells, which indicate disease activity,” said M. Francesca Cordeiro, PhD, MRCP, FRCOphth, at the Imperial College London.

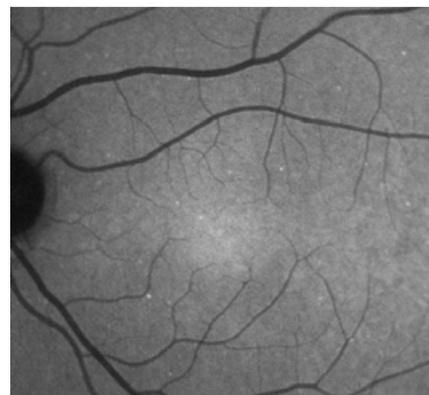
**Counting sick cells.** This phase 1 clinical trial involved 8 patients with glaucomatous neurodegeneration and evidence of progressive disease, plus 8 healthy controls. All received intravenous ANX776 (annexin 5, a cellular

protein that binds to an apoptosis marker, compounded with fluorescent dye DY-776).

Retinal angiograms and optical coherence tomography images were acquired before, during, and after injection. Apoptotic cells appeared as unique hyperfluorescent spots on the retina. The number of spots, or the DARC count, was significantly higher (2.37-fold) in glaucoma patients, compared with healthy controls.

In other findings, the DARC count significantly correlated with decreased central corneal thickness and increased cup-disc ratios in glaucoma patients. In healthy controls, the DARC count was correlated with increased age. In addition, no adverse effects were noted in either the glaucoma patients or the healthy controls.

**Surprise finding.** The DARC count was greater in patients who later showed increasing rates of disease progression in any parameter—rim area, retinal nerve fiber layer, or visual field. “Increased DARC activity was predictive of increased structural and/or functional



**CELL DEATH.** This image of a patient's retina shows hyperfluorescent signals. Each white spot is a single sick retinal nerve cell, labeled in vivo with the DARC technique.

rates of progression,” Dr. Cordeiro said of the unexpected post hoc finding.

**Up next.** The predictive nature of the technique has potential clinical implications. DARC might help identify glaucoma suspects more quickly, said Dr. Cordeiro. It also might help researchers assess response to treatment.

Phase 2 studies will assess DARC in

### CATARACT

## Zonular Weakness and Lens Movement

**JAPANESE RESEARCHERS HAVE CLASSIFIED ZONULAR** weakness based on the distance the lens shifts at the start of cataract surgery.<sup>1</sup> “This classification of zonular weakness may be useful for selecting the appropriate surgical device and procedure during cataract surgery, both of which are dependent on the degree of zonular instability,” said Shigeo Yaguchi, MD, PhD, at Kozawa Eye Hospital and Diabetes Center in Mito, Japan.

The study builds on the team's previous animal research, which demonstrated that the shifted distance of the lens capsule at the start of continuous curvilinear capsulorrhexis (CCC) correlated with the degree of zonular weakness.<sup>2</sup>

**Study design.** This retrospective interventional case series involved 316 consecutive patients (402 eyes) undergoing CCC, phacoemulsification, and implantation of an intraocular lens (IOL). All procedures were performed by a single surgeon. Lens movement was captured on video, retrospectively correlated to surgical interventions, and classified into 3 grades, based on the distance the lens traveled at the start of CCC.

**Results.** Grade I eyes (68.6% of eyes) experienced a shift of < 0.20 mm. Eyes classified as Grade II (25.4% of eyes) and Grade III (6%) experienced shifts of 0.20-0.39 mm and  $\geq$  0.4 mm, respectively.

As in the earlier animal study, the need for surgical interventions—the use of a capsular stabilization device and scleral suture fixation of the IOL—was positively correlated with increasing zonular weakness. The researchers also noted a correlation between the shifted distance of the lens and the presence of anterior capsule striae, a characteristic sign of zonular instability during CCC.

**Clinical implications.** Widespread adoption of the classification system needs to wait for development of video equipment that can capture lens movement during real-time surgery, said Dr. Yaguchi.

For now, he said, “All surgeons can make their own classification of zonular weakness based on the degree of lens movement at CCC. If [similar] data from many surgeons are gathered, the classification would be more reliable.”

—Miriam Karmel

1 Yaguchi S et al. *PLoS One*. 2017;12(4):e0176169.

2 Yaguchi Y et al. *J Clin Exp Ophthalmol*. 2016;7:541.

**Relevant financial disclosures**—Dr. Yaguchi: None.

age-related macular degeneration, optic neuritis, and Alzheimer disease. Dr. Cordeiro is also developing a noninvasive DARC compound. “We believe a less-invasive delivery system would allow for more widespread screening and diagnostic testing,” she said.

—Miriam Karmel

I Cordeiro MF et al. *Brain*. 2017. Published online Apr. 26, 2017.

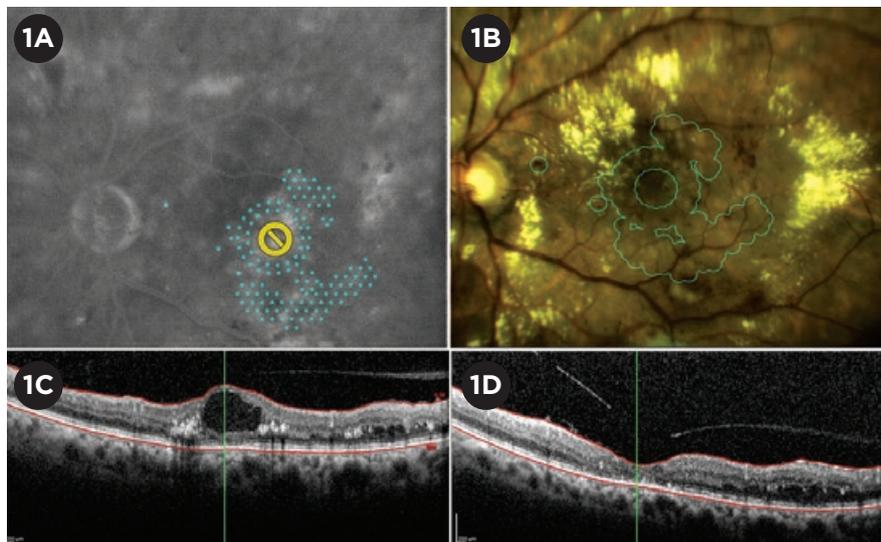
**Relevant financial disclosures**—Dr. Cordeiro is a named inventor on DARC technology patents owned by University College London. The project has been funded through the Wellcome Trust charity through an academic pathway.

## RETINA

# Using Telemedicine to Treat DME

**IN THE FIRST STUDY OF ITS KIND,** ophthalmology researchers on opposite sides of the globe have used telemedicine as a tool for treatment, rather than for screening and diagnosis. In 10 patients with diabetic macular edema (DME), 16 eyes underwent navigated focal laser photocoagulation using a novel teleretinal treatment plan.<sup>1</sup>

**Long-distance consult.** A clinic in Riyadh, Saudi Arabia (Clinic 1) performed the initial imaging with spectral-domain optical coherence tomography (SD-OCT) and fluorescein angiography. The angiograms were then registered to the patient’s fundus image using the Navilas laser system’s



**BEFORE AND AFTER.** (1A) Image of teleophthalmology treatment plan (blue dots) on fluorescein angiogram in an eye with DME. (1B) Post-treatment color fundus image showing hard exudates (yellow) and laser burns (blue circles). (1C) SD-OCT B-scan before laser treatment demonstrates hard exudates (intraretinal hyper-reflective bodies) and foveal cyst/macular edema. (1D) SD-OCT B-scan following treatment demonstrates reduction in exudates and the amount of macular edema.

software and sent in an encrypted format to a second location in West Columbia, South Carolina (Clinic 2). Using the same Navilas system, a surgeon at Clinic 2 assessed an off-line treatment plan that targeted the treatment zones (areas of leaking microaneurysms). The surgeon then transmitted the treatment plans back to Clinic 1, where surgeons successfully executed the plans without any changes in all 16 eyes.

**No registration errors.** Image registration is a critical component of the retinal telephotocoagulation introduced in this study. “And we found the regis-

tration algorithms to be very precise,” said lead author Igor Kozak, MD, PhD, at Moorfields Eye Hospital Centre in Abu Dhabi, United Arab Emirates. “From prior studies, we know that the perfect alignment takes anywhere from 5 to 9 registration marks on the retina. We were getting a perfect match at times with just 3 or 4.” Consequently, the researchers were able to transfer images between clinics without registration error.

**Looking ahead.** Although this study provides an example of real-time teleophthalmology, it is also possible to use a store-and-forward application between multiple clinics. “Ideally, we would like to involve more clinics at many locations,” said Dr. Kozak.

“We also believe that using a centralized image center could help standardize treatment in trials, where lasers are currently used in different ways at the discretion of the treating physician—often leading to interoperator variability.”

—Annie Stuart

1 Kozak I et al. *Graefes Arch Clin Exp Ophthalmol*. 2017. Published online Apr 26, 2017.

**Relevant financial disclosures**—Dr. Kozak: None.

## Teletreatment for DME

### Clinic 1

Navilas is installed in Clinic 1

Clinic 1 images the patient and creates a plan

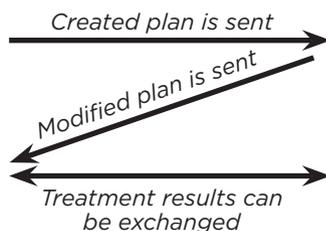
Clinic 1 treats the patient with modified plan

### Clinic 2

Navilas contact is installed on laptop in Clinic 2

Clinic 2 reviews and modifies the plan

Clinic 2 can review the report of the treatment



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