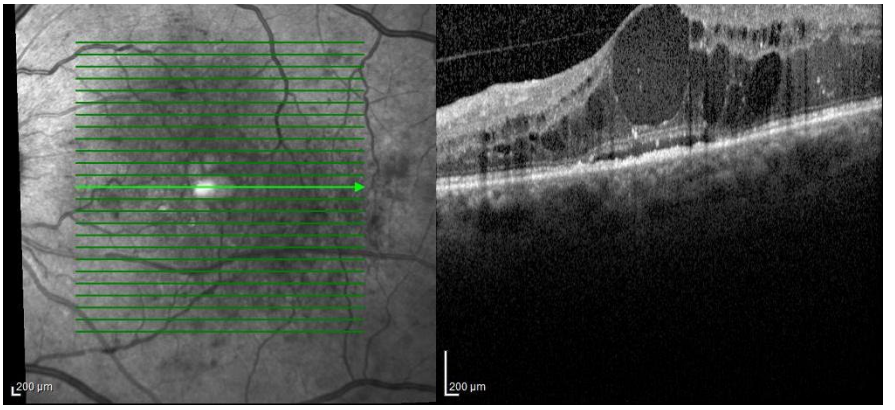


WATCHFUL WAITING? *This patient's DME (shown here at initial presentation) was treated with an anti-VEGF injection. Observation without treatment may be appropriate for selected eyes, results of Protocol V indicate.*

COMPREHENSIVE

Careful Observation Preserves VA in Certain DME Eyes

UNLESS VISION BEGINS DETERIORATING, observation without treatment appears to be a safe and effective management strategy in patients with center-involved diabetic macular edema (CI-DME) and good baseline visual acuity (VA), a landmark study by the Diabetic Retinopathy Clinical Research network has concluded.[1]

Protocol V. The prospective, randomized clinical trial, called Protocol V, compared visual outcomes in 702 eyes with CI-DME that were managed initially with aflibercept (Eylea), laser photocoagulation, or observation. All study subjects began the trial with VA of at least 20/25, and aflibercept treatment was initiated in the observation eyes (and in the laser-treated group) if vision worsened during follow-up.

After two years, there was no significant difference in final mean VA among the three groups, the researchers reported. The percentage of eyes with at least a 5-letter VA decrease compared to baseline was 16% (33/205), 17% (36/212), and 19% (39/208) in the aflibercept, laser, and observation groups, respectively.

Furthermore, two-thirds of the observation eyes and three-quarters of the laser-treated eyes never required any intravitreal injections during the two-year period, said Carl W. Baker, MD, the research network's Protocol V chair.

Support for watchful waiting. The evidence that a large subset of DME patients can be managed successfully with watchful waiting is important, because approximately 40% of DME eyes presenting to ophthalmologists have vision of 20/25 or better, said Dr. Baker, a vitreoretinal specialist who practices in Paducah, Kentucky.

"Vitreoretinal specialists see a lot of DME patients like these, but until this point we haven't really known the best way to treat them," he said. "Our study demonstrated that with these patients you could wait until vision drops and, with careful observation, you end up with the same chance for good results after two years."

Areas of concern. In clinical practice, following the study's findings could pose issues of compliance, Dr. Baker said, because patients under observation must unfailingly return for frequent examinations every eight to 16 weeks. "We don't know how the issues of compliance might affect outcomes in these three different groups," he noted.

Concerns also have been raised that the Protocol V findings could negatively impact decisions about reimbursement for intravitreal injections, Dr. Baker said. "It's important for us to sit down with clinicians inside and outside our research network and discuss the implications of these results" as they relate to working with third-party payers, he said. "We certainly would not want this to limit the availability of treatment options for our patients."

Dr. Baker said the results support a more personalized approach to interventions for DME. "This is another point we are going to make with the payers: that these strategies were shown to be successful but that we used the individual patient's progress or loss of vision to determine whether they were going to get the injectable medicine. Each individual DME patient had different needs that had to be met," he said.

Next steps. The Protocol V researchers, who practice at 91 sites in the United States and Canada, plan to conduct further analyses of study data to try to better define factors affecting DME progression. They also will look for biomarkers that might be used to identify patients most at risk, Dr. Baker said. —*Linda Roach*

1 Baker CW et al., for the DRCR Retina Network. *JAMA*. Published online April 29, 2019.
Relevant financial disclosures—Dr. Baker: Alcon: S; Genentech: S; Novartis: S; Regeneron: S.

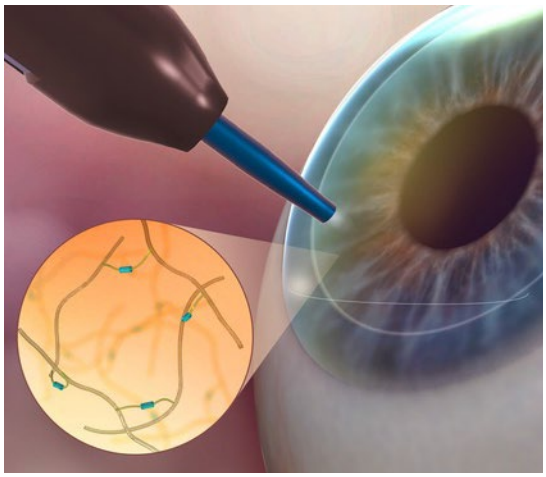
EXTRA **MORE ONLINE.** For more on Protocol V, listen at aao.org/audio/episode-168-drcr-net-protocol-v-study-results-real. The two-part episode covers study design, results, and real-world implications.

CORNEA

Novel Bioadhesive Gel for Corneal Repair

A TEAM OF RESEARCHERS HAS described a simple treatment for the repair of corneal wounds that involves nothing more than a tube of adhesive and visible light.[1] In animal models, GelCore (for "gel for corneal regeneration"), a transparent bioadhesive gel that is still in development, sealed the eyeball and filled structural defects in the cornea for long periods of time without sutures, grafts, or bandage contact lenses.

"GelCore provides an alternative to current standard treatment options," said Nasim Annabi, PhD, at the University of California, Los Angeles. "It is designed to be applied easily, without the need for an operating theater, surgical skills, or even surgery rooms." She singled out its potential on battlefields, where ocular injuries account for over 10% of injuries sustained by soldiers in combat.



NO SUTURES. *The biopolymer solution is injected into the corneal defect and exposed to visible light, forming the hydrogel.*

Gelatin plus light. GelCore is a naturally derived biopolymer with characteristics similar to the native cornea. It is made from chemically modified

CATARACT

Preoperative Astigmatism Planning: High-Tech Isn't Necessarily Better

A STUDY EVALUATING OUTCOMES AFTER ASTIGMATISM correction found that an image-guided system and intraoperative aberrometer, when used together, yielded outcomes that were not significantly better than the surgeon's standard of care.[1]

The findings, however, are dependent on the surgeon's use of "modern and advanced formulas with accurate preoperative measurements and detailed attention to all aspects of the preoperative evaluation," said Kerry D. Solomon, MD, a cataract specialist in Mount Pleasant, South Carolina.

Study design. This prospective case series involved patients who were having uncomplicated bilateral cataract extraction or refractive lens exchange with IOL implantation and astigmatism correction. Dr. Solomon performed all of the surgeries.

The patients served as their own controls, and their eyes were randomly assigned to two groups: 1) Group A eyes received Dr. Solomon's standard of care. He used Lenstar LS 900 (Haag-Streit) keratotomy and calculator/nomogram to determine toric power and orientation of astigmatic incisions. 2) For eyes in Group B, Dr. Solomon used the Verion image-guided system (Alcon) to preoperatively determine the placement of the toric IOL or incision. He also used the Optiwave Refractive Analysis system with VerifEye+ (Alcon) for intraoperative aberrometry calculations.

Results. All told, 38 eyes received toric IOLs, and 40 eyes received manual limbal-relaxing incisions. No significant differences in outcomes between the two groups were noted. Other results were as follows:

- On average, toric IOLs resulted in approximately 0.25 D less cylinder than corneal astigmatic incisions. This was consistent with a large meta-analysis reporting lower residual astigmatism with toric IOLs than with relaxing limbal incisions.[2]
- At three months, the IOL in four eyes (11%; two in each group) was more than 10 degrees of absolute orientation from the intended orientation. No eye with a toric IOL had a secondary surgical intervention to reorient the IOL.
- The reduction in residual astigmatism did not improve other clinical outcomes, such as uncorrected and corrected distance visual acuity.

What if? Might the results differ in the hands of other surgeons? "We don't know for sure if—or how—having a different or less experienced surgeon would have affected the results," Dr. Solomon said. "But we believe that using older formulas and not following our standard procedures could affect the results."

—Miriam Karmel

1 Solomon KD et al. *J Cataract Refract Surg.* 2019;45(5):569-575.
2 Kessel L et al. *Ophthalmology*. 2016;123(2):275-286.
Relevant financial disclosures—Dr. Solomon: Alcon: C,S.

Masoud Moosavi Basri

porcine gelatin mixed with light-activated compounds. After application to the wound and brief exposure to a visible light cross-linking system, GelCore solidifies and firmly adheres to the corneal tissue, sealing the defect without sutures. To overcome biosafety concerns, the light intensity used in the cross-linking system is well below the maximum exposure limit, the researchers said.

Early results. Tests in rabbit eyes indicated that GelCore effectively sealed corneal defects and also promoted re-epithelization. In tests of wound closure strength, shear resistance, and burst pressure, GelCore performed significantly better than existing adhesives, which lack both high adhesion to wet corneal tissue and long-term retention.

"The glues in current use are associated with low biocompatibility, low adhesion, and poor transparency, and they are undesirably rough and difficult to handle," said Dr. Annabi. "Our biomaterial has shown prolonged retention even when filling in large corneal tissue defects. And it could regenerate the damaged corneal tissue."

Potential uses. GelCore is designed mainly for corneal deep scars, but the researchers are working on different formulations for uses ranging from large lacerations and corneal scars to infection and inflammation.

Dr. Annabi noted that its physical and chemical properties can be fine-tuned for use not only in the cornea but also elsewhere in the body, including the lungs, skin, and heart. Moreover, she said, the gel can be used as a platform for delivering antimicrobial agents or drugs to a targeted site to foster wound healing and prevent infection.

Years to market. Since testing in human patients has not yet begun, it could take five to six years to reach the market, Dr. Annabi said.

—Miriam Karmel

1 Sani ES et al. *Sci. Adv.* Published online March 20, 2019.

Relevant financial disclosures—Dr. Annabi: NIH: S; UCLA: S; U.S. Department of Defense: S.

RETINA

Simple Fixes Improve Retinal Detachment Outcomes

Two simple changes in office routines can significantly reduce the incidence of keratopathy after complex retinal detachment (RD) surgery with pars plana vitrectomy and silicone oil tamponade, a study at the University of California, San Francisco (UCSF) has found.[1]

The changes involved:

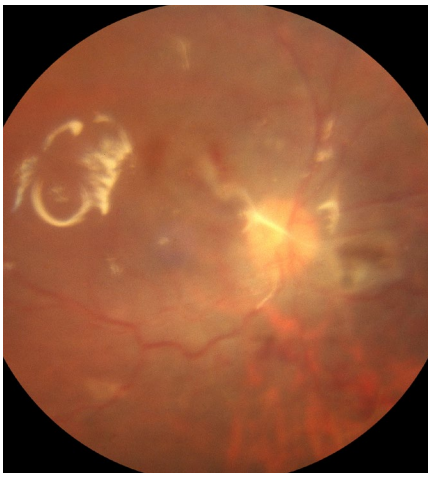
- keeping a registry of patients who received silicone oil, and
- calling to remind them to return for follow-up appointments.

After UCSF vitreoretinal surgeons adopted these procedures, the proportion of patients with complex RD who developed keratopathy fell from 33.3% to 12.8%. "We were surprised that it was so simple to achieve such a difference," said coauthor Jay M. Stewart, MD, at UCSF and Zuckerberg San Francisco General Hospital.

Instigation. Dr. Stewart said the vitreoretinal division in the hospital's ophthalmology department implemented this registry and reminder system in 2014, after physicians and staff noticed that patients were experiencing complications in the months after complex RD surgery.

These adverse outcomes appeared to be related to a lack of follow-up and the duration of the silicone oil in their eyes, Dr. Stewart said. "We encountered complications that could have been avoided if the oil had been removed sooner."

Improved outcomes. After early indications that the reminders were working, the practice did a retrospective records review to compare outcomes in 48 eyes treated before the system was in place (control group), and 39 eyes treated afterward. The review showed statistically significant reductions not only in keratopathy cases but also in two other key areas:



TAMPONADE. *Silicone oil was used in this patient with an RD (note retinal surface reflex). A lengthy period of tamponade has been shown to be the greatest risk factor for silicone oil emulsification, which can lead to keratopathy, glaucoma, and cataracts.*

- The number of patients lost to follow-up was 23 (47.9%) in the control group, versus six (15.4%) in the treatment group ($p = 0.0015$).
- The mean duration before silicone oil removal was 79.6 ± 91.7 weeks (mean ± standard deviation) in the control group and 36.3 ± 31.5 weeks in the treatment group ($p = 0.015$).

With regard to other outcomes, intraocular pressure measurements did not vary significantly between the two groups. Finally, cataract formation was not analyzed as an outcome measure in this study.

Standard practice. Dr. Stewart said the registry and reminder system is now standard practice in the hospital's clinic. "If patients don't show up, then they start getting chased down by the staff" until they do return, he said. "Establishing a line of communication directly between the clinic and the patient gets it back on their radar. It reinforces to them that we consider the appointment to be important—and that there's value in keeping it." *—Linda Roach*

1 Ma D et al. *Ophthalmol Retina.* 2019;3(7):543-547.

Relevant financial disclosures—Dr. Stewart: None.

See the financial disclosure key, page 10. **For full disclosures,** including category descriptions, view this News in Review at aao.org/eyenet.