

News in Review

COMMENTARY AND PERSPECTIVE

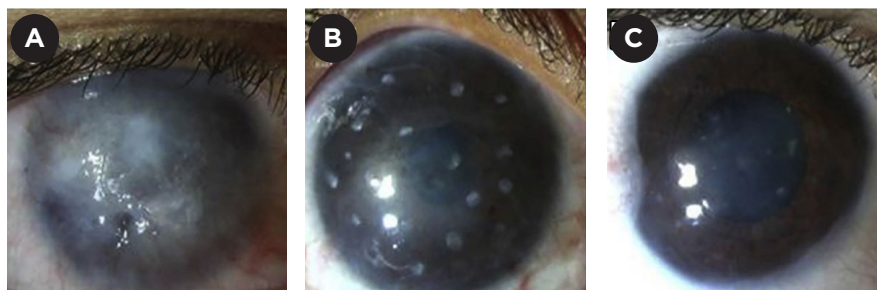
A Simpler Method for Limbal Cell Transplants

SAME-DAY TRANSPLANTATION OF tiny pieces of autologous limbal stem cell tissue onto a patient's burned cornea can restore the ocular surface long term, without requiring expensive ex vivo cultivation of a larger limbal epithelial sheet before the transplant, a large case series has found.

This simple limbal epithelial transplantation (SLET) procedure repaired the corneal epithelium and maintained it for at least 1 year in 76% of 125 study eyes, the researchers at the L.V. Prasad Eye Institute, in Hyderabad, India, reported.¹ That was comparable to the group's previously reported success rate of 71.4% with cultivated limbal epithelial transplantation (CLET).² Success was defined as a completely epithelialized, clinically stable, and avascular corneal surface.

This technique was particularly advantageous in children, who had a success rate of 71% with SLET vs. 37% with CLET, said study coauthor Virender S. Sangwan, MBBS, MS. "SLET works superbly well in the pediatric population," said Dr. Sangwan, who is the Dr. Paul Dubord Chair in Cornea and director of the Center for Ocular Regeneration at the L.V. Prasad Institute.

Visual outcomes. Patients in the study had unilateral chemical or thermal ocular surface burns. Prior to surgery, 93.3% of the children (n = 60)



TRANSPLANT PROGRESS. (A) Preoperative state of child's eye with a chemical burn. (B) SLET progress at 1 month; intact transplants are visible over avascular, totally epithelialized cornea. (C) Eye at 2 years. The small area of conjunctivalization was present at 6 months and has remained stable since then.

and 92.3% of the adults (n = 65) had best-corrected visual acuity (BCVA) of 20/200 or worse. After surgery and a median follow-up of 1.5 years:

- In the eyes in which SLET was successful (n = 95), 67% improved to BCVA of 20/60 or better (p < .0001). The continued poor acuity in the other eyes was due to dense amblyopia, stromal scarring, or cataract.
- BCVA of 20/200 or worse fell to 38% for children and 30% for adults.
- Risk factors associated with transplant failure were history of acid burns; presence of symblepharon extending onto the cornea; concurrent keratoplasty; and postoperative loss of the transplanted tissue.

Technique for transplant. As described by the authors, autologous SLET requires a limbal biopsy sample, measuring 1 clock-hour, from the patient's uninjured fellow eye. The tissue is divided into 6 to 8 pieces, which are laid onto an amniotic membrane scaffold atop the bared cornea and then secured with fibrin glue and a bandage contact lens.

The tiny limbal tissue fragments can

regenerate the entire corneal surface, eliminating the expensive and technology-dependent practice of expanding the biopsy sample in the laboratory before transplantation, the authors wrote. Further, this method requires harvesting substantially less tissue from the fellow eye than either CLET or standard autologous limbal stem cell grafting.

"It seems that the conventional assumption of needing 3 to 6 clock-hours of donor tissue based on animal studies may not necessarily hold true in humans," they wrote. "It does not seem to matter whether a 1-clock-hour limbal biopsy sample is cultured ex vivo on a Petri dish with laboratory reagents or in vivo on the corneal surface itself."

Wider adoption encouraged. Dr. Sangwan's group and others previously have reported positive outcomes with SLET,³⁻⁶ fueling early adoption of the procedure. "My colleagues and I have trained groups from Southeast Asia, Africa, North America, Brazil, Mexico, and many other countries," he said.

Now, because of its larger population and longer follow-up, this study

validates the earlier research and supports wider adoption of the technique, Dr. Sangwan said.

“Based on accumulated personal experience and published literature, I am more than 100% confident in recommending SLET for patients anywhere in the world,” Dr. Sangwan said. “Surgeons need minimal training for this surgery, and they can expect results as good as in my hands.”
—Linda Roach

1 Basu S et al. *Ophthalmology*. 2016;123(5):1000-1010.

2 Sangwan VS et al. *Br J Ophthalmol*. 2011;95(11):1525-1529.

3 Sejpal K et al. *JAMA Ophthalmol*. 2013;131(6):731-736.

4 Vazirani J et al. *Br J Ophthalmol*. Published online Jan. 27, 2016. doi:10.1136/bjophthalmol-2015-307348.

5 Amescua G et al. *Am J Ophthalmol*. 2014;158(3):469-475.e2.

6 Mittal V et al. *Cornea*. 2015;34(10):1227-1232.

Relevant financial disclosures—Dr. Sangwan: None.

TELEOPHTHALMOLOGY

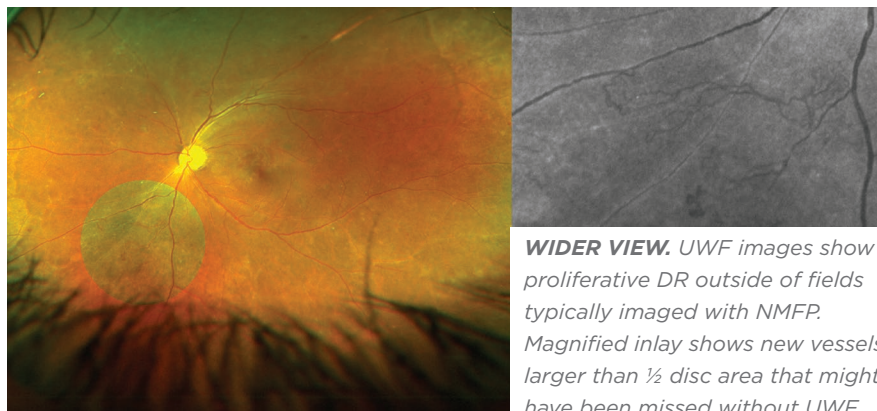
Ultra-widefield Imaging Boosts Retinopathy Dx

THE HIGH COST OF ULTRA-WIDEFIELD imaging systems to remotely monitor diabetic eye disease might give ophthalmologists pause, but great benefits could lie in store for teleophthalmology programs that adopt this technology, a large study of Indian Health Service (IHS) patients suggests.

Reduction in ungradable images.

This 16-month study of remote imaging in more than 50,000 eyes found that the number of patients with ungradable retinal images plummeted by almost 90% when the images were acquired via nonmydriatic ultra-widefield (UWF) digital imaging using scanning laser ophthalmoscopy, compared with standard nonmydriatic multifield fundus photography (NMFP).¹

UWF also identified nearly twice as many cases of diabetic retinopathy ($p < .0001$) as NMFP did, researchers from the IHS-Joslin Vision Network



WIDER VIEW. UWF images show proliferative DR outside of fields typically imaged with NMFP. Magnified inlay shows new vessels larger than $\frac{1}{2}$ disc area that might have been missed without UWF.

Teleophthalmology Program reported. And predominantly peripheral DR lesions—located outside of the standard ETDRS fields—were present in more than 21% of DR patients imaged with UWF.

However, these better views of the retina came at a cost—more than \$70,000 for each UWF device, the authors wrote.

Better imaging decreases patient burden. The nationwide IHS-Joslin teleophthalmology program monitors the eyes of about 18,000 American Indian and Alaska Native diabetic patients annually. Digital retinal images from 97 IHS facilities in 25 states across the country are transmitted to a centralized reading center for grading of disease severity on the ETDRS scale.

On an annualized basis, the reduction in ungradable images with UWF translated into 4,000 fewer diabetic patients who, because of poor image quality, had to travel to tertiary care centers for a follow-up exam, said coauthor Paolo S. Silva, MD, chief of telemedicine at the Joslin Diabetes Center in Boston.

“At this point, cost is a limiting factor, and our study did not look specifically at cost-effectiveness,” Dr. Silva said. “But ultra-widefield imaging potentially will enable us to bring in only those patients who really need tertiary care. So, especially in large programs, in my opinion the efficiency benefits of ultra-widefield imaging outweigh its costs.”
—Linda Roach

1 Silva PS et al. *Ophthalmology*. Published online March 1, 2016.

Relevant financial disclosures—Dr. Silva: None.

VITREORETINAL SURGERY

Assessing Anti-coagulant Risks

THE FIRST RETROSPECTIVE REVIEW

of its kind suggests that patients may safely continue novel oral anticoagulants (NOACs) during vitreoretinal surgeries—procedures that carry inherent risk for hemorrhagic complications.¹ “Regardless, every situation requires individualization and careful consideration of the patient’s medical history and overall health,” said coauthor Harpreet S. Walia, MD, who is a vitreoretinal surgeon with Georgia Retina in Atlanta.

Benefits and indications. Dr. Walia and lead author M. Gilbert Grand, MD, evaluated the effects of 4 NOACs—rivaroxaban (Xarelto), apixaban (Eliquis), dabigatran (Pradaxa), and prasugrel (Effient)—which offer several benefits over older types of antithrombotics, including a rapid onset of action, few drug interactions, and no need for routine coagulation monitoring. Over time, vitreoretinal surgeons are likely to encounter increasing numbers of patients taking these drugs.

In the study, the NOACs were used most often to prevent thromboembolism after angioplasty (57.6%), followed by reduction of stroke risk and systemic embolism in patients with nonvalvular atrial fibrillation (36.4%). Other patients were on the drugs for recurrent deep vein thrombosis (DVT) or for DVT prophylaxis after hip surgery.

Comparable hemorrhage rates. The researchers compared 36 eyes of 33 patients on 1 of the 4 NOACs against

65 control eyes, all of which underwent vitreoretinal surgery at the Retina Institute in St. Louis from 2012 to 2015. Performed mostly under local regional anesthesia, the procedures included 3-port, 23-gauge pars plana vitrectomy, scleral buckling, or a combination of both. Patients were followed postoperatively for a minimum of 3 months.

No eyes in either group experienced perioperative complications of retinal, suprachoroidal, or subretinal hemorrhage, said Dr. Walia. Four eyes in the NOACs group experienced postoperative vitreous cavity hemorrhage: 2 of them required additional surgery for retinal detachment, and 2 resolved without intervention. In the control group, 6 eyes experienced postoperative vitreous cavity hemorrhage, of which 4 required reoperation. There was no significant difference between the groups

in rate of hemorrhage.

“Although we were pleasantly surprised by the results,” said Dr. Walia, “these results are consistent with those described in the literature for other antithrombotics such as warfarin, aspirin, and clopidogrel.”

Caveats. Dr. Walia emphasized the need to confer with the patient and prescribing physician about the seriousness of the patient’s thrombotic condition as well as the nature of the ophthalmic condition and imminent surgery. For example, stopping anticoagulants for elective surgeries, such as cataract or epiretinal membrane, may be more practical than for emergency surgeries such as retinal detachment or endophthalmitis, he said. “In cases like these, we don’t have the luxury to stop these drugs prior to surgery.”

Ophthalmologists have not yet

reached consensus on this issue, said Dr. Walia. However, he said, when combined with other data—including metadata comparing NOACs and other antithrombotics—results from this study show that the visual risks of continuing NOACs during vitreoretinal surgery are low, especially when compared with the risks of discontinuation.

—Annie Stuart

1 Grand MG, Walia HS. *Retina*. 2016;36(2):299-304.

Relevant financial disclosures—Dr. Walia: None.

FURTHER READING. Ophthalmologists in other subspecialties must also grapple with the question of NOAC use. For a discussion of considerations in oculoplastic surgery, see “Perioperative Management of Antithrombotics,” *EyeNet*, April 2016.

GLAUCOMA MANAGEMENT

Outreach Reduces Missed Appointments

If you want your glaucoma patients to keep their appointments, a personal phone call and letter can help. It worked for patients in a randomized study at the Wills Eye Hospital Glaucoma Service who received personalized appointment reminders.¹ Those patients (n = 130) were 23% more likely to keep their appointments than patients (n = 126) who did not receive such reminders. Baseline demographics were similar in the 2 study groups: A large majority of the patients were African-American, older than 65 years, and diagnosed with primary open-angle glaucoma.

Low tech, high touch. Appointment adherence is critical to glaucoma care, which is predicated on monitoring disease progression and therapeutic regimen efficacy, the investigators noted. Yet prior to the study, approximately 30% of patients at the participating clinic were lost to follow-up. They either canceled appointments without rescheduling or simply did not show up.

“In our study, a very simple personalized appointment reminder consisting of a brief phone call and letter proved to be a low-cost approach to improve adherence to glaucoma appointments,” said coinvestigator Laura T. Pizzi, PharmD, MPH, applied health economics researcher at Thomas Jefferson University.

Balancing the costs. The study did not address visual outcomes or long-term cost implications, but Dr. Pizzi cited other research estimating that the cost of glaucoma care rises considerably as the disease advances.²

“Assuming one agrees with the assertion that improved adherence to glaucoma care delays long-term consequences, there is an economic argument to be made in support of low-cost adherence reminder programs,” she said. At \$11.32 per patient, such outreach is a worthwhile investment in reducing the long-term cost of vision loss, the researchers suggested.

While a dedicated appointment staff may be too costly for most ophthalmology practices, Dr. Pizzi suggested that existing office staff could be deployed to give personal reminders. In addition, the study assessed different models to potentially lower costs through use of volunteers. “The American health care system is complex and often impersonal,” she said. “This study supports the idea that giving patients personal attention is a powerful motivator toward their engagement in care.”

—Miriam Karmel

1 Pizzi LT et al. *Appl Health Econ Health Policy*. Published online Feb. 29, 2016.

2 Lee PP et al. *Arch Ophthalmol*. 2006;124(1):12-19.

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