

What Is New in the US Pipeline?

A review of compelling technologies not yet available or approved by the FDA.

BY GEORGE O. WARING IV, MD

A number of promising technologies are either entering into or emerging from the US development and regulatory pipeline. These technologies range from therapeutics to diagnostics, all playing an important role in advanced ocular surgery. This article serves to highlight compelling technologies not yet available or approved by the FDA and is not meant to be all-inclusive. Furthermore, note that the innovation and regulatory channels are quite fluid, and technologies change names, designs, and regulatory status daily. Herein is a glimpse of the future.

CORNEAL COLLAGEN CROSS-LINKING

Corneal collagen cross-linking (CXL) has been used for years in Europe to treat patients with keratoectasia (Figure 1). Safety and efficacy data have been published and are well accepted. New technologies and strategies continue to emerge, with the American-European Congress of Ophthalmic Surgery CXL Trial/Avedro, Inc., and the CXL-USA trials actively recruiting or treating patients, among others. The primary indication for CXL is still the stabilization of keratoectasia. Exciting new indications, however, are emerging, including epithelial-on (epi-on) treatments with bio-enhanced riboflavin solutions. Epi-on treatments have the clear benefit of quick recovery and less discomfort and a better safety profile.^{1,2} More comparative evidence is needed to determine efficacy compared to the traditional epithelium-off or epi-off technique, but initial results are promising.^{3,4} “LASIK extra” or combined “limited” cross-linking with LASIK for patients who may be borderline candidates or at higher risk for regression is another exciting new use of cross-linking. Some early evidence from Japan suggests that this



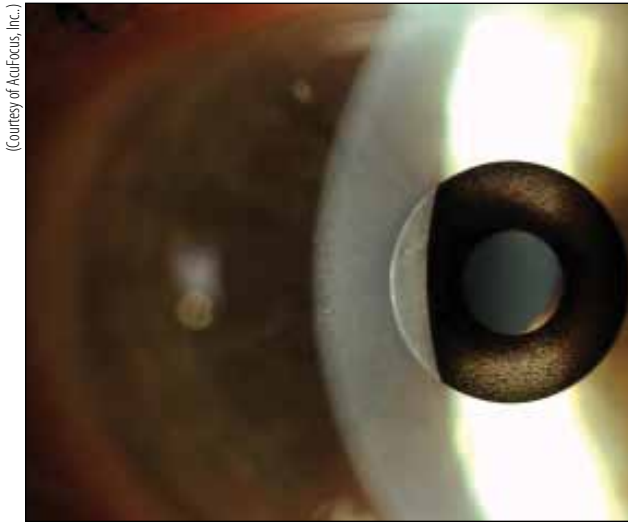
(Courtesy of George O. Waring IV, MD)

Figure 1. Corneal collagen cross-linking.

procedure is safe and may lead to improved refractive stability after LASIK.⁵ Topography-guided customized treatments are also being developed to preferentially treat the most severely affected parts of the cornea. Finite element models have suggested that this may lead to improved corneal shape after cross-linking.

PRESBYOPIC INLAYS

A number of corneal inlays for the surgical management of presbyopia are currently in development or



(Courtesy of AcuFocus, Inc.)

Figure 2. The Kamra intracorneal inlay for the surgical treatment of presbyopia (Courtesy of AcuFocus, Inc.).

under study. These inlays can be implanted through a corneal pocket or under a lamellar corneal flap; all are typically implanted in the nondominant eye. The Kamra intracorneal inlay (AcuFocus, Inc.) is a 5- μ m-thick biocompatible inlay made of polyvinylidene fluoride, inserted under either a lamellar flap or corneal pocket (Figure 2). The inlay has a 1.6-mm central annulus that acts as a pinhole, and its outer diameter is 3.8 mm. This small aperture allows nonbent rays of light to filter through, providing a broad depth of focus. A key benefit of a small aperture inlay is the stability of near and intermediate acuity, despite the progressive nature of presbyopia.⁶

Of the inlays currently being investigated, the Presbia Flexivue Microlens (PresbiTech, Inc.) is the only one to use refractive add power. The hydrophilic acrylic lens is 3 mm in diameter and about 15 μ m in edge thickness. The device is placed in a corneal tunnel in the nondominant eye at a depth of 200 μ m.

The Raindrop (ReVision Optics, Inc.) is a 2-mm-diameter permeable hydrogel lenticule that is implanted under a lamellar flap (about 120-130 μ m depth) in the nondominant eye for the treatment of plano presbyopia. It creates a central steepening for near and intermediate vision, and light rays paracentral to the inlay remain focused on the retina. Distance acuity is minimally affected, as light rays paracentral to the 2-mm inlay remain primarily focused on the retina, particularly with a dilated pupil. Pupillary constriction creates a pseudoaccommodative state, utilizing the steepened central cornea.^{7,8}

“The device is one of the few being developed to measure biomechanical properties of the cornea, an area of great interest to the corneal and refractive surgeon.”

ASTIGMATISM-CORRECTING IOLs

The IOLs in the pipeline warrant an entire article. It is worth mentioning that the AcrySof IQ Restor +3.0 Multifocal Toric IOL (Alcon Laboratories, Inc) has been a mainstay of simultaneous treatment of presbyopia and astigmatism outside the United States since introduced at the European Society of Cataract & Refractive Surgery annual meeting in 2010. Enrollment has been completed for the US FDA trials. The Crystalens toric accommodative IOL (Bausch + Lomb) is in the US regulatory pipeline, and reports from early data are quite encouraging. The Light Adjustable Lens (Calhoun Vision) is a photosensitive silicone IOL that can be adjusted postoperatively to increase or decrease the lens power to correct sphere or astigmatism (by changing power in one axis). Patients undergo routine IOL implantation, and then lens power is adjusted 2 weeks postoperatively. The power can be adjusted, and once on target, the IOL power is “locked in.” Phase 2 trials for myopic correction are complete, and the company is moving toward phase 3 trials for astigmatic adjustments. A central add may be induced in the future to increase spherical aberration for increased depth of focus.

DIAGNOSTICS

The Corvis ST (Oculus Optikgeräte GmbH) is a dynamic tonometer combined with a rotating Schiempflug camera that recently received FDA approval for tonometry and pachymetry, according to the company; the biochemical response feature is not yet available. The device is one of few developed to measure biomechanical properties of the cornea, an area of great interest to the corneal and refractive surgeon. Dynamic videos of corneal deformation with an applied force are generated, and metrics are extrapolated based on a number of biomechanical factors. This device has great potential for evaluating ectatic eyes after cross-linking and potentially for screening for refractive surgery, particularly in patients with subclinical ectasia.

The Salzburg Reading Desk (SRD Vision) represents a new paradigm in diagnostics: functional vision testing. This is one of the first devices of its kind that objectively measures reading speed at different distances. A number of peer-reviewed articles have been published demonstrating the applications and efficacy of the device, and with the emerging subspecialty of surgical correction of presbyopia, devices such as these are likely to become more commonplace.⁹

INFORMATICS

Accelerated Vision has introduced a comprehensive, secure, cloud-based data management and analytics system. Accelerated Vision streamlines data capture, organization, and access with strategies that auto-populate secure online source documents and data files from most digital diagnostic devices and lasers. Full data analysis is available with standardized graphing, and the company also ensures and monitors effective research practices. It is hoped that this will revolutionize data transfer for industry-affiliated clinical research.

CONCLUSION

The future is bright for our industry with plenty of technology in the pipeline for advanced ophthalmic

surgical care. These new devices are poised to improve the patients' (and surgeons') experience and, hopefully, outcomes. ■

George O. Waring IV, MD, is the director of refractive surgery at the Storm Eye Institute and assistant professor of ophthalmology at the Medical University of South Carolina in Charleston. Dr. Waring is also the medical director of Magill Vision Center in Mt. Pleasant, South Carolina. Dr. Waring is a consultant to and on the medical advisory boards of companies mentioned in this article. Dr. Waring may be reached at georgewaringiv@gmail.com.



1. Filippello M, Stagni E, O'Brart D. Transepithelial corneal collagen crosslinking: bilateral study. *J Cataract Refract Surg.* 2012;38(2):283-291. Erratum in: *J Cataract Refract Surg.* 2012;38(8):1515.
2. Leccisotti A. Transepithelial crosslinking. *J Cataract Refract Surg.* 2012;38(9):1706.
3. Zhang ZY, Zhang XR. Efficacy and safety of transepithelial corneal collagen crosslinking. *J Cataract Refract Surg.* 2012;38(7):1304; author reply 1304-1305.
4. Caporossi A, Mazzotta C, Baiocchi S, et al. Transepithelial corneal collagen crosslinking for keratoconus: qualitative investigation by in vivo HRT II confocal analysis. *Eur J Ophthalmol.* 2012;22(Suppl 7):S81-88.
5. Celik HU, Alagöz N, Yildirim Y, et al. Accelerated corneal crosslinking concurrent with laser in situ keratomileusis. *J Cataract Refract Surg.* 2012;38(8):1424-1431.
6. Rasp M, Bachernegg A, Seyeddain O, et al. Bilateral reading performance of 4 multifocal intraocular lens models and a monofocal intraocular lens under bright lighting conditions. *J Cataract Refract Surg.* 2012;38(11):1950-1961.
7. Dexl AK, Seyeddain O, Riha W, et al. Reading performance and patient satisfaction after corneal inlay implantation for presbyopia correction: two-year follow-up. *J Cataract Refract Surg.* 2012;38(10):1808-1816.
8. Dexl AK, Seyeddain O, Riha W, et al. Reading performance after implantation of a modified corneal inlay design for the surgical correction of presbyopia: 1-year follow-up. *Am J Ophthalmol.* 2012;153(5):994-1001.
9. Dexl AK, Schlögel H, Wolfbauer M, Grabner G. Device for improving quantification of reading acuity and reading speed. *J Refract Surg.* 2010;26(9):682-688.