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COVER FEATURE

Corneal collagen crosslinking

Corneal crosslinking's refractive possibilities

by Vanessa Caceres- EyeWorld Contributing Writer

AT A GLANCE

- Data from a clinical trial with Intacs and CXL shows that the combined use can be complementary.
- Topography-guided PRK and CXL has consistently shown good results. However, patients should expect improvements in BSCVA vs. UCVA.
- LASIK combined with concomitant adjunct CXL can possibly improve long-term stability for hyperopes and higher myopes, but requires further study.
- Results from CXL with RK are highly variable.

How this versatile approach fares in combination with refractive procedures

As ophthalmologists in the U.S. continue to celebrate the Food and Drug Administration's (FDA) approval of corneal collagen crosslinking (CXL) for keratoconus, they also look ahead to CXL's use in combination with refractive procedures. The combined uses are not all approved in the U.S. yet. EyeWorld asked ophthalmologists experienced with CXL about its efficacy with several refractive procedures.

Intacs and CXL

Intacs (Addition Technology, Lombard, Illinois; Oasis Medical, San Dimas, California) and CXL have two complementary goals, said Peter Hersh, MD, director, Cornea and Laser Eye Institute, Teaneck, New Jersey; professor, Rutgers Medical School, Piscataway, New Jersey; and visiting research collaborator, Princeton University, Princeton, New Jersey. "The goal of Intacs is to decrease the cone height and make the corneal topography more regular to improve spectacle-corrected vision and contact lens wear," Dr. Hersh said. The goal of CXL is to strengthen the corneal biomechanics to decrease the progression of keratoconus and corneal ectasia. In studies led by Dr. Hersh, there was about a 1.6 D improvement in corneal topography 1 year after CXL; most patients stabilize rather than improve their corneal topography. "Thus, the goals of Intacs and CXL are different and potentially complementary," he said. The best candidates for Intacs are patients who are contact lens intolerant and who have poor spectacle-corrected vision; the best CXL candidates are those who have progressive keratoconus and want to limit further deterioration. A randomized clinical trial underway by Dr. Hersh and colleagues is looking at the results of Intacs and CXL and whether it is better to use Intacs first and perform CXL 3 months later, or if the procedures should be performed on the same day. "We are carrying out formal data analysis, but results to date do suggest the procedures complement each other," he said. "Most patients have seen their keratoconus stabilize after the procedures, and Intacs have substantially improved corneal topography." So far, the data do not show a major difference between the simultaneous versus sequential Intacs/CXL groups, Dr. Hersh added.

John Kanellopoulos, MD, medical director, Laservision.gr Eye Institute, Athens, and clinical professor of ophthalmology, New York University Medical School, New York, said that although combining Intacs and CXL does not have much long-term evidence of stability yet, he does see some potential promise in the concept. "It probably makes sense to place the Intacs first in a biomechanically 'fluid,' cornea, and then perform

collagen crosslinking, either within the same treatment or following a certain amount of time to lock in the cornea shape change in these eyes,” he said. The use of a plastic foreign material in the cornea has been associated with some serious complications, Dr. Kanellopoulos said. However, he thinks that clinicians could further study an allograft or recombinant collagen version to help achieve long-term stability and efficacy. “The combination of CXL either as a primary procedure in these theoretical allograft Intacs- like implants or in the diseased cornea may be a fruitful adjunct treatment,” he said.

CXL and topography-guided partial PRK

Since introduction of the Athens protocol in 2005, Dr. Kanellopoulos and colleagues have used topography-guided partial PRK and CXL to reduce significant corneal irregularity. “This is our preferred technique for mild, moderate, and even advanced keratoconus, and sometimes in patients who are contact lens intolerant and have a corneal thickness of 370 microns and higher at the thinnest cornea point,” he said. “We have found that the best outcomes are in patients who have a dioptric difference of 10 D or less across the cornea,” said Raymond Stein, MD, medical director, Bochner Eye Institute, and associate professor of ophthalmology, University of Toronto, Toronto, Ontario. “This allows for flattening of the steep area by 5 D or less and steepening of the flat area by 5 D or less.” Topography-guided PRK combined with CXL has shown the greatest improvement in best spectacle-corrected visual acuity (BSCVA) compared with CXL alone, Dr. Stein added. However, surgeons must explain to patients that the goal is better BSCVA and not uncorrected visual acuity (UCVA), as patients still typically need correction with glasses or soft contact lenses, he added.

In a study of topography-guided PRK and CXL led by Simon Holland, MB, FRCSC, Pacific Laser Eye Centre, Vancouver, British Columbia, and David T.C. Lin, MD, medical director, Pacific Laser Eye Centre, two-thirds of post-LASIK ectasia patients had a 20/40 or better UCVA with the Schwind Amaris laser (Schwind Eye-Tech-Solutions, Kleinostheim, Germany), and nearly half had the same result with the WaveLight Allegretto laser (Alcon, Fort Worth, Texas). Side effects such as delayed epithelialization, haze, and progression were rare, Dr. Holland said.

Their studies show this approach as a potentially effective treatment for contact lens intolerant patients, Drs. Holland and Lin concluded. Although there were similar results with both devices, the Schwind Amaris laser had advantages with iris tracking, cyclotorsion control, and image capture.

Dr. Holland said he and Dr. Lin have performed about 1,200 topography-guided cases in the past 7 years.

The only drawback that Dr. Kanellopoulos has found is that topography-guided PRK and CXL addresses more anterior corneal surface normalization than posterior cornea surface normalization.

LASIK and concomitant adjunct CXL

The use of LASIK and concomitant adjunct CXL—known commercially as LASIK Xtra (Avedro, Waltham, Massachusetts)—was introduced by Dr. Kanellopoulos and colleagues in 2009. It combines a higher fluence CXL in routine LASIK cases; he has used it since then in higher-risk cases, which are usually younger myopic patients with an almost borderline residual corneal thickness of at least 300 microns under the stromal bed following ablation. This approach has led to more stability for higher myopes as well as a better epithelium remodeling profile and an ex vivo increase in biomechanical stability of the residual stroma by 100%. Yet, “Under no means does the procedure justify treating with LASIK form fruste keratoconic cases or cases that result in residual stromal bed of less than 300 microns, in my opinion,” he cautioned. Although LASIK Xtra is not approved in the U.S., Dr. Hersh does see some valuable safety goals from it: strengthening of the cornea and improving long-term stability outcomes. “It can be viewed as an extra safety element in patients who may have some theoretically greater risk, such as those who have thinner corneas and those who have higher degrees of correction,” Dr. Hersh said. Clinical experience from Dr. Kanellopoulos has also described a

potential adjunct utility for LASIK Xtra in hyperopic patients. He and co-authors have reported since 2011 long-term stability of the corneal steepening achieved with hyperopic LASIK in the eyes that had hyperopic LASIK Xtra. The LASIK Xtra eyes proved more stable over the first 2 years following their correction compared with the contralateral eyes that had hyperopic LASIK alone. The latter eyes showed progressive flattening over 1 to 2 years of 1 to 2 D and recurrence of hyperopia.

Dr. Stein said he does not perform LASIK and concomitant adjunct CXL. “The incidence of ectasia is rare today with proper screening that evaluates the anterior curvature, posterior elevation, and a corneal thickness map. On cases of questionable keratoconus in patients over 40 that have thick corneas, I perform PRK and limited CXL,” he said.

Further studies should focus on the clinical situations in which LASIK Xtra would be most helpful, Dr. Hersh said.

CXL and radial keratotomy

The use of radial keratotomy (RK) and CXL does seem to provide some stability in diurnal fluctuation, Dr. Kanellopoulos said. “In cases where a through-cornea incision and a large epithelial plug are present, the actual CXL treatment may exaggerate the hyperopic effect by ‘stretching out’ the cornea incisions, which may be considered a disadvantage as far as the refractive error,” he said. However, the stabilization in diurnal fluctuation can be a first step to follow a PRK or LASIK procedure that would further correct the refractive error. Dr. Kanellopoulos acknowledged that this can be a challenging patient set. “Our results with follow-up of up to 9 years have been highly variable,” Dr. Stein said. “The best outcomes are in patients who have had four to eight incisions. In general, patients with 12 to 16 cuts do not do well with CXL in stabilizing their diurnal fluctuation.” The use of RK with CXL is also not approved in the U.S., Dr. Hersh said, and would benefit from further study regarding its potential effectiveness.

Editors’ note: Dr. Hersh has financial interests with Avedro. Dr. Holland has financial interests with Alcon, Allergan (Dublin), and Clarion Medical Technologies (Cambridge, Ontario). Dr. Kanellopoulos has financial interests with Alcon, Allergan, Avedro, and other ophthalmic companies. Dr. Stein has no financial interests related to his comments.

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