Preventing Ectasia With Cross-linking After PRK or LASIK

Prophylactic cross-linking stabilizes the cornea and promotes the success of laser refractive surgery.

BY A. JOHN KANELLOPOULOS, MD

Corneal collagen cross-linking (CXL) has been established as an effective surgical treatment to increase the biomechanical stability of the cornea. Surgeons first used the procedure to treat idiopathic keratoectasia such as keratoconus and pellucid marginal degeneration and also iatrogenic ectasia such as post-LASIK ectasia and more rare forms of post-PRK ectasia. Five years ago, my team in Athens, Greece, introduced the concept of performing prophylactic, high-fluence CXL after LASIK or PRK.

IMPETUS

During the past 10 years, I have had the opportunity to practice internationally as well as in New York City. I have been struck by the high prevalence of keratoconus in the Eastern Mediterranean. In my experience, one in every 100 to 200 young men in Greece has some form of clinical or subclinical keratoconus (vs a reported incidence of 1:2,000 in the United States). For the past several years, it has been routine in my practice for the siblings of patients who have undergone a successful LASIK procedure to undergo an evaluation. To my surprise (and terror), many of them have overt topographic keratoconus. This finding naturally made me anxious about my LASIK patients’ future. Their preoperative examinations were normal, but they might have been at an age when the biomechanical stability of the cornea had not been fully established. Moreover, I have reviewed evidence from John Marshall, PhD (personal communication, 2011), that performing refractive surgery, especially LASIK, reduces the biomechanical stability of the cornea by about 20%, mainly due to the vertical interruption of anterior corneal lamellae. It therefore was a logical next step for my team and me to employ CXL as a prophylaxis in what I

Figure 1. The surgeon has repositioned the LASIK flap. After soaking with riboflavin, the stroma has acquired a yellow tinge.

Figure 2. Optical coherence tomography after LASIK shows hyper-reflective evidence of CXL around the flap interface.
considered to be high-risk LASIK or PRK cases.

I arbitrarily categorize as high-risk LASIK cases those involving patients under 25 years of age who have a refractive error of greater than 6.00 D, patients who have more than 1.00 D of astigmatism, and patients who have greater than 0.50 D of asymmetry in the astigmatism of their two eyes. Obviously, I consider patients who have a first- or second-degree relative with documented keratoconus to be high risk. I should note that these criteria are applied to patients with normal corneal topography and tomography. I am not considering the combined procedure for patients with forme fruste keratoconus or other corneal irregularities. Additionally, I require a residual stromal bed of at least 350 µm for LASIK.

With regard to PRK, I perform prophylactic CXL based on the aforementioned criteria but also on corneas that have the appearance of forme fruste keratoconus and those with a preoperative thickness below 500 µm.

PROCEDURES AND EARLY RESULTS
CXL Combined With LASIK

My protocol for prophylactic CXL, when combined with LASIK or PRK, was to use about one-half to one-third of the classic Dresden protocol. The specifics of my approach to combined prophylactic CXL and LASIK in my study are as follows.

After completing the LASIK ablation, I placed one drop of 0.1% riboflavin sodium phosphate on the stromal bed and waited 1 minute while taking care not to soak the folded flap. I then repositioned the LASIK flap and thoroughly irrigated the residual riboflavin from the eye, after which I applied 10 mW/cm² of high-fluence ultraviolet (UV) light (Figure 1).

Prophylactic CXL minimally affected my LASIK nomogram. Patients’ visual rehabilitation was immediate, and I encountered no complications. Of course, the amount of rigidity restored to the eye after the LASIK procedure is difficult to measure, although the eyes that underwent combined LASIK and CXL have thus far required fewer retreatments. The follow-up period now extends to 5 years.

Optical coherence tomography has demonstrated hyper-reflective activity (100-150 µm) over and, to a greater degree, under the LASIK flap in the eyes that have undergone CXL after LASIK (Figure 2). In addition, optical coherence tomography has revealed a diminution of the clear space typically observed within the flap interface, a finding that suggests better adhesion of the flap to the interface. Anecdotally, I have found it more difficult to relift the flap after combined LASIK-CXL procedures than after LASIK alone (http://www.youtube.com/watch?v=onup8JWRUN8).

Recently, my colleagues and I reported the results of a long-term, randomized study of prophylactic CXL combined with hyperopic LASIK in one of the patients’ two eyes (Figures 3-5). Since our initial work, we have...
CXL Combined With PRK

I have published my approach to combining CXL and PRK.8 My results with combined PRK-CXL have been similar to mine with combined LASIK-CXL.

Over the years, I have found that CXL can also be used to modulate corneal scarring after PRK. CXL (Continued on page 54)
(Continued from page 52)
decreases the number of keratocytes, which slowly repopulate the cornea during the first 3 to 6 months after PRK.\textsuperscript{9} This effect was also evident in a study of topography-guided PRK performed sequentially with versus on the same day as CXL for the treatment of keratoconus.\textsuperscript{8}

CONCLUSION
The indications for CXL seem to be expanding dramatically. In my clinical practice, I have routinely used prophylactic CXL in high-risk LASIK cases. Refractive surgeons' performance of CXL after hyperopic LASIK may also become routine for reducing long-term flattening of the cornea and, thus, hyperopic regression. In addition, CXL is proving effective at decreasing corneal scarring after PRK.

Our investigative team in Athens has been working on using verteporfin (Visudyne; Novartis AG) instead of riboflavin as a CXL photosensitizer (Figure 6). The beauty of this potential application would be that verteporfin is sensitized by red rather than UV light and that the FDA has approved the drug, although this use would be off label.

Note: The FDA has not approved CXL or topography-guided laser refractive surgery.

A. John Kanellopoulos, MD, is the director of the LaserVision.gr Eye Institute in Athens, Greece; an attending surgeon at the Department of Ophthalmology, Manhattan Eye, Ear, and Throat Hospital in New York; and a clinical professor of ophthalmology at New York University Medical School in New York. He is a consultant to Alcon Laboratories, Inc.; Avedro, Inc.; Seros Medical, LLC; and WaveLight Laser Technologie AG. Dr. Kanellopoulos may be reached at +30 21 07 47 27 77; ajkmd@mac.com.