Point/Counterpoint: My Ideal Ablation Pattern for Combined CXL Treatments

Surgeons share their preferred methods to combine laser and CXL.

BY A. JOHN KANELLOPOULOS, MD, AND LEOPOLDO SPADEA, MD

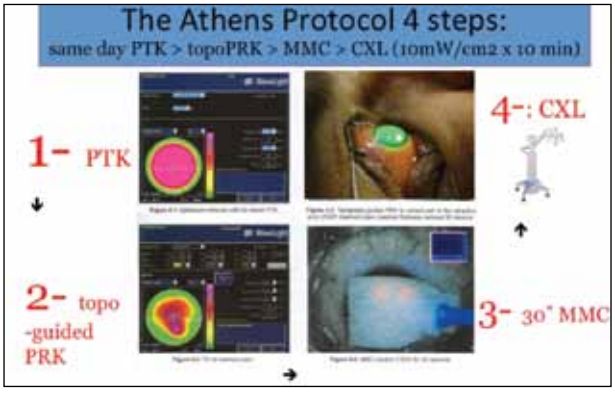
The Athens Protocol: Topography-Guided Partial PRK With CXL

An effective way to stabilize and visually rehabilitate patients with keratoconus and post-LASIK ectasia.

By A. John Kanellopoulos, MD

Our investigative team at the Laser Vision Eye Institute has studied the clinical application of corneal collagen cross-linking (CXL; not approved for use in the United States) in patients with keratoconus and post-LASIK ectasia for more than 10 years and in more than 2,000 eyes.[1-29] We introduced the use of CXL through a femtosecond laser-created intrastromal corneal pocket,[3,6] the use of higher-fluence CXL,[3,5-12,14,15,21,26] and the use of CXL prophylactically in myopic LASIK and as an efficacy booster in hyperopic LASIK.[14,21] Most recently, we introduced the use of high-fluence CXL in femtosecond laser-assisted astigmatic keratotomy procedures in order to enhance the effect and/or reduce the incision arc.[30]

Our biggest contribution to the global ophthalmic community, however, may be the introduction of topography-guided (not available in the United States) normalizing surface ablation plus CXL as a visual rehabilitation tool.[2] The concept of ablating a thin, ectatic cornea usually generates fear in surgeons and patients alike. Nevertheless, we have found that the apparent disadvantage of thinning the cornea is accompanied by remarkable vision-rehabilitating improvement and synergy from the CXL component.



(All figures courtesy of A. John Kanellopoulos, MD.)

Figure 1. The basic steps of the Athens protocol. The photherapeutic keratectomy (PTK) treatment plan on the WaveLight platform (1). Following PTK, areas of Bowman membrane have been ablated, confirming that the epithelium over the cone is thinner (2). Mitomycin C is applied (3) prior to the riboflavin and CXL (4).

We initially performed topography-guided partial PRK in patients who showed stabilization after CXL but had poor visual rehabilitation due to remaining significant corneal irregularity. Soon, however, we began to perform both treatments on the same day, with topography-guided PRK applied first, followed immediately by high-fluence CXL. With 1 to 3 years of follow-up in many cases, the BCVA gains achieved by most patients were impressive. Hundreds of cases followed, and we reported the results and complications in large groups of patients treated with this protocol for keratoconus and post-LASIK

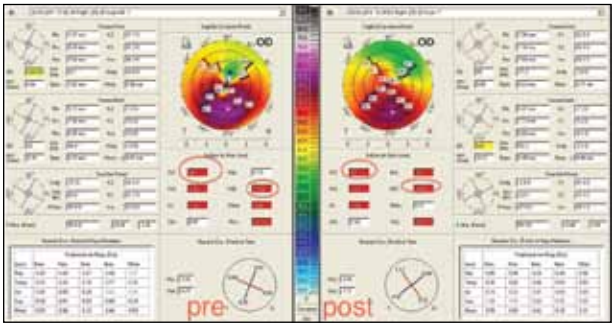


Figure 2. Improvement of topometric indices before and after treatment with the Athens protocol.

Figure 3. The right eye of a 27-year-old man with advanced keratoconus. Preoperative BCVA was 20/50 with refraction of -2.50 -5.00 × 80. After application of the Athens protocol, the patient achieved a UCVA of 20/30 and BCVA of 20/20 with -1.00 -1.50 × 85. The slit-lamp photograph shows the corneal clarity and ground-glass appearance typical of CXL-treated eyes.

Figure 4. Anterior segment optical coherence tomography (OCT) of the same eye 7 months after the Athens protocol. One can appreciate the anterior cornea hyperreflectivity consistent with CXL and the demarcation line at about 300-µm depth depicting the depth of effective CXL. Clinicians familiar with these findings following CXL alone may appreciate the enhanced depth and wider diameter of the CXL effect noted on the OCT images following the Athens protocol.

ectasia.[26] Several esteemed colleagues have also presented similar approaches of combined PRK and CXL.

Our findings suggest that simultaneous topography-guided partial PRK with CXL offers a safe and effective approach for normalizing the cornea and enhancing visual function in eyes with ectatic conditions. The core importance of CXL in this technique is to address highly irregular astigmatism in eyes with keratoconus and post-LASIK ectasia. Our theoretical and clinical evidence supports the use of this technique, dubbed the *Athens protocol*, in which CXL and topography-guided surface ablation are performed in the same session rather than sequentially (Figure 1).

In our experience, surface ablation using a topography-guided excimer laser platform (Allegretto Wave 200-Hz and 400-Hz models and recently the WaveLight EX500; all from Alcon Laboratories, Inc.) effectively and predictably normalizes the corneal surface and improves functional vision. We have documented a synergistic effect when this procedure is performed simultaneously with CXL. Safety with this combination approach has been favorable as well. The minor complications of postoperative haze and delayed epithelial healing have occurred in a small number of eyes in our large series.[26]

MEETING VISUAL REHABILITATION NEEDS

Although the efficacy of CXL for stabilizing keratectasia is well established and the procedure causes some corneal flattening, significant residual astigmatism that limits effective soft contact lens or spectacle wear may be a persistent problem for patients who are unable to wear rigid gas permeable contact lenses. This situation creates an indication to perform subsequent topography-guided partial PRK or to implant intrastromal corneal ring segments (ICRS). The latter option is used by some colleagues but in our hands has very variable efficacy and may be counterintuitive, as the main mechanism of action of the ICRS relies on high elasticity of the cornea. The stiffening effect of CXL may make these eyes poor responders to subsequent ICRS implantation.

Surface ablation of a keratoconic eye may sound unorthodox, but the goal of using topography-guided software is to normalize the corneal surface and improve BCVA. This is a therapeutic procedure in our opinion, not a refractive one; in fact, some eyes become more myopic postoperatively but have significantly better corneal regularity and improvement in BCVA. We have chosen to remove no more than 50 µm of stroma, which at most usually treats 2.00 to 2.50 D of astigmatism and up to 1.00 D of myopia.

The pivotal element in this technique is the proprietary WaveLight topography-guided platform that utilizes Placido disc images and/or Pentacam Comprehensive Eye Scanner (Oculus Optikgeräte GmbH) tomographic maps to calculate a treatment consisting of combined myopic and hyperopic subsegments to normalize the irregular

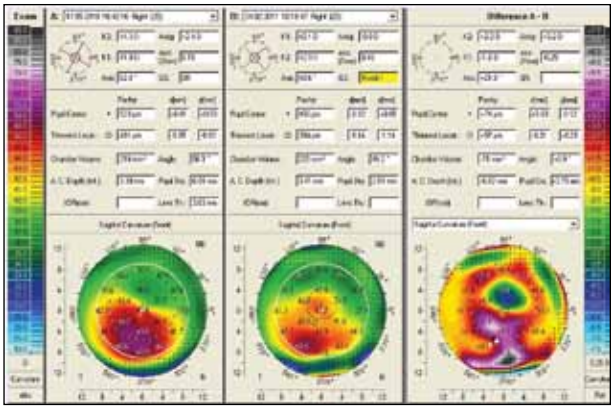


Figure 5. Pentacam images preoperatively (left) and 7 months postoperatively (center), showing significant normalization of the cone, keratometric flattening, and improved symmetry. Difference map is at right.

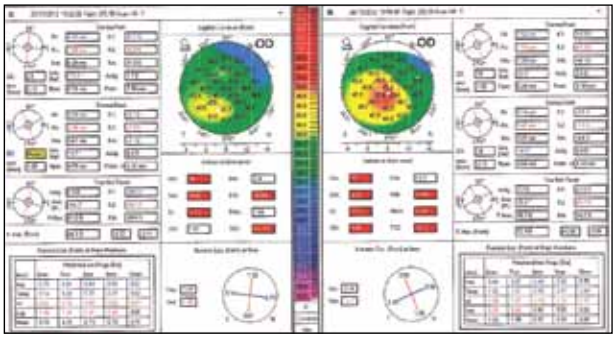


Figure 6. Topometric comparison of postoperative (left) and preoperative (right) tomographic maps of an eye with keratoconus treated with the Athens protocol by Dr. Baddar.

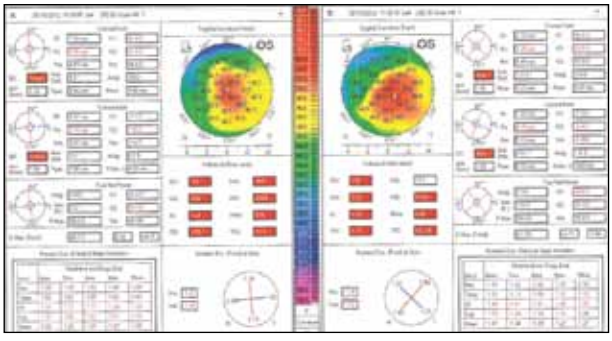


Figure 7. Similar images of the left fellow eye of the same keratoconus patient treated with Ferrara Rings and CXL by Dr. Baddar's team. Note improvements in the index of high decentration and index of surface variance. Nevertheless, this patient and most of the 25 patients enrolled in this comparison study preferred their Athens protocol-treated eye due to better quality of vision and lesser discomfort. Eyes treated with ICRS and CXL recovered much faster.

corneal surface. We are currently reviewing long-term results of a very large case series (more than 500 cases) to determine which modality is more effective, and the preliminary data suggest the Pentacam-driven platform. Experience has taught us that visual function in these cases correlates closely with two main topometric corneal indices, the index of high decentration and the index of surface variance. The aim of these treatments is improve these two indices of ectasia-related topometric irregularity (Figure 2).

ATHENS PROTOCOL

The Athens protocol begins with a 6.5-mm PTK to remove 50 µm of epithelium. Then topography-guided partial PRK is performed. The topography reference image for this application is generated by the Oculyzer II (a Pentacam HR-based tomographic capture device; Alcon Laboratories, Inc.). The excimer laser ablation resembles part of a hyperopic treatment combined with part of an eccentric myopic treatment over the cone. It is performed using a 5.5-mm effective optical zone and targets steepening of the area adjacent to the cone in an attempt to regularize the corneal surface.

Mitomycin C (0.002 mg/mL) is applied for 30 seconds, followed by our version of the CXL procedure. Ultraviolet A (UVA) light is applied at 5-mW fluence for 18 minutes with our own riboflavin solution formulated with 0.1% sodium phosphate, slightly hypotonic (prepared in the United States by Leiter's Pharmacy). This part of our technique was designed with CXL expert Satish Herekar, MS, a science fellow with Avedro, Inc. For a video of the surgical technique, visit http://tinyurl.com/d6up9mu. The corneal epithelium and Bowman membrane can act as barriers to UVA light penetration into the stroma. Because these tissues are removed in the PTK and/or PRK procedure, it seems intuitive that the efficacy of CXL would increase; our clinical findings support this theory. For example, in a patient who had CXL alone in one eye and the Athens Protocol in the other, OCT hyperreflectivity maps show that the area of crosslinking is much broader and denser in the eye that received the combination treatment (Figures 3 and 4). We recently described these OCT maps as a sign of the extent of CXL.[24]

We also theorized that a PRK-treated eye represents a better biomechanical model for performing CXL (Figure 5). In theory, an eye with a regularized surface, as opposed to one in which there is ongoing strain from intraocular pressure and eye rubbing localized over the cone's peak, would be better strengthened by CXL and more likely to remain stable after the procedure.

We believe redistribution of corneal strain by remodeling of the cornea with surface ablation is a significant factor in

the synergistic effect achieved when performing PRK and CXL together. The order of treatment in the Athens protocol also avoids removing cross-linked cornea, as would occur if CXL were performed first followed by PRK.[22]

CLINICAL DATA

In a comparison of two large, consecutive series of eyes treated either with PRK and CXL at the same session or with CXL first followed by topography-guided surface ablation 1 year later, statistically significant differences in several outcome parameters favored the same-day procedure. The study included 127 eyes in the sequential group and 198 eyes treated with the Athens protocol.[5]

In the sequential group, mean logMAR UCVA improved from 0.90 to 0.49, and mean logMAR BCVA improved from 0.41 to 0.16. Mean keratometry reading decreased by 2.75 D and mean manifest refraction spherical equivalent by 2.50 D. The mean postoperative haze score was 1.2. For eyes in the simultaneous group, there was a significantly greater improvement in mean logMAR UCVA (from 0.96 to 0.30) and mean logMAR BCVA (from 0.39 to 0.11) as well as a significantly greater mean reduction in manifest refraction spherical equivalent (-3.20 D) and keratometry (-3.50 D). The mean haze score in the simultaneous group was 0.5, which was significantly lower than the control group's score. Central corneal thickness decreased by 70 µm after both procedures, and there was no significant change in endothelial cell count in either group.

These findings show that performing the two procedures in the same session offers the advantages of less PRK-associated scarring and better riboflavin and UVA penetration to achieve a wider and deeper CXL effect with greater corneal flattening.

ATHENS PROTOCOL VERSUS ICRS

Sherif Baddar, MD, of Cairo, Egypt, is conducting an interesting study as a postdoctoral thesis, evaluating the outcomes of patients with keratoconus who are treated with the Athens Protocol in one eye and ICRS implantation (Ferrara Rings; Ferrara Ophthalmics) and CXL in the fellow eye. Preliminary results show improvements in both groups, although BCVA and the index of height decentration improvement appear to be significantly better in the Athens protocol group (Figures 6 and 7).

CONCLUSION

In our experience, same-day, simultaneous topography-guided PRK and CXL is a safe and effective therapeutic intervention in highly irregular corneas with keratoconus and progressive post-LASIK ectasia. The Athens protocol appears to be superior to sequential CXL and PRK.

A. John Kanellopoulos, MD, is the director of the LaserVision.gr Eye Institute in Athens, Greece, and is a clinical professor of ophthalmology at New York University School of Medicine. He is a consultant to Alcon Laboratories, Inc., and Avedro, Inc. Dr. Kanellopoulos may be reached at +30 21 07 47 27 77; ajkmd@mac.com.

1. Hafezi F, Kanellopoulos AJ, Wiltfang R, Seiler T. Corneal collagen crosslinking with riboflavin and ultraviolet A to treat induced keratectasia after laser in situ keratomileusis. *J Cataract Refract Surg*. 2007;33:2035-2040.
2. Kanellopoulos AJ, Binder PS. Collagen cross-linking (CCL) sequential topography-guided PRK: a temporizing alternative for keratoconus to penetrating keratoplasty. *Cornea*. 2007;26(7):891-895.
3. Krueger RR, Ramos-Esteban JC, Kanellopoulos AJ. Staged intrastromal delivery of riboflavin with UVA cross-linking in advanced bullous keratopathy: laboratory investigation and first clinical case. *J Refract Surg*. 2008;24(7):730-736.
4. Hayes S, Kamma-Lorger CS. Corneal collagen cross-linking in bullous keratopathy. *J Refract Surg*. 2009;25(8):687; author reply [Kanellopoulos] 687-688.
5. Kanellopoulos AJ. Comparison of sequential vs same-day simultaneous collagen cross-linking and topography-guided PRK for treatment of keratoconus. *J Refract Surg*. 2009;25(9):812-818.
6. Kanellopoulos AJ. Collagen cross-linking in early keratoconus with riboflavin in a femtosecond laser-created pocket: initial clinical results. *J Refract Surg*. 2009;11:1034-1038.
7. Krueger RR, Kanellopoulos AJ. Stability of simultaneous topography-guided photorefractive keratectomy and riboflavin/UVA cross-linking for progressive keratoconus: case reports. *J Refract Surg*. 2010;26(10):827-832.
8. Kanellopoulos AJ, Skouteris V. Secondary ectasia due to forceps injury at childbirth: management with combined topography-guided partial PRK and collagen cross-linking (Athens Protocol) and subsequent phakic IOL implantation. *J Refract Surg*. 2011;27(9):635-636.
9. Kanellopoulos AJ, Binder PS. Management of corneal ectasia after LASIK with combined, same-day, topography-guided partial transepithelial PRK and collagen cross-linking: The Athens Protocol. *J Refract Surg*. 2011;27(5):323-331.
10. Kanellopoulos AJ. Long-term results of a prospective randomized bilateral eye comparison trial of higher fluence shorter duration ultraviolet A radiation, and riboflavin collagen cross linking for progressive keratoconus. *Clin Ophthalmol*. 2012;6:97-101.
11. Kanellopoulos AJ. The management of cornea blindness from severe corneal scarring, with the Athens Protocol (transepithelial topography-guided PRK therapeutic remodelling, combined with same-day, collagen cross linking). *Clin Ophthalmol*. 2012;6:87-90.
12. Kanellopoulos AJ. Laboratory evaluation of selective in situ refractive cornea collagen shrinkage with continuous wave infrared laser combined with transepithelial CXL: a novel refractive procedure. *Clin Ophthalmol*. 2012;6:645-652.
13. Kanellopoulos AJ, Aslanides I, Asimellis G. Correlation between epithelial thickness in normal corneas, untreated ectatic corneas, and ectatic corneas previously treated with CXL; is overall epithelial thickness a very early ectasia prognostic factor? *Clin Ophthalmol*. 2012;6 789-800.
14. Kanellopoulos AJ. Long-term safety and efficacy follow-up of prophylactic higher fluence collagen cross-linking in high myopic laser-assisted in situ keratomileusis. *Clin Ophthalmol*. 2012;6:1125-1130.
15. Kanellopoulos AJ. Cross-linking plus topography-guided PRK for post-LASIK ectasia management. In: Garg A, Alio JL, Lin JT, et al, eds. *Mastering Advanced Surface Ablation Techniques*. New Delhi: Jaypee Brothers; 2007:204-214.
16. Kanellopoulos AJ. PRK and C3-R. In: *Modern Management of Keratoconus*. Boxer Wachler BD, ed. New Delhi: Jaypee Brothers; 2007:219-228.
17. Kanellopoulos AJ. Cross-linking plus topography-guided PRK for post-LASIK ectasia management. In: Garg A, Rosen E, eds. *Instant Clinical Diagnosis in Ophthalmology Refractive Surgery*. New Delhi: Jaypee Brothers; 2008:258-269.
18. Kanellopoulos AJ. Cross linking plus topography guided PRK for post-LASIK ectasia management. In: Garg A, Pinelli R, O'Brart D, Lovisolo CF, eds. *Mastering Corneal Collagen Cross-linking Techniques (C3- CCL/CxL)*. New Delhi: Jaypee Brothers; 2008:69-80.
19. Kanellopoulos AJ. Simultaneous collagen crosslinking (CXL) and topography-guided PRK (tPRK) for keratoconus (KCN). In: Garg AI, Alio JL, eds. *Surgical Techniques in Ophthalmology: Refractive Surgery*. Panama: Jaypee-Highlights; 2009: 60-63.
20. Kanellopoulos AJ. In-flap simultaneous collagen crosslinking (CXL) and topography-guided (tPRK) for early post-LASIK ectasia - a novel technique. In: Garg A, Alio JL, eds. *Surgical Techniques in Ophthalmology: Refractive Surgery*. Panama: Jaypee-Highlights; 2009:233-236.
21. Kanellopoulos AJ. Prophylactic collagen crosslinking in high risk femtosecond assisted-LASIK: a novel technique. In: Garg A, Alio JL, eds. *Surgical Techniques in Ophthalmology: Refractive Surgery*. Panama: Jaypee-Highlights; 2009:423-426.
22. Kanellopoulos AJ. Simultaneous prophylactic collagen cross-linking (CXL) following high-risk topography-guided PRK (tPRK). In: Garg A, Alio JL, eds. *Surgical Techniques in Ophthalmology: Refractive Surgery*. Panama: Jaypee-Highlights; 2009:427-430.
23. Kanellopoulos AJ. Simultaneous collagen cross-linking (CXL) and topography-guided PRK (tPRK) for keratoconus (KCN). In: Garg A, Alio JL, eds. *Surgical Techniques in Ophthalmology: Corneal Surgery*. Panama: Jaypee- Highlights; 2009:18-21.
24. Kanellopoulos AJ. The Athens protocol: PRK and CXL. In: Burratto L, ed. *PRK: Present, Past and Future*. Thorofare, NJ: Slack Incorporated; 2012:85-88.
25. Kilic A, Kanellopoulos AJ. Corneal crosslinking treatment and femtosecond laser pocket. In: Garg A, Alio JL, eds. *Femtosecond Laser Techniques & Technology*. Panama: Jaypee-Highlights; 2012:34-37.
26. Kanellopoulos AJ, Cho M. Complications with the use of collagen cross-linking. In: Agarwal A, Jacob S, eds. *Complications in Ocular Surgery*. Thorofare, NJ: Slack Incorporated; 2012:115-120.
27. Kanellopoulos AJ. Post-LASIK ectasia management. *Cataract & Refractive Surgery Today Europe*. May/June 2006;(3):40-42.
28. Karmel M. Collagen cross-linking: new applications emerging but U.S. studies falter. *Eyenet*. 2010; 39-43.
29. Kanellopoulos AJ. Minor complications can occur with collagen cross-linking. *Ocular Surgery News*. 2011. http://tinyurl.com/brew69k
30. Bourdou S, Kanellopoulos AJ. Reduced cylinder with femtosecond laser-assisted cataract surgery: a contralateral eye study. Poster presented at: American Academy of Ophthalmology Annual Meeting, Refractive Surgery Subspecialty Day; November 9-10, 2012; Chicago, IL.

(All figures courtesy of Leopoldo Spadea, MD.)

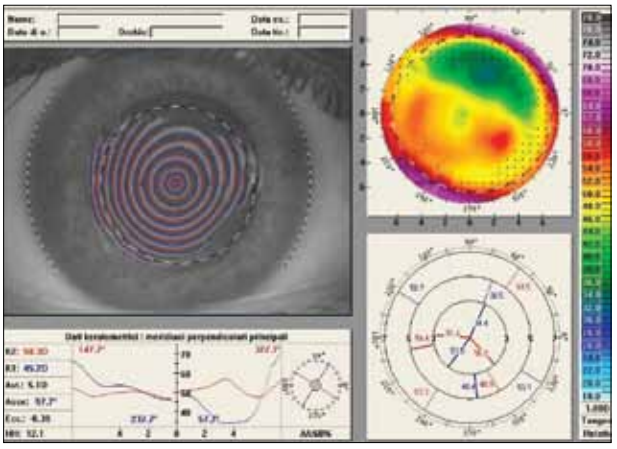


Figure 1. Videokeratographic map of a right eye before the treatment. The topographic pattern highlights irregular astigmatism (relative scale, tangential algorithm).

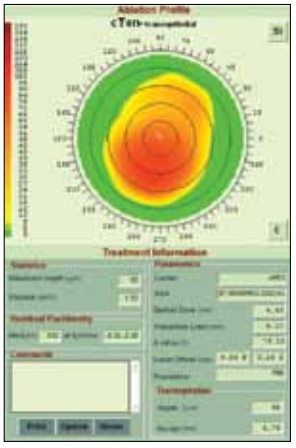


Figure 2. Pattern of transepithelial customized ablation.

The Ideal Ablation Pattern for Combined Treatments: CXL Plus PRK

Customized ablation and cross-linking can stabilize the cornea after lamellar surgery.

By Leopoldo Spadea, MD

Conventional excimer laser surface ablation has shown efficacy in visual rehabilitation of eyes with very irregular corneas after lamellar keratoplasty. However, postoperative complications such as unpredictable refractive outcome, refractive regression, and corneal haze are commonly seen, limiting the use of noncustomized PRK in these eyes.[1] Excimer laser customized ablation shows promise to be a powerful technique to treat such corneal irregularities.

Corneal ectasia after lamellar keratoplasty has occasionally been reported, but its incidence has not been assessed. Corneal collagen cross-linking (CXL) induced by application of riboflavin and ultraviolet A (UVA) light has been shown to increase the biomechanical stability of corneas with lamellar flaps, arresting and even partially reversing iatrogenic keratectasia after LASIK.[2]

Keratoconus is a degenerative disorder in which the cornea thins and steepens, affecting vision. For many years, full-thickness keratoplasty was the principal surgical treatment for patients with advanced keratoconus, but more recently, lamellar corneal approaches have been advocated as less invasive surgical alternatives. One of these, excimer laser-assisted lamellar keratoplasty (ELLK), has been proposed to augment thin corneas in keratoconus and keratectasia after LASIK.[3]

Some time ago, we saw one patient who developed corneal ectasia after ELLK for keratoconus and a secondary PRK for residual refractive correction.[4] In this 33-year-old woman, CXL resulted in improvement of visual acuity and preservation of a clear lamellar graft with 2 years' follow-up.

To further assess this therapeutic combination of CXL and PRK as a prophylaxis against ectasia after lamellar keratoplasty, we conducted a larger study.[5] This study evaluated the efficacy, predictability, safety, and stability of the combined treatment of customized excimer laser PRK and prophylactic CXL for residual refractive error in 14 patients previously treated with ELLK for keratoconus (Figure 1). The aim was for customized PRK to regularize the central cornea and CXL to strengthen and stabilize the cornea in these eyes.

SURGICAL TECHNOLOGY

The iVis Suite integrated platform (iVis Technologies; not available in the United States) was used to perform customized excimer laser PRK. The platform consists of surgical planning software (Central Corneal Regularization [CCR]), a corneal morphology data source (Precisio), and a high-frequency excimer laser (iRES; all from iVis Technologies).

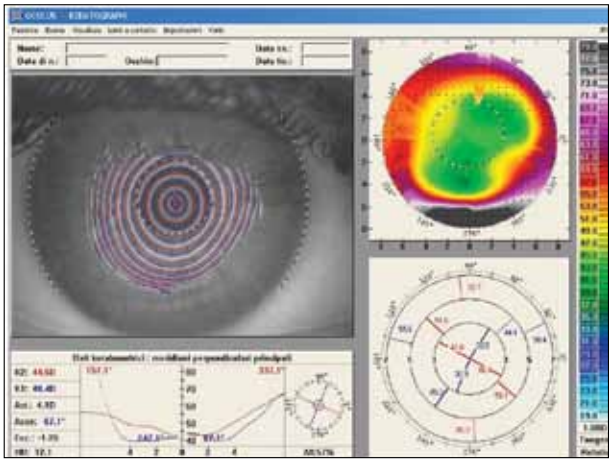


Figure 3. Videokeratographic map of the same eye shown in Figure 1 at 2 years after customized PRK and CXL. The topographic pattern shows an improvement in corneal profile with central flattening (relative scale, tangential algorithm).

"Epithelial ablation was enlarged to 9 mm to perform subsequent standard CXL. This transepithelial customized refractive treatment standardizes the technique, making it no-touch surgery."

Treatment began with acquisition of reliable corneal topography. Excimer laser photoablation was performed using the high-frequency excimer laser with the following parameters: gaussian flying-spot size, 650 µm; frequency, 1,000 Hz; and wavelength, 193 nm. All ablation profiles were calculated with corneal apex as the ablation center. This choice creates a postoperative corneal surface symmetrical with respect to the preoperative morphology of the cornea, which will likely be more physiologically accepted by the patient.

The postoperative curvature of the cornea was obtained by combining two methods: (1) The corneal surface was standardized to the lowest preoperative keratometric reading by flattening the steepest axis, and (2) the spherical component of the manifest refraction was added with a positive or negative sign to the standardized keratometric value to obtain the desired (ideal) postoperative surface. The system calculated the ablation profile as the difference, within the optical zone, between the ideal postoperative surface and the preoperative corneal shape, with the aims of minimizing corneal ablation and regularizing a small central corneal area. Epithelial ablation was enlarged to 9 mm to perform subsequent standard CXL. This transepithelial customized refractive treatment standardizes the technique, making it no-touch surgery.

The maximum net mean ablation depth was 100 µm (range, 80-135), and the minimum mean estimated residual stromal thickness was set at 463 µm (range, 411-569; Figure 2).

Ablation procedures were performed under topical anesthesia. At the end of ablation, after application of topical pilocarpine 1%, riboflavin solution (Ricrolin; Sooft Italia Spa) was applied for corneal soaking for 15 minutes. UVA illumination was then applied with the solid-state Vega (Ofta high-tech Innovazione Tenico Chirurgica; not available in the United States) UV-A light source for 30 minutes, irradiating an area 9 mm in diameter and applying the riboflavin solution every 2.5 minutes. Energy was delivered at 3 mW/cm².

At the end of the treatment, a therapeutic bandage soft contact lens was applied, and ofloxacin drops were ordered at three times a day for 2 weeks. Topical corticosteroid (butyrate clobetasone 0.1%) drops were also prescribed three times a day for 1 month and then subsequently tapered and titrated.

RESULTS

The study included 14 eyes of 14 patients who had initially undergone ELLK for keratoconus and subsequently presented with ametropia (-6.11 D ±2.48 standard deviation [SD]; range, -2.50 to -9.50). The combination customized PRK and CXL procedures were performed in these 14 eyes a mean 40.1 ±12.4 SD months after ELLK.

At a mean 15 ±6.5 SD (range, 6-24) months after customized PRK plus CXL, all eyes gained at least 1 line of Snellen distance UCVA (range, 1-10) from preoperative levels, no patient lost lines of distance BCVA, and four patients gained 3 lines of BCVA. The mean postoperative manifest refraction spherical equivalent was -0.79 D ±2.09 SD (range, +1 to -3). The mean topographic keratometric astigmatism was 5.02 D ±2.93 SD (range, 0.8-8.9; Figure 3). All corneas remained clear, with haze less than grade 1.

CONCLUSION

The combination of customized PRK and CXL provided safe and effective results in these eyes with residual ametropia after ELLK for keratoconus. The combined procedure provided corneal regularization and refractive improvement in these difficult-to-treat eyes. ■

This article is reprinted with permission from the March 2013 issue of Cataract & Refractive Surgery Today Europe.

Leopoldo Spadea, MD, is an associate clinical professor of ophthalmology, chief of corneal and refractive surgery in the eye elinic at S. Salvatore Hospital, University of L'Aquila, Italy. He acknowledged no financial interest in the products or companies mentioned herein.
Prof. Spadea may be reached at +39 0862 319671; lspadea@cc.univaq.it.

1. Bilgihan K, Ozdek SC, Akata F, Hasanreisoglu B. Photorefractive keratectomy for post-penetrating keratoplasty myopia and astigmatism. *J Cataract Refract Surg*. 2000;26:1590-1595.
2. Hafezi F, Kanellopoulos J, Wiltfang R, Seiler T. Corneal collagen crosslinking with riboflavin and ultraviolet A to treat induced keratectasia after laser in situ keratomileusis. *J Cataract Refract Surg*. 2007;33:2035-2040.
3. Bilgihan K, Ozdek SC, Sari A, Hasanreisoglu B. Excimer laser-assisted anterior lamellar keratoplasty for keratoconus, corneal problems after laser in situ keratomileusis, and corneal stromal opacities. *J Cataract Refract Surg*. 2006;32(8):1264-1269.
4. Spadea L. Collagen crosslinking for ectasia following PRK performed in excimer laser-assisted keratoplasty for keratoconus. *Eur J Ophthalmol*. 2012;22(2):274-277.
5. Spadea L, Paroli M. Simultaneous topography-guided PRK followed by corneal collagen cross-linking after lamellar keratoplasty for keratoconus. *Clin Ophthalmol*. 2012;6:1793-1800.