Corneal cross-linking (CXL) has established a new paradigm for the treatment of progressive ectasia and keratoconus.1,2 The visual rehabilitation of patients who achieve stability after CXL can be challenging if they were intolerant of rigid gas permeable contact lenses or if they had poor vision with glasses and/or soft contact lenses prior to treatment. The problem led my colleagues and me to introduce the topography-guided normalization of corneas that remain highly irregular despite some flattening effect from CXL.3,4

EARLY EFFORTS
At the outset, we waited at least 6 months after CXL to perform topography-guided partial PRK. Because these were “uncharted waters,” we set an arbitrary 50-µm limit to the ablation over the cone. Admittedly, such conservative treatment did little to correct refractive error.5-12

We decided that, if the corneal parameters permitted, we would treat up to 70% of the sphere and cylinder but always maintain that 50-µm maximum ablation over the thinnest part of the cone. The refractive effects of this treatment strategy were impressive: the great majority of patients obtained a BCVA of 20/40. Few complications occurred aside from some PRK-related haze and occasionally delayed epithelial healing.13 We therefore began to discuss our findings with prospective CXL patients and to offer them the option of CXL and partial topography-guided PRK as a combined, same-day procedure.

ADVANTAGES
Our early experience identified three advantages of our combined approach. First, there is no need to remove cross-linked cornea (the CXL effect is greater closer to the surface). With...
A Clinical Example

A 23-year-old man had progressive keratoconus in his right eye. In 2008, his refraction was -5.00 -3.00 × 130, and his BSCVA measured 20/60. The patient underwent treatment using the Athens protocol in 2009: topography-guided PRK -2.00 -1.50 × 121 (the topography axis) combined with same-day corneal collagen cross-linking.

Eight years later, his keratoconus is stable, and the patient has a distance UCVA of 20/25. His refraction is currently +0.50 -100 × 050 = 20/20 (Figure).

Figure. Preoperative measurements (left). Eight years postoperatively (middle). The difference between the pre- and postoperative measurements (right) demonstrates the high degree of treatment accuracy and remarkable flattening of almost 9.00 D at the peak of the cone.

a sequential approach, surface ablation removes some of the most biomechanically stable corneal tissue produced by CXL. Second, we observed less corneal haze and scarring in these eyes. A third and surprising finding was that performing CXL and topography-guided PRK at the same time had a synergistic effect: we achieved greater corneal flattening and a more dramatic refractive effect (see A Clinical Example).

Results and Refinement

We carefully studied our results in approximately 200 procedures of CXL first and topography-guided partial PRK performed 6 months later at the earliest, and we compared them to the results of more than 200 cases in which CXL and PRK were performed simultaneously. We named the combined same-day procedure the “Athens Protocol” and have since reported on over 1,000 cases, both primary keratoconus and post-LASIK ectasia, and their long-term follow-up.

We have since enhanced the Athens protocol. Because the epithelium of these eyes is invariably highly irregular, we remove the tissue via phototherapeutic keratectomy using a 7-mm optical zone and a depth of 50 µm. We use the epithelium as a “masking agent” for the topography-guided PRK procedure. Another change we have made is a transition to higher-fluence ultraviolet light for CXL: 6 mW/cm² applied for 15 minutes for the same total energy of 5.4 J. Moreover, like most investigators globally, we use riboflavin solution based in saline rather than dextran for better absorption and less dehydration of the stroma.

Combined versus Sequential Treatment

The argument against the combined procedure is as follows: one cannot predict the long-term refractive effects of CXL, so it is not possible to predict what the refractive error produced by the combination technique will be. We have indeed observed a few cases of a slight refractive overcorrection after more than 10 years of follow-up, when the postoperative refraction was initially targeted for the first couple of years. Another significant concern regarding the Athens protocol is the combined ultraviolet assault on the epithelium from PRK and CXL, with delayed epithelial healing and stromal loss as potential sequela.

Sequential treatment is certainly a valid option. After performing CXL, the ophthalmologist monitors the patient’s visual rehabilitation and considers the possibility of contact lenses or a phakic IOL if anisometropia or residual refractive error persists. If needed, the surgeon performs a partial topography-guided PRK 6 months or longer after CXL, when most of the healing has taken place. Again, the disadvantage is that PRK will remove some of the most biomechanically stable tissue produced by the CXL procedure.

The combined approach reduces patient morbidity. In our experience, it is also far more attractive to patients. Proper informed consent is needed so they understand that the Athens protocol cannot be a fully predictable refractive procedure—not comparable to today’s routine PRK and LASIK. Further visual rehabilitation with soft contact lenses, glasses, or potentially a future refractive procedure on the cornea or with a phakic IOL may be required if emmetropia or a result approaching it is desired.

Our preference is to inform patients about both options, share with them our experience and clinical outcomes, and let them decide (see Watch It Now). To promote a well-educated and thoroughly discussed decision, we ask the family to be present, because most of our candidates are teenaged boys or young adult men (early twenties).

Conclusion

The big lesson we have drawn from our extensive study of corneal diagnostics is that not everything that looks like ectasia or keratoconus progression on topography or tomography is what it seems. A multifactorial assessment of the cornea is necessary to remove bias for potential epithelial remodeling, the use of contact lenses, etc. As far as combining CXL with partial PRK or performing the procedures sequentially, once surgeons acquire experience with both approaches, they will determine what best meets their patients’ needs.


A. John Kanellopoulos, MD
- medical director, The Laservision Research and Clinical Institute, Athens, Greece
- clinical professor of ophthalmology, New York University School of Medicine, New York
- +30 210 7472777; ajkmd@mac.com; Twitter @KanellopoulosMD
- financial disclosure: consultant to AJKMD events, Alcon, Allergan, Avedro, Carl Zeiss Meditec, i-Optics, ISP Surgical, and Keramed