

# Combining Keraflex and Corneal Collagen Crosslinking

This keratoconus treatment may potentially achieve 10.00 to 35.00 D of corneal flattening.

**BY ARTHUR B. CUMMINGS, MB ChB, FCS(SA), MMed (OPHTH), FRCS(EDIN)**

Corneal collagen crosslinking (CXL) was introduced more than 10 years ago, with the first treatment performed in Dresden, Germany. I started using CXL for the treatment of keratoconus in January 2007, as soon as the device received the Conformité Européenne (CE) Mark. In my experience, keratoconus progression either stopped (95% of cases) or slowed (5% of cases) after CXL treatment, but only on occasion did corneal topography and refractive outcomes such as UCVA, BCVA, and refraction improve. When there were improvements in corneal shape, they were typically modest.

I recently started performing CXL after using Keraflex KXS (Avedro, Inc., Waltham, Massachusetts), a microwave pulse treatment delivered to the cornea to improve its shape. In my experience, this combination procedure yields better overall results than CXL alone.

## ENHANCING CORNEAL SHAPE

Our 1-year data show that patients achieve a mean 2.10 D of corneal flattening with CXL alone. Even though this should be celebrated, the celebration is muted when we have halted keratoconus progression but the patient's UCVA, BCVA, refraction, and corneal topography remain less than ideal. Had we not performed CXL, the odds are great that keratoconus would have progressed, especially in younger patients. But, by itself, CXL essentially locks in a nonideal corneal shape.

Many strategies have been suggested to create an ideal corneal shape before performing CXL. For instance, when it is used in topography-guided mode, the WaveLight Allegretto laser (Alcon Laboratories, Inc., Fort Worth, Texas) can provide a limited surface ablation treatment to improve the shape of the cornea. A. John Kanellopoulos, MD, of Athens, Greece, has used this treatment on more than 1,000 eyes prior to CXL. When I use this strategy, I always perform

a procedure we call *simultaneous laser crosslinking* (SimLC), a refraction-free, topography-guided PRK to smooth the corneal surface and limit ablation depth, before CXL. At 3 years' follow-up, our center's outcomes after combined SimLC and CXL are better than CXL alone. The average corneal flattening was 5.90 D with SimLC; results are stable through 3 years.

The limiting factor in treatments such as these is that keratoconus is associated with thin corneas that cannot afford further tissue removal before CXL is used to lock in the improved shape. To avoid removal of tissue, we have also tried Intacs (Addition Technology, Inc., Des Plaines, Illinois) to reshape the cornea; however, the use of Intacs is not always possible due to thin and/or very steep corneas.

Thermal energy can also be used to flatten the cornea before CXL treatment. For example, NearVision CK (Refractec, Irvine, California) uses individual thermal spots to flatten the cornea. When thermal energy alone is used,



Figure 1. Five days post-Keraflex. A bandage contact lens is in situ.

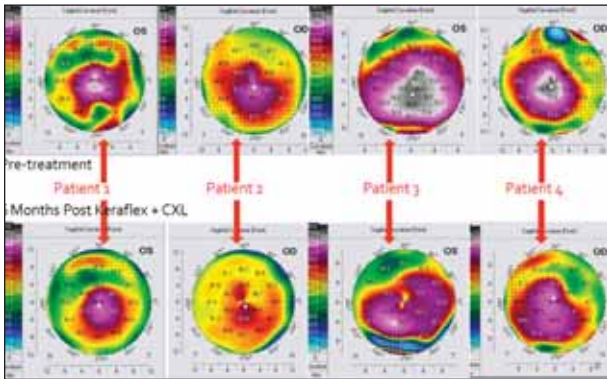


Figure 2. Keraflex with sequential CXL: Topographic results at 6-month follow-up.

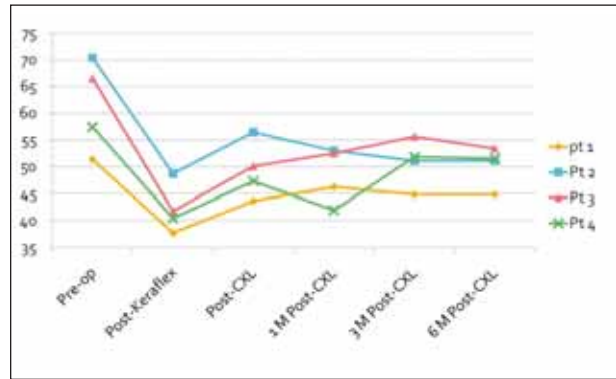


Figure 3. Average-K in eyes that underwent Keraflex with sequential CXL.

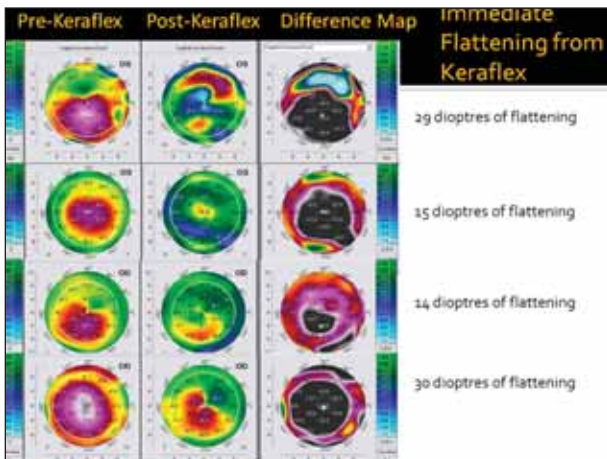


Figure 4. An immediate flattening effect of Keraflex is seen in four eyes that underwent Keraflex and simultaneous KXL.

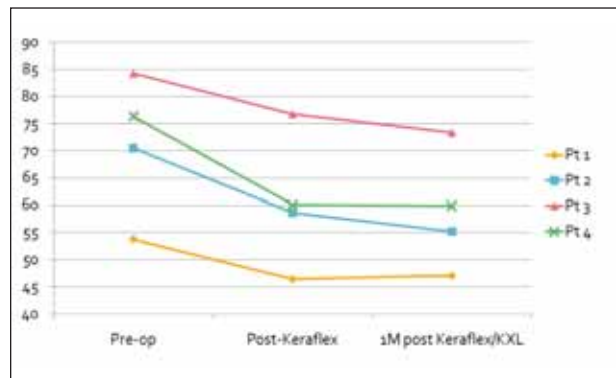


Figure 5. K-Max in eyes that underwent Keraflex with simultaneous KXL with 1 month follow-up.

the corneal shape will eventually regress. But when it is used in combination with CXL, results are more stable.

**LOW-ENERGY MICROWAVE PULSE**

I recently started using the Vadera KXS system (Avedro, Inc.) to flatten the cornea before CXL. In this treatment, a low-energy microwave pulse is applied to the cornea to

shrink corneal collagen and form a toroidal lesion in the upper 150 µm of the stroma. For a video of the procedure, visit <http://eyetube.net/?v=fuheh>.

My first four cases using Keraflex for the treatment of keratoconus were performed in October 2010 (Figures 1 through 3). In these eyes, CXL was performed 4 to 7 days later using the Dresden protocol (30 minutes of ultraviolet-A illumination at 3 mW/cm<sup>2</sup>). In March 2011, I treated an additional six eyes with Keraflex immediately followed by

**TAKE-HOME MESSAGE**

- By itself, CXL essentially locks in a nonideal corneal shape.
- When thermal energy is used alone, the corneal shape will eventually regress.
- Combining CXL with a thermal energy treatment produces more stable results than either used alone.
- The improvement in UCVA and BCVA, refraction, refractive cylinder, and topography were significantly better when CXL was performed after Keraflex than with CXL alone or when CXL was combined with SimLC or Intacs.

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KXL, which is an accelerated CXL approach that applies only 3 minutes of illumination at 30 mW/cm<sup>2</sup> (Figures 4 and 5). With both strategies, we have achieved between 10.00 and 35.00 D of corneal flattening depending on the magnitude of the refractive error (spherical equivalent) to be addressed and the amount of energy delivered to the cornea.

If CXL is delayed by a few days, approximately 6.00 to 8.00 D of regression occurs between procedures. In the four cases we have performed with this method, one eye experienced 1.00 D of regression, one eye remained stable, and in two eyes the corneas continued to flatten. Topography was analyzed using keratometry (K)-Average and K-Max. The same dramatic flattening effect was seen in the six eyes that underwent Keraflex and simultaneous KXL. However, these eyes regressed only 1.00 or 2.00 D before KXL, and they seemed to be locked in more aggressively. I am not sure whether this is an effect of the KXL (rather than CXL) or whether it has to do with the timing of the CXL (simultaneous vs sequential). I have no evidence that this (simultaneous) is a better strategy in the long-term, but it appears to be more effective at 1 month.

The improvement in UCVA and BCVA, refraction, refractive cylinder, and topography were significantly better when CXL was performed after Keraflex, both sequentially and simultaneously, than it was with CXL alone or when CXL was combined with SimLC or Intacs. Additionally, no tissue is removed using Keraflex, and no foreign bodies are inserted into a weakened cornea as with intrastromal corneal ring segments.

## CONCLUSION

I was apprehensive about Keraflex. I thought its effect would regress and the patient would be no better off than if he or she had had CXL only. However, I was pleasantly surprised with the outcomes at 6 months, and corneas treated with CXL have maintained the initial flattening effect. It remains to be seen whether these corneas will maintain their current shapes through 1 and 2 years and even longer; only time will provide these answers.

I know of no other modality that can achieve the same degree of corneal flattening and hence visual improvement in such a safe manner. I assume that Keraflex can be repeated in the future if necessary, but I do not have clinical evidence to support this statement. I currently find that, when I use combination treatments, I opt for Keraflex more frequently than SimLC or Intacs. Keraflex has been a welcome

addition to the Wellington Eye Clinic, and 10 patients are already grateful for this advancement. ■

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