

# Conductive Keratoplasty Followed by Collagen Cross-Linking With Riboflavin–UV-A in Patients With Keratoconus

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**Purpose:** To evaluate the combined effect of conductive keratoplasty (CK) followed by corneal collagen cross-linking (CXL) in 2 patients with keratoconus.

**Methods:** CK spots were applied on the flatter side of the cornea followed by CXL using riboflavin and UV-A light.

**Results:** Immediately after CK, a significant corneal topographic improvement was observed. The CK effect regressed 3 months postoperatively and remained unchanged until the sixth postoperative month in both patients.

**Conclusion:** Corneal remodeling with CK in patients with keratoconus seems to have a temporary effect despite the subsequent application of CXL.

**Key Words:** keratoconus, corneal collagen cross-linking, conductive keratoplasty

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Keratoconus is a progressive corneal disorder that involves loss of corneal biomechanical stability and results in the development of irregular astigmatism.<sup>1</sup> Riboflavin–UV-A corneal collagen cross-linking (CXL) is currently used to solidify the ectatic cornea in keratoconus and post refractive corneal ectasia.<sup>2–4</sup> The stabilization effect is sustained for several years after application of the procedure.<sup>3–7</sup> In severe ectasia, improvement of visual acuity can be achieved only if irregular astigmatism is addressed.

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One technique considered effective for the correction of corneal irregularities is conductive keratoplasty (CK).<sup>8–13</sup> This technique is based on corneal remodeling through heating of collagen fibrils with radio frequencies applied to several spots on the cornea according to the intended correction.<sup>9–15</sup> Because this method does not involve removal of tissue, it may be of particular benefit for patients with thin corneas as occurs in keratoconus.<sup>11</sup>

The combined application of these procedures (CK and CXL) has not been reported previously in the literature, although ablation of cross-linked cornea for the correction of keratoconus has been described.<sup>16</sup> We present 2 cases in which we used CK followed by the application of CXL to achieve stable corneal remodeling in patients with advanced keratoconus.

## MATERIALS AND METHODS

### Patients

Two patients with bilateral keratoconus presented to our institute. Patients were evaluated by assessment of uncorrected and best spectacle-corrected visual acuity (UCVA and BSCVA, respectively) and tonometry, corneal topography, central and peripheral corneal pachymetry, and fundus examination. Both patients had more advanced keratoconus in 1 eye. Combined treatment, using CK followed by the application of CXL, was performed.

### Surgical Procedures

All surgical procedures were performed in our center by the same surgeon (G.D.K.). CK was performed with a ViewPoint CK System under topical anesthesia. One drop of proparacaine 0.5% was administered in the operative eye 15 minutes before the procedure followed by a second drop immediately before surgery. The ocular surface was prepared with povidone-iodine, and eyelids were retracted using a ViewPoint CK speculum. Careful attention was given to corneal marking with a gentian violet-dampened CK marker. The ocular surface was irrigated with balanced salt solution and dried with a fiber-free sponge. According to the markings, the spots were applied to the cornea at the periphery of the topographically flatter area. The surgeon determined the number of the spots to be applied in each case depending on the severity of the irregularity and topography. The outcome of the initially planned treatment was evaluated 30 minutes after the procedure, with additional

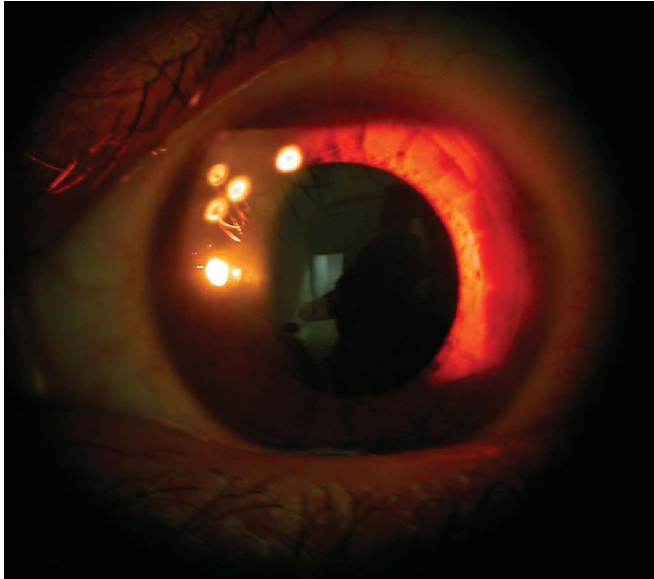
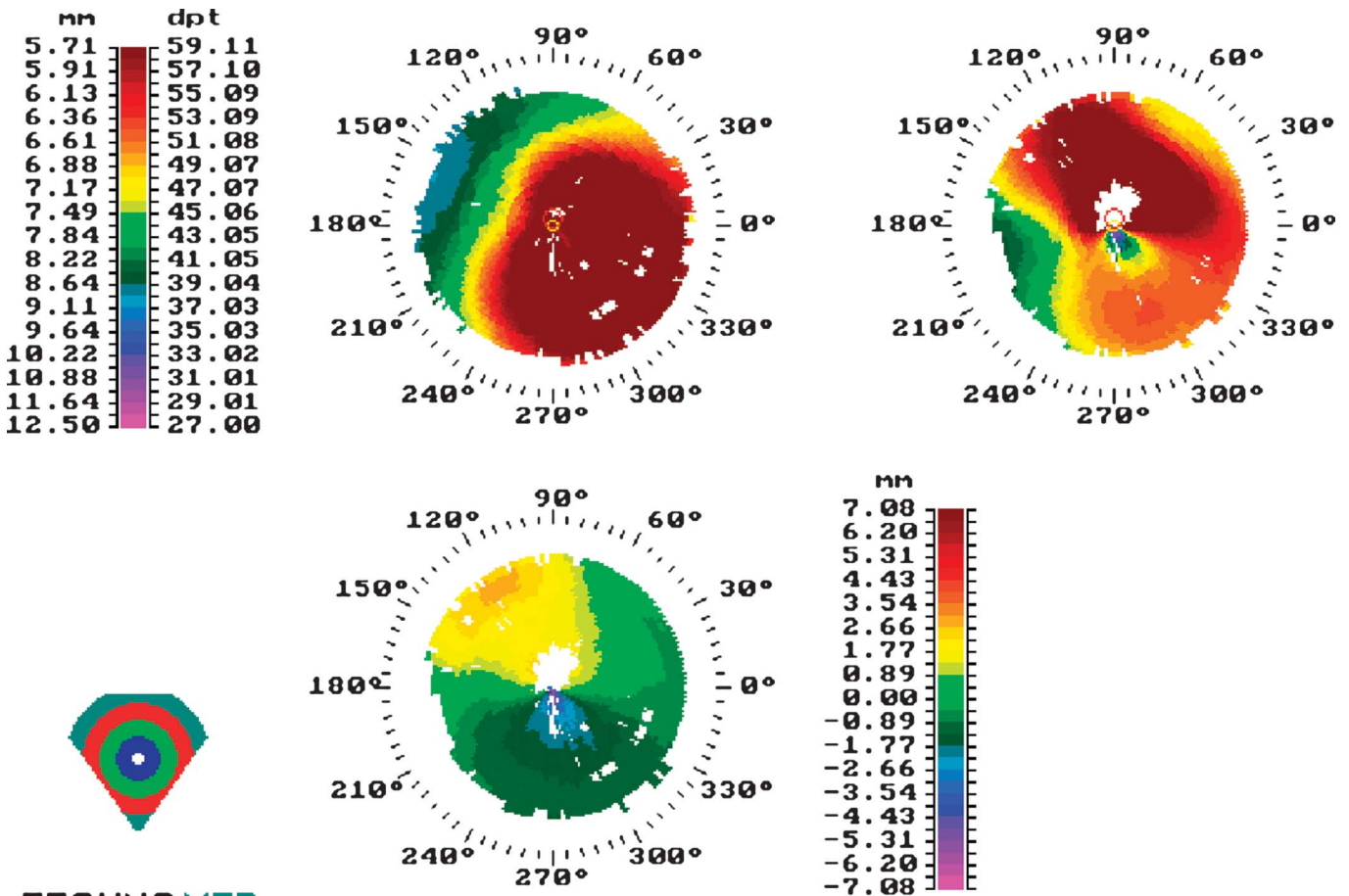


FIGURE 1. Slit-lamp photograph showing the application and placement of CK spots in case 1.

spots applied if the result was inadequate. The treatment spots were applied to the cornea with the Keratoplast tip (Refractec, Inc) placed perpendicular to the corneal surface. All eyes were treated with the standardized setting of 350 kHz, 60% power for 0.6 seconds per spot. At the completion of the procedure, topical tobramycin 0.3% and 1 drop of flurbiprofen 0.03% were applied to treated eyes. Patients were examined by slit-lamp microscopy 1 hour after the procedure and were evaluated with topography immediately after surgery and before the cross-linking treatment.

Both patients underwent CXL 24 hours (case 1) and immediately after (case 2) CK. The surgical procedure was conducted under sterile conditions. After topical anesthesia using tetracaine 1% and oxybuprocaine 0.4% eyedrops, the corneal epithelium was mechanically removed. Then, riboflavin (0.1% solution, 10 mg riboflavin-5-phosphate/10 mL dextran-T-500 20% solution) was applied every 3 minutes for approximately 30 minutes until the stroma was completely penetrated and the aqueous was stained yellow (riboflavin shielding). UV-A irradiation was accomplished using a commercially available UV-A system (UV-X; PESCHKE Medtrade) with Koehler optics. Before treatment, the intended 3 mW/cm<sup>2</sup> surface irradiance (5.4 J/cm<sup>2</sup> surface dose after



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FIGURE 2. Pre-CK (top left), immediately after CK (top right), and difference topographic map (bottom) showing the effect of CK in case 1.

30 minutes) was calibrated using the UV-A meter YK-34UV (Lutron Electronic), which is supplied with the UV-X device. During treatment, riboflavin solution was applied every 2–3 minutes to ensure saturation. After the treatment, a bandage contact lens was applied, remaining in place until the epithelium healed completely, and topical fluorometholone 0.1% eye-drops (FML Liquifilm) was applied twice daily for 2 weeks.

The patients had been thoroughly informed about the experimental nature of the combination of these interventions, possible outcomes, and current clinical experience with the procedures and gave their written consent according to the Declaration of Helsinki and institutional guidelines.

## RESULTS

### Case 1

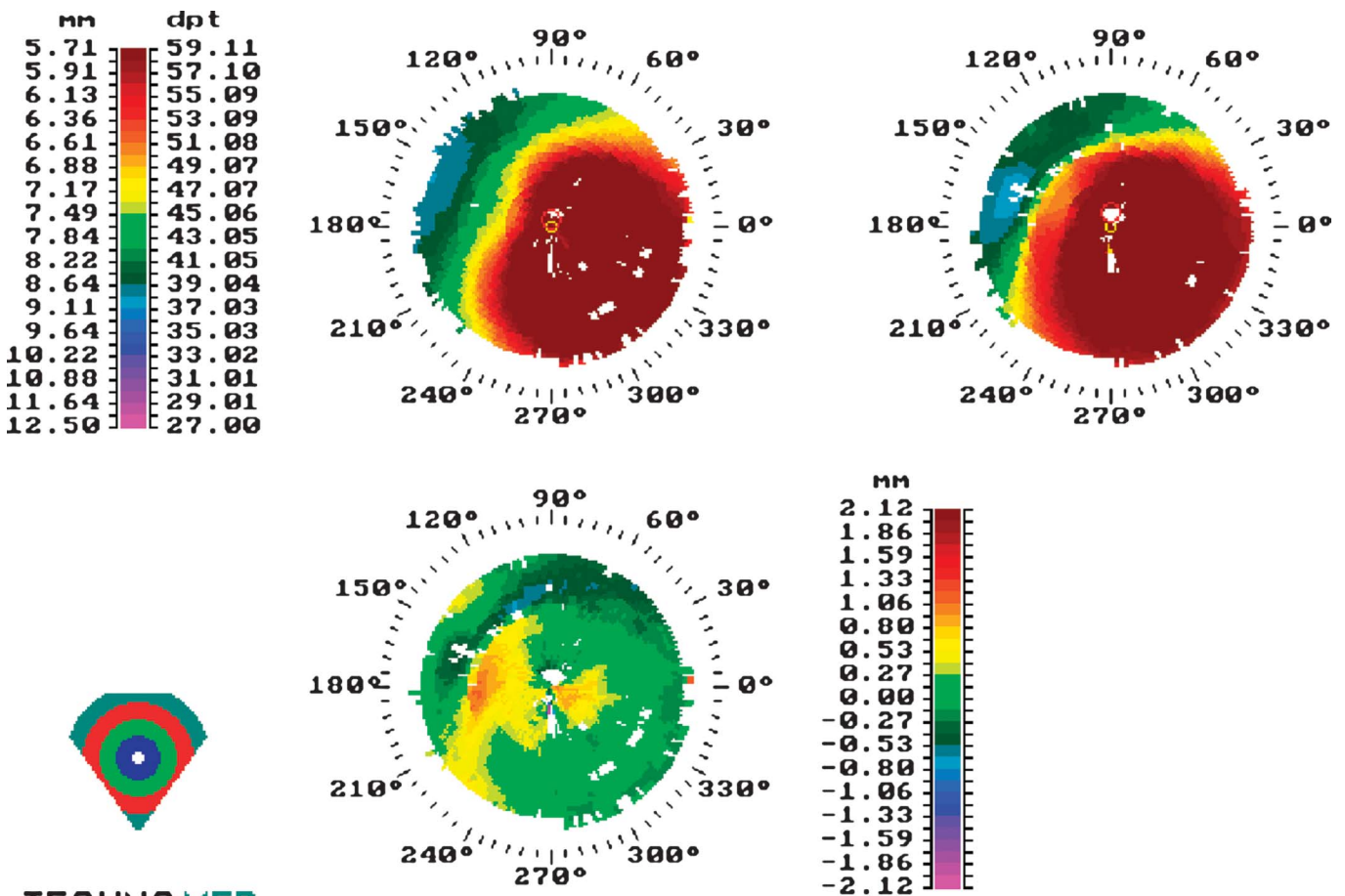
A 22-year-old male presented to our institute seeking treatment for bilateral keratoconus. UCVA in the right eye was 20/50 correcting to 20/15 with  $-3.00 -1.00 \times 45$  degrees and in the left eye 20/100 correcting to 20/30 with  $-4.00 -7.00 \times 155$  degrees. The topographic evaluation of his cornea revealed a clearly keratoconic pattern in both eyes but more progressive in the left eye.

Nine months later, he again presented to our institute with decreased vision in both eyes. UCVA was 20/50 in the right eye and count fingers in the left eye. BSCVA was 20/20 with  $-1.75 -2.50 \times 45$  degrees in the right eye and 20/80 with  $-6.50 -7.00 \times 160$  degrees in the left. BSCVA with rigid contact lenses was 20/20 in the right eye and 20/50 in the left. The topographic evaluation confirmed bilateral keratoconic progression, more advanced in the left eye. Central corneal thickness was 501  $\mu\text{m}$  in the right eye and 497  $\mu\text{m}$  in the left eye. We proposed CK followed by collagen cross-linking as a less invasive procedure with possible improvement of topographic irregularities and visual acuity.

During the CK procedure, 4 spots were applied: 3 spots at the 7 mm and 1 spot at the 8 mm diameter at the topographically flatter area of the cornea (Fig. 1). Corneal pachymetry was performed before application of the CK spots to ensure that corneal thickness was more than 550  $\mu\text{m}$  at the CK spot placement.

Topographic evaluation on the first day after CK revealed a significant improvement of irregular astigmatism, derived from the steepening of the flat meridians (Fig. 2). CXL was performed the first day after CK. No adverse effects were observed during the procedures or during the follow-up period.

Three months after the cross-linking treatment, the topographic pattern was similar to the preoperative, indicating that the CK remodeling had regressed (Fig 3). UCVA was count fingers and BSCVA was 20/80 with  $-6.00 -7.00 \times 170$  degrees as in the



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FIGURE 3. Pre-CK (top left), 2 months after CK (top right) and difference in topographic map (bottom) showing regressed effect of CK in case 1.

preoperative measurements. Six months and 8 months postoperatively, all parameters (UCVA, manifest refraction, BSCVA, and corneal topography) remained unchanged.

### Case 2

A 23-year-old male with diagnosis of bilateral progressive keratoconus presented to our institute complaining of severe deterioration in vision during recent months. His UCVA in the right eye was 20/100, correcting to 20/63 with +2.00 -6.00 × 75 degrees and in the left eye 20/32 correcting to 20/25 with +2.50 -2.00 × 85 degrees. The topographic evaluation of his cornea revealed a clear keratoconic pattern in both eyes but more advanced in the right eye (Fig. 4A). Central corneal thickness was 444 μm in the right eye and 455 μm in the left eye. The combination treatment of CK and sequential cross-linking was proposed as a treatment for his right eye.

Peripheral corneal pachymetry was performed to ensure that corneal thickness was more than 550 μm, and 6 spots were applied at the flatter area: 4 spots at 7 mm and 2 spots at the 8 mm diameter.

A significant improvement of corneal irregularities on topography was noted immediately after CK treatment (Fig. 4B). On the same day, CXL was subsequently performed. No complications were observed during the procedures or during the follow-up period.

Two months postoperatively UCVA was 20/100 correcting to 20/63 with +2.50 -5.75 × 80 degrees with topography similar to preoperative findings (Fig. 4C). At the sixth postoperative month, all parameters (UCVA, manifest refraction, BSCVA, and corneal topography) remained unchanged.

### DISCUSSION

CK is a tissue saving technique that can be used with minimal risk of further destabilizing corneal biomechanics.<sup>8</sup> The technique is based on the use of high-frequency (radio frequency 350 kHz) low-energy current delivered within the stroma of the peripheral cornea with a keratoplasty tip inserted in the cornea. Tissue temperatures rise because of electric impedance in the flow of energy through collagen fibrils, causing collagen shrinkage to occur when the temperature reaches 65°C. This results in corneal remodeling depending on where the spots and device tip are applied. The use of CK spots applied in concentric rings at the mid periphery of the cornea for refractive purposes is well documented and has been studied both in animals and in humans. CK for the correction of low to moderate hyperopia is reported safe and effective, with stable results.<sup>14,15</sup> Alió et al<sup>11</sup> applied CK spots to the flatter areas of the irregular cornea of 3 patients with keratoconus to induce a modeling biomechanical effect that resulted in an immediate improvement in corneal regularity, UCVA, and BSCVA. They also reported regression of the result in one of the cases.

The promising results of CXL in stabilizing keratoconus lead to additional research for treatments that could improve the quality of vision in patients with keratoconus. Kanellopoulos and Binder<sup>16</sup> described the application of topography-guided photorefractive keratectomy on the cornea of a patient with keratoconus who had undergone CXL 24 months earlier. Visual acuity improved, and the patient's condition seemed stable 18 months after photorefractive keratectomy. Although the method seems to be effective, it has the drawback that tissue removal from a cornea with keratoconus may possibly induce destabilization of corneal biomechanics and

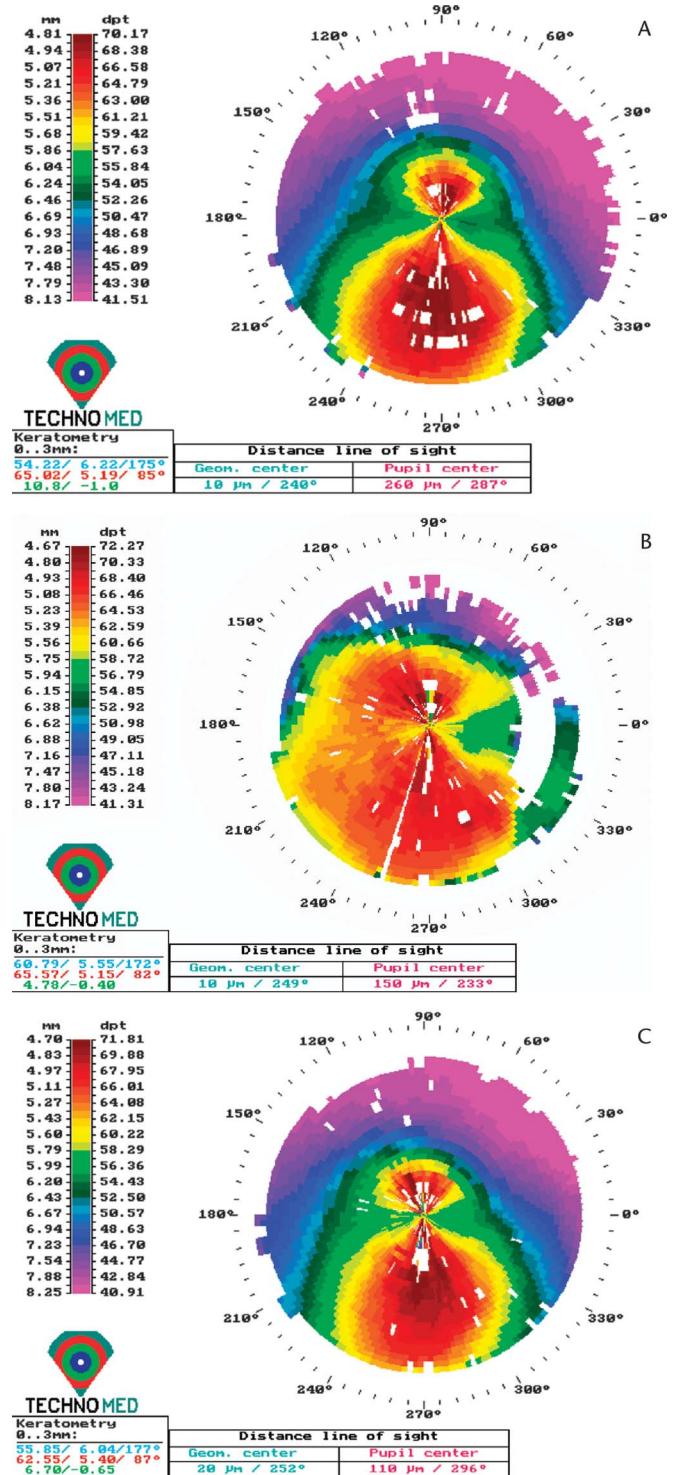


FIGURE 4. Pre-CK (A), immediately after CK (B), and 2 months after corneal cross-linking (C) topography in case 2.

progression of the ectasia. On the contrary, CK is a tissue saving technique that can be applied on a keratoconic cornea without the disadvantage of inducing a weakening effect. The subsequent application of CXL using riboflavin and UV-A

light had the potential to stabilize the cornea not only in regard to progression of keratoconus but also in the remodeling effect of CK.

Despite these theoretical advantages of the combination of CK and CXL, in our experience, there was a significant regression of the initial result. Refractive regression after CK is a well-known complication.<sup>11,17,18</sup> It can be attributed to factors such as the severity of the corneal irregularity and the attempted correction, which differs from studies where CK is applied for low to moderate hyperopic or astigmatic corrections. Patient age is also a significant factor affecting corneal biomechanics.<sup>19</sup> Regression is more likely to occur in younger patients, as seen in our case reports, than in patients older than 40 years, as shown in studies using CK hyperopic corrections.<sup>17,19</sup>

In conclusion, the combination of CK followed by CXL did not offer additional benefit in comparison with CXL alone in this preliminary report of 2 cases. Corneal remodeling with CK seems to be temporal despite the post-CK application of CXL. Further studies in additional patients using modified approaches, such as application of additional spots or reversing the sequence of the procedures, may show benefit and improve patient outcomes.

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