Corneal Crosslinking and Visual Rehabilitation in Keratoconus in One Session Without Epithelial Debridement: New Technique

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Abstract: A new surgical technique for the treatment of keratoconus is presented. This technique combines a new corneal crosslinking method with implantation of a flexible full-ring implant into a "closed" corneal pocket via a narrow incision tunnel in 1 surgical session. Riboflavin is not applied in the form of eyedrops onto a corneal surface after epithelial removal but is instilled into the corneal pocket without the need for epithelial debridement. A case of advanced keratoconus treated in this manner is presented. Uncorrected visual acuity increased by 7 lines from 0.05 to 0.25, and the average central *K* reading decreased by 11 diopters. The haze seen during the early postoperative period diminished in the first month after surgery.

Key Words: corneal cross-linking, cornea, keratoconus, intracorneal implant, MyoRing, CISIS, visual rehabilitation, keratoplasty

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Ultraviolet-A irradiation of the cornea after application of riboflavin induces crosslinks between the collagen elements with subsequent stiffening of the tissue.[1] Although this treatment may stop progression of keratoconus, the ability to achieve visual rehabilitation for improved visual outcome is limited.[2,3] Therefore, combining corneal crosslinking (CXL) with visual rehabilitation methods—such as intracorneal implants, topography-guided photorefractive keratectomy, or phacic intraocular lens—may improve the long-term visual results in patients with keratoconus.[4–6] The standard CXL treatment requires epithelial debridement, which results in pain and discomfort to the patient. Leaving the epithelium untouched, however, may significantly impair the efficacy of the crosslinking process.[7,8] The inability of the dye to penetrate the intact epithelium sufficiently increases the risk of UV damage to the eye. However, bypassing the epithelium by injecting riboflavin directly into an intracorneal pocket seems to be safe and effective, preserving the epithelium and avoiding pain and discomfort seen after epithelial removal.[9] We present a case of keratoconus treated with a new technique of CXL without epithelial removal combined with corneal intrastromal implantation surgery (CISIS), characterized by implantation of a flexible full-ring implant into a corneal pocket.[10–12]

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CASE REPORT

We report a 36-year-old lady suffering from advanced keratoconus (stage 3 after Krumeich classification[13]). The preoperative examination showed a clear cornea with Vogts striae but without scarring. The central corneal thickness was 395 μm. The pre- and postoperative data are shown in Table 1. Figure 1 shows the tangential map of the pre- and postoperative topography.

SURGICAL TECHNIQUE

The surgical technique is characterized by a 4-step procedure:

1. Creation of a corneal pocket.
2. Instillation of riboflavin into the corneal pocket.
3. UV irradiation without epithelial debridement.
4. MyoRing implantation into the corneal pocket.

After topical anesthesia, a "closed" intracorneal pocket was created via a small incision tunnel by means of the PocketMaker microkeratome (DIOPTEX GmbH, Linz, Austria), as described elsewhere.[10–12] The device uses a precisely guided and microvibrating diamond blade to create a corneal pocket of 9 mm in diameter at 300-μm depth via a 4-mm-wide intracorneal tunnel. A sterile standard dose of riboflavin (0.1% riboflavin in 3 mL of 20% dextran 500 solution and MEDIO-CROSS 3 mL; Steffens Kronen-Apotheke, Kiel, Germany) was continuously injected over 3 minutes into the corneal pocket via a standard canula of 0.3-mm diameter through the incision tunnel (Fig. 2). The instillation of the dye resulted in a "yellowish turbidity" in the anterior and the posterior stroma in slit-lamp microscopy indicating that the dye distributes posteriorly and anteriorly from the pocket. The cornea was subjected to a 30-minute irradiation treatment with UV-A light of 365 nm (Peschke Meditrade GmbH, Clemont-Ferrand, Switzerland) and UV intensity of 3 mW/cm^2. Within 5 minutes after UV-A irradiation, a flexible MyoRing intracorneal implant (DIOPTEX GmbH) was inserted into the corneal pocket via the small

TABLE 1. The Pre- and Postoperative Data

	Sphere (D)	Cylinder (D)	Spherical Equivalent (D)	UCVA	BSCVA	*K*1 (D)	*K*2 (D)	*K* (D)
Preoperative data	−6.00	−4.00	−8.00	0.05	0.40	62.11	56.35	59.23
Postoperative data	−0.50	−2.50	−1.75	0.25	0.67	48.56	47.38	47.97

*K*1 and *K*2 are the keratometry readings obtained from the 3-mm zone. *K* represents the average *K* reading according to $(K1 + K2)/2$.

incision tunnel, as shown and described elsewhere.[10,11] The intracorneal tunnel is selfsealing, and the procedure requires no suturing. Central corneal thickness recordings were performed throughout the UV-A irradiation procedure and shown to be consistently 400 μm or higher. The thickness of the cornea was measured by means of ultrasound pachymetry (Quantel Medical SA, France).

RESULTS

After 3 months, uncorrected visual acuity (UCVA) improved by 7 lines, best spectacle–corrected visual acuity (BSCVA) improved by more than 2 lines, and *K* flattened by 11 diopter (D). Pre- and postoperative data including UCVA, BSCVA, *K*1, *K*2, *K*, and the manifest sphere and manifest cylinder are shown in Table 1. The cornea was hazy in the early postoperative phase. Figure 3 shows the hazy cornea 1 day after combined CISIS-CXL treatment. The turbidity of the cornea (haze) appeared evenly distributed over the entire corneal thickness and treated diameter with a slightly higher density in the anterior cornea. After 1 month, however, the haze was almost completely resolved (Fig. 4). The changes in topography are shown in Figure 1.

DISCUSSION

Collagen crosslinking takes about 1 year to stabilize without any relevant improvement of the visual outcome.[2,3] In mild cases of keratoconus, vision can be improved after CXL by means of additional visual rehabilitation measures, such as contact lenses, intracorneal ring segments, topography-guided photorefractive keratectomy and phacic intraocular lenses.[4–6] A recent study on Intacs treatment in advanced keratoconus showed an improvement of the mean UCVA from 0.05 to 0.16 and a reduction in the average *K* reading of 3.6 D from 53 to 49.4 D.[14] Although a comparison of penetrating keratoplasty with Intacs treatment revealed that ring segment treatment in keratoconus[15] is superior in terms of complications, side effects, and patient discomfort, keratoplasty still seems to be the treatment of choice for advanced cases.

Our technique of combining CXL with CISIS uses a corneal pocket for bypassing the epithelium to apply intracorneal riboflavin and implanting a flexible full-ring implant. Bypassing the epithelium to apply intracorneal riboflavin is achieved by irrigating the corneal pocket with riboflavin. This keeps the corneal epithelium in sound condition and avoids the pain and discomfort seen after conventional CXL. Our technique of bypassing the epithelium to apply riboflavin differs from that of Kanellopoulos[9] in several points. To create the intracorneal pocket, we used the PocketMaker microkeratome with a special diamond blade instead of a femtosecond laser. Our pocket is 9 mm in diameter and has a depth of 300 μm instead of 7-mm diameter and 100-μm depth. The diameter of the 9-mm pocket corresponds to the diameter of exposed stroma after epithelial removal in standard CXL.[16] Our decision to create the pocket with a depth of 300 μm stems from the CISIS procedure, which requires 300-μm depth for MyoRing implanation.[10,11] In contrast to the corneal flap cut in laser in situ keratomileusis, a corneal pocket should not weaken the cornea regardless of pocket diameter and depth.[11] Unlike Kanellopoulos,[9] who used the intracorneal pocket for preserving the epithelium in CXL in mild cases of keratoconus without the need of an additional visual rehabilitation procedure, we additionally used the intracorneal pocket for taking up the MyoRing to achieve additional visual rehabilitation.

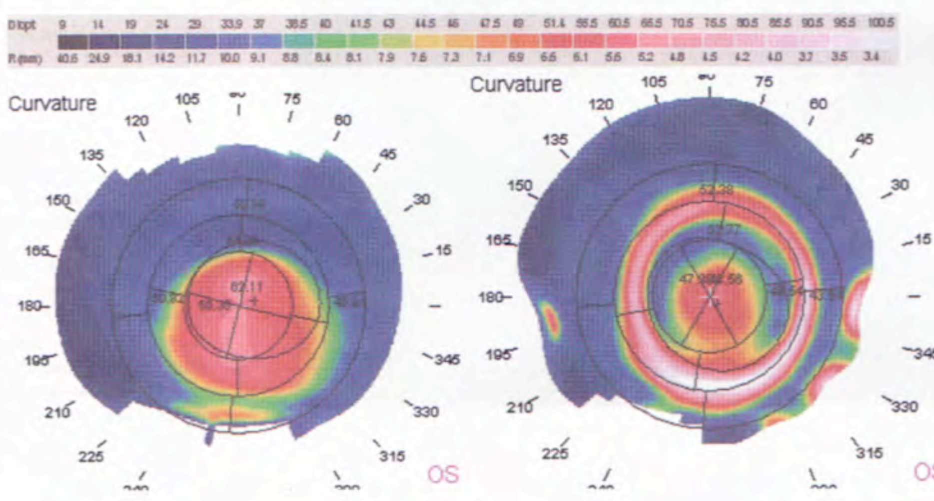

FIGURE 1. Tangential map of the preoperative (A) and postoperative (B) topography.The tangential map represents the local curvature and is able to recognize sharp power transitions more readily compared with axial map representations. Therefore, the representation of the MyoRing is better in a tangential map (red circle in the postoperative picture), allowing precise evaluation of the centration of the implant. The black numbers inside the map represent the keratometry (*K*1 and *K*2) obtained from the 3-, 5-, and 7-mm zones, respectively.

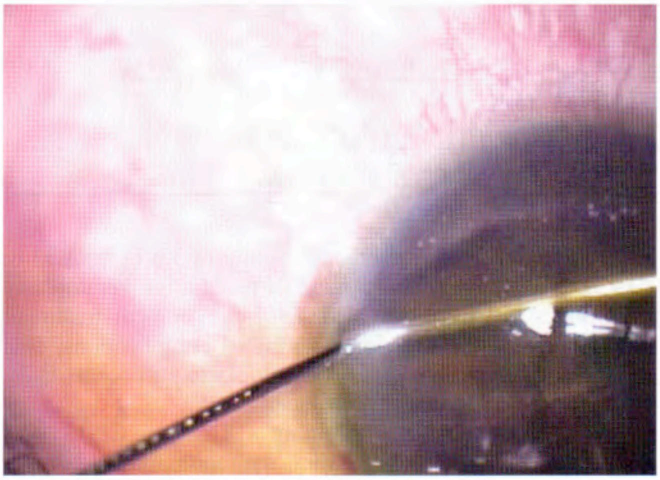

FIGURE 2. The instillation of riboflavin into the corneal pocket. The pocket was slowly rinsed with 3 mL of riboflavin solution (yellow dye) over 3 minutes.

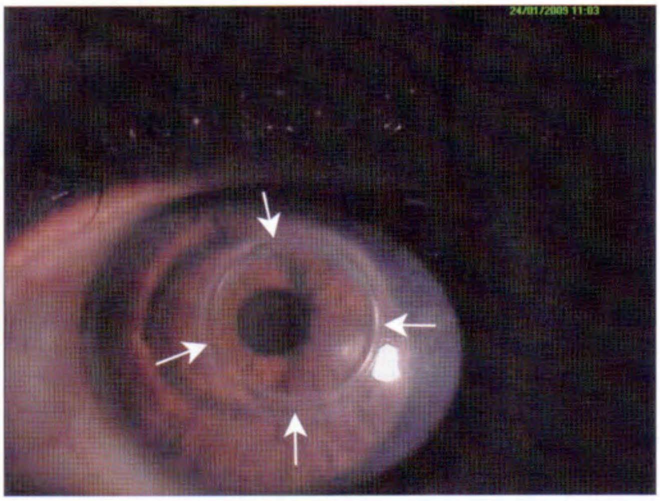

FIGURE 4. The cornea 1 month after surgery. The haze has vanished and the cornea is clear. The white arrows indicate the position of the MyoRing implant.

Our treatment resulted in an improvement of UCVA by 7 lines from 0.05 to 0.25 after 3 months. As can be seen in Table 1, the treated case is an advanced case with average *K* reading close to 60 D, central corneal thickness of 395 μm, BSCVA of 0.4, and a manifest cylinder of 4 D, respectively. The cornea had no scars.

In our case, the cornea was hazy in the early postoperative period (Fig. 2) but cleared up quite quickly within the first postoperative month (Fig. 3). Haziness in the early postoperative period is not uncommon even in standard CXL.[17] Reducing exposure time to UV light and increasing UV intensity may diminish the likelihood of haze in the early postoperative phase of future treatments. Kanellopoulos[9] did not report any significant haze in the early postoperative period. He exposed the cornea to 7 mW/cm^2 of UV intensity for 15 minutes and instilled only 0.2 mL of 0.1% riboflavin solution instead of 3 mL in our case.

The follow-up period is short, and a larger number of cases needs to be examined. However, the clinical results of the presented case are promising and indicate that this new surgical approach to keratoconus treatment not only helps to avoid the pain and discomfort seen in conventional CXL but may also decisively improve the patient's vision.

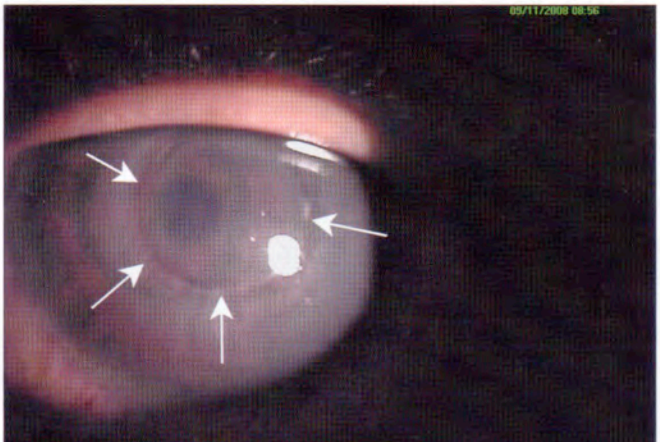

FIGURE 3. The corneal haze 1 day after surgery. The haze is diffuse throughout the entire corneal stroma. The MyoRing implant is indicated by the white arrows.

REFERENCES

1. Spoerl E, Huhle M, Seiler T. Induction of cross-links in corneal tissue. *Exp Eye Res*. 1998;66:97–103.
2. Raiskup-Wolf F, Hoyer A, Spoerl E, et al. Collagen cross-linking with riboflavin and ultraviolet-A light in keratoconus: long term results. *J Cataract Refract Surg*. 2008;34:796–801.
3. Grewal DS, Brar GS, Jain R, et al. Corneal collagen cross-linking using riboflavin and ultraviolet-A light for keratoconus. One-year analysis using Scheimpflug imaging. *J Cataract Refract Surg*. 2009;35:425–432.
4. Chan CC, Sharma M, Wachler BS. Effect of inferior-segment Intacs with and without C3-R on keratoconus. *J Cataract Refract Surg*. 2007;33:75–80.
5. Kannelopoulos AJ, Binder PS. Collagen cross-linking (CCL) with sequential topography-guided PRK; a temporizing alternative to penetrating keratoplasty. *Cornea*. 2007;26:891–895.
6. El-Reggal TM, Abdel Fattah AA. Sequential Intacs and Verisyse phacic intraocular lens for refractive improvement in keratoconic eyes. *J Cataract Refract Surg*. 2007;33:966–970.
7. Hayes S, OBrart PO, Lamdin LS, et al. Effect of complete epithelial debridement before riboflavin-ultraviolet-A corneal collagen cross-linking therapy. *J Cataract Refract Surg*. 2008;34:657–661.
8. Wollensack G, Iomdina E. Biomechanical and histological changes after corneal cross-linking with and without epithelial debridement. *J Cataract Refract Surg*. 2009;35:540–546.
9. Kanellopoulos AJ. Collagen cross-linking in early keratoconus with riboflavin in a femtosecond laser-created pocket: initial clinical results. *J Refract Surg*. 2009;25:1034–1037.

10. Daxer A. Corneal intrastromal implantation surgery for the treatment of moderate and high myopia. *J Cataract Refract Surg*. 2008;34:194–198.
11. Daxer A. Adjustable intra-corneal ring in a lamellar pocket for keratoconus. *J Refract Surg*. 2010;26:217–221.
12. Daxer A. CISIS: reversible treatment of high myopia and keratoconus [in German]. *Spektrum Augenheilkd*. 2009;23:39–41.
13. Krumeich JH, Daniel J. Live epikeratophakia and deep lamellar keratoplasty for stage-specific surgical treatment of keratoconus [in German]. *Klin Monatsbl Augenheilkd*. 1997;211:94–100.
14. Shetty R, Kurian M, Anand D, et al. Intacs in advanced keratoconus. *Cornea*. 2008;27:1022–1029.
15. Rodriguez LA, Guillen PB, Benavides, MA, et al. Penetrating keratoplasty versus intrastromal corneal ring segments to correct bilateral corneal ectasia: preliminary study. *J Cataract Refract Surg*. 2007;33:488–496.
16. Koppen C, Vryghem JC, Gobin L, et al. Keratitis and corneal scarring after UVA/riboflavin cross-linking for keratoconus. *J Refract Surg*. 2009;25:S819–S823.
17. Mazzotta C, Balestrazzi A, Baiocchi S, et al. Stromal haze after combined riboflavin-UVA corneal collagen cross-linking in keratoconus: in vivo confocal microscopic evaluation. *Clin Experiment Ophthalmol*. 2007;35:580–582.