

An Alternative Treatment for Keratoconus

Collagen cross-linking with ultraviolet A light and riboflavin followed by customized topography-guided PRK may be an alternative to penetrating keratoplasty.

BY A. JOHN KANELLOPOULOS, MD

Keratoconus is usually a bilateral, asymmetric, progressive, and non-inflammatory degeneration of the cornea. Its incidence is approximately 1 in 2,000 in the general population. The disorder usually starts during puberty, and it progresses in approximately 20% of those affected to such an extent that penetrating keratoplasty (PKP) is indicated.¹ Today, PKP remains the global gold standard for rehabilitating the vision of patients with advanced keratoconus.¹ The intermediate and long-term visual rehabilitation in these patients remains challenging.¹ An alternative treatment to PKP may be a procedure that includes collagen cross-linking with ultraviolet A light and riboflavin followed by customized topography-guided PRK (the treatment).

CASE REPORT

Keratoconic Patient

A male patient 26 years of age with a long history of keratoconus and rigid gas-permeable contact lens wear for more than 8 years presented to my office. Due to the development of debilitating giant papillary conjunctivitis, contact lens use by the patient became intolerable. His UCVA was 20/40 OD

and 20/100 OS, BSCVA was 20/15 OD and 20/50 OS, and his refraction -0.75 -0.75 X 80 OD and -3.75 -4.50 X 110 OS. Spectacle use was associated with significant decrease in his visual quality and increase anisometropia problems.

I initially evaluated the patient for a corneal transplantation at the recommendation of several cornea specialists the patient had consulted previously (Figures 1 and 2). The corneal thickness was 520 μ m and 440 μ m in the right and left eye, respectively. The endothelial cell count was 2,800 and 2,750 cells/mm² in the right and left eye, respectively, as measure by Orbscan (Bausch & Lomb, Rochester, NY) and ultrasound.

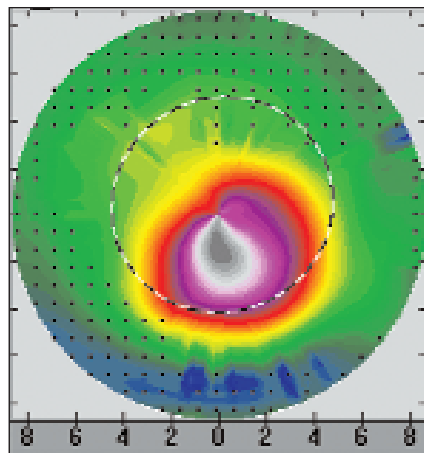


Figure 1. Pictured is the corneal topography of the patient's left eye, which was most affected by keratoconus. His BSCVA was 20/400.

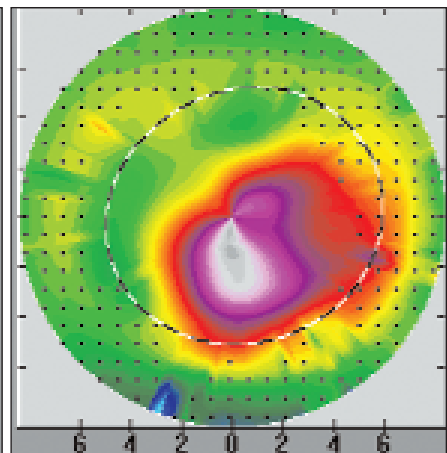


Figure 2. Twelve months following the treatment, the patient's central steepening is still present, although it has reduced. His UCVA was 20/200 and BSCVA was 20/70.

The patient and I spoke at length about his treatment options. I described the pros and cons of PKP¹ and detailed the use of Intacs (Addition Technology Inc., Des Plaines, IL) as a substitute treatment.² I also shared my experience and that of my colleagues with the treatment.³ The patient decided to undergo the treatment prior to considering PKP.

Treatment Protocol

The treatment was completed in two steps. The patient first underwent collagen cross-linking to stabilize corneal ectasia. This technique is described in several laboratory and clinical studies.^{2,4-10}

Before treating the patient, I removed his corneal epithelium via 20% ethyl alcohol solution, which remained on the corneal surface for 20 seconds.

Special emphasis should be taken preoperatively to document his minimal corneal thickness because of potential cytotoxic effects of ultraviolet A on corneal endothelial cells. Previous experimental studies in the rabbit cornea have investigated dose-dependent cytotoxicity to the corneal endothelium. Those studies have clearly shown that the surface irradiance according to the protocol described herein, may not be used in corneas thinner than 400 μm (including the epithelial layer) in lieu of potential endothelial damage.²

For the treatment I used the Keracure prototypic device (Priavision, Menlo Park, CA) prototypic device. It emits 370nm of ultraviolet A light and $3\text{mV}/\text{cm}^2$ radiance through four light emitting diodes for 30 minutes (defined by an automatic, built-in timer). The nursing staff simultaneously administered 0.1% riboflavin ophthalmic solution (Priavision) to the de-epithelialized cornea, one drop every 2 minutes, in order to “soak” the stromal bed. The riboflavin facilitates collagen cross-linking and, impor-

tantly, protects the iris, crystalline lens, and retina from ultraviolet A radiance.

A bandage contact lens was placed onto the de-epithelialized, cross-linked cornea. The patient received ofloxacin and prednisolone acetate 1% q.i.d. for 10 days. The contact lens was removed on postoperative day 4, when the patient’s cornea had completely re-epithelialized.

Postoperative Results and Refractive Surgery

The patient’s UCVA and BSCVA improved to 20/80 and 20/40, respectively, with a refraction of -3.50 -4.00×115 at 3 months postoperatively. Based on the stability of these parameters and the corneal topography between months 1 and 12 of this treatment, the patient and I decided to proceed with a limited topography-guided PRK in order to reduce the amount of irregular astigmatism and to facilitate visual rehabilitation (Figures 3 and 4).

At the time of refractive surgery, the patient’s cornea at its thinnest measured $450\mu\text{m}$ with pachymetry. I reduced the treatment values for myopia from -3.50D to -2.50D and from -4.00D to -3.00D for astigmatism. I decreased the treatment zone to 5.5mm from the standard 6.5mm that we use in routine PRK procedures. I performed the PRK using the 400Hz Allegretto Wave Eye-Q Excimer Laser System’s (Wavelight, Inc., Sterling, VA) topography-guided, customized program known as T-CAT treatment to visually rehabilitate this

contact lens-intolerant patient. The T-CAT with the 400Hz Allegretto Wave Eye-Q Excimer Laser System allows for treatment zones of 5.0 to 7.0mm in 0.5-mm increments.¹¹ My goal was to remove no more than $50\mu\text{m}$ of central corneal tissue (Figure 5).

I placed 20% diluted alcohol on the corneal surface for 20 seconds to remove the epithelium, and then I per-

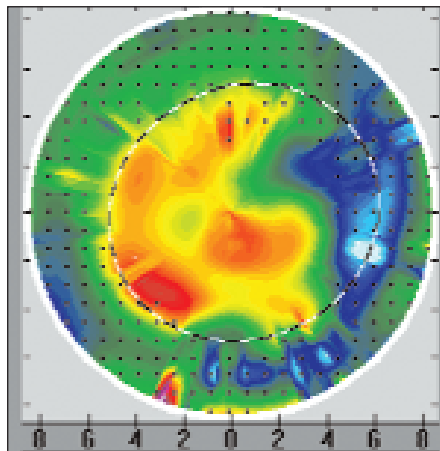


Figure 3. Pictured is a comparative map of Figure 1 minus Figure 2 that depicts the actual improvement in corneal curvature at 12 months postoperatively.

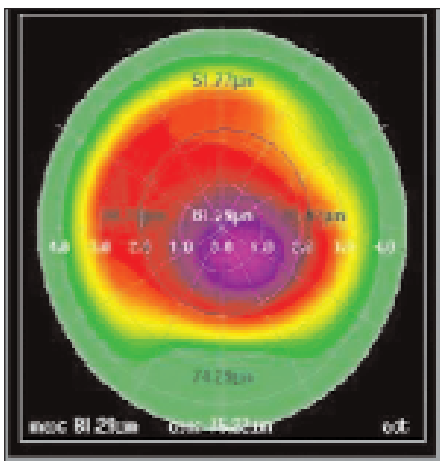


Figure 4. Pictured is an estimated corneal topography ablation pattern for the laser treatment plan of the topography-guided procedure the author performed on the patient. This ablation pattern is highly irregular, with flattening of the cone apex and steepening of the rest of the central cornea (with a deeper ablation inferiorly and right to the center that matches, through the central cornea irregularity) as in the previously mentioned figures.

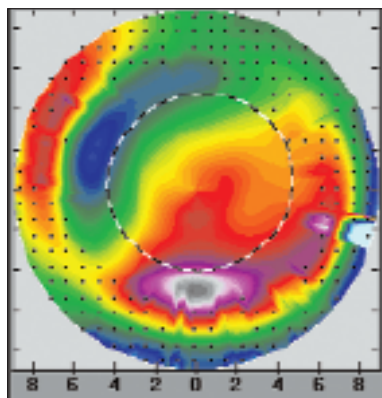


Figure 5. Corneal topography 15 months following topography-guided PRK on the patient's left eye. The central cornea appeared more regular and much flatter postoperatively. His BSCVA and UCVA were 20/15 and 20/20, respectively.

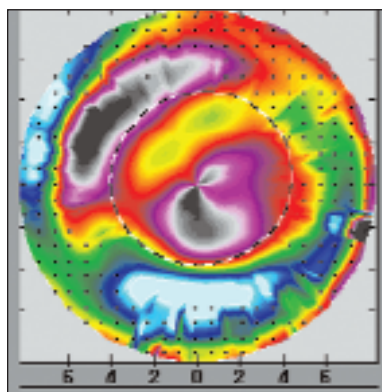


Figure 6. Pictured is a comparative map of Figure 2 minus Figure 5 that depicts the improvement experienced by the patient 15 months after PRK. The difference resembles the topography-guided ablation pattern shown in Figure 5 and illustrates the specificity of the treatment in reducing the pathogenic corneal irregularity, which the author theorized contributed to the drastic improvement in BSCVA.

formed the laser treatment. I applied a Weck-Cel sponge (Medtronic Xomed Ophthalmics, Inc., Minneapolis, MN) soaked in mitomycin C 0.2% solution to the ablated tissue for 30 seconds and then irrigated the tissue with 10mL of chilled balanced salt solution. Finally, I applied a bandage contact lens on the cornea.

The laser treatment must be applied with caution because more rigid corneas (the actual effect that the cross-linking achieves) may have a different ablation

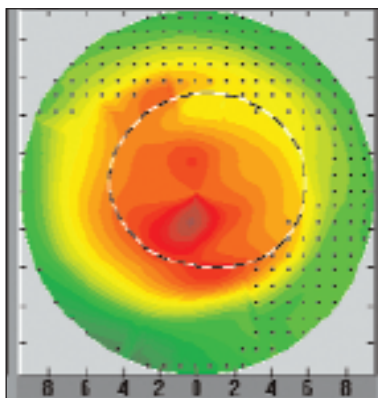


Figure 7. Pictured is the topography of the patient's right untreated eye on presentation.

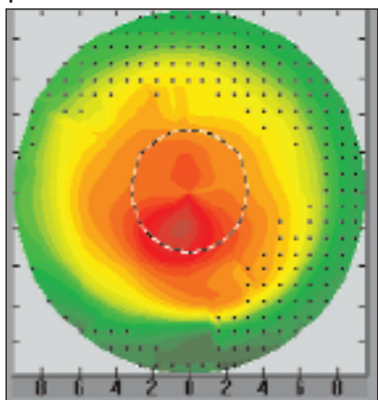


Figure 8. Pictured is the topography of the patients' untreated right eye 12 months after he had received the treatment in his fellow eye. The ectatic progression of the untreated right eye is demonstrated by comparing this topography to Figure 1. Noteworthy is that the irregular infero steepening has drastically worsened in 12 months.

formed the laser treatment. I applied a Weck-Cel sponge (Medtronic Xomed Ophthalmics, Inc., Minneapolis, MN) soaked in mitomycin C 0.2% solution to the ablated tissue for 30 seconds and then irrigated the tissue with 10mL of chilled balanced salt solution. Finally, I applied a bandage contact lens on the cornea.

depth per pulse than the untreated cornea. In this case the correction achieved was more than what was expected from the treatment planned, suggesting that a special nomogram is required for the ablation of a previously cross-linked cornea. In short, aim for less. Therefore, my recommendation would be to use 75% to 80% of the measured sphere and cylinder as a correction parameter when planning the ablation with the T-CAT software.

The patient's visual treatment was very rewarding on postoperative day 7 following the bandage lens' removal on day 5. One can appreciate the difference map between pre- and post-ultraviolet A, collagen cross-linked treatment (Figure 6), as well as the difference map between pre- and posttopography-guided treatment (Figures 7), and the actual ablation profile that was used for the treatment (Figure 5). The qualitative changes on the cornea surface are interesting. In both the treatment plan and the difference map (Figure 8) there is strong evidence of a deeper ablation over the steep cone area. Another important factor is the attempt in the treatment plan and actual effect in the difference map of a mid-peripheral steepening effect of the diametrically opposite cornea to the cone center. This effect is achieved by flattening the outer edge of the mid cornea that is to be steepened. Normalization of the cornea is achieved with the T-CAT software by (1) flattening the cone apex a small diameter via an eccentric PTK-like treatment, and (2) steepening its diametrical opposite cornea to achieve an effect that resembles a hyperopic treatment. The advantage of a topography-guided treatment in this case is that it removes far less (almost 1/3 less) of tissue in comparison to similar wavefront-guided treatments. This advantage is very important especially in keratoconic patients because there is tremendous limitation in the amount of tissue that can be removed.

I prescribed topical ofloxacin and prednisolone acetate 1% q.i.d. for 10 days postoperatively. The patient then used prednisolone acetate 1% alone q.i.d. for 3 additional weeks and b.i.d. for the next 4 weeks. I encouraged him to pro-

protect his eyes from all natural light with sunglasses and to take 1,000mg of vitamin C daily for 60 days (my standard protocol for post-PRK patients).

At 1 month postoperatively, the patient's UCVA was 20/20, and he reported seeing well at night. During the first 18 months postoperatively, he enjoyed a UCVA of 20/20 and a BSCVA 20/15 with plano -0.50 X 150. He considers his left treated eye as best when compared to his right eye. The corneal endothelium had 2,750 cells/mm² at 1 month after the treatment, and it had not changed at 1 and 12 months after topography-guided PRK. The post-operative regression of ectasia was impressive and stable for 12 months (Figure 6).

CONCLUSION

The persistence of stable results more than 1 year postoperatively indicate the utility of the treatment, and suggests that the procedure may in the near future have wider applications for preventing the development of keratoconus, ectasia, and other biomechanical corneal changes following LASIK. I feel that this treatment may hold significant promise for the management of keratoconus, and may help

“Larger comparative studies establishing the safety and efficacy of this treatment and longer follow up are necessary to further validate the results discussed herein.”

relieve the tremendous burden this condition places on patient's everyday life when they cannot wear contact lenses. The treatment's utility may further be improved by adjusting the nomogram. For example, reducing the treatment for myopia and astigmatism by 25% (as described earlier), something that each surgeon may adjust in regards to the laser platform that he uses, in the ablation of cross-linked cornea tissue to avoid a refractive overcorrection. Larger comparative studies establishing the safety and efficacy of this treatment and longer follow up, however, are necessary to further validate these results discussed herein and potentially make this treatment available in early cases of keratoconus. ■

CORNEAL COLLAGEN CROSS-LINKING WITH RIBOFLAVIN SHOWS POTENTIAL

BY BRIAN S. BOXER WACHLER, MD

Corneal collagen cross-linking has been shown to strengthen the cornea by greater cross-linking and the increased diameter of collagen fibrils, which yielded a physically stronger cornea in patients and in the laboratory.^{1,2} A logical next step is to evaluate the use of surface laser treatment, which minimizes biomechanical changes in previously compromised corneas. In his article, the results presented by A. John Kanellopoulos, MD, appear very promising. I agree with him that it is prudent to limit the amount tissue removed. In theory, there is a point at which subtracting too much tissue can lead to “re-ectasia” despite prior cross-linking. Dr. Kanellopoulos' case report makes me optimistic about the procedure's future applications. ■

Brian S. Boxer Wachler, MD, is Director of the Boxer Wachler Vision Institute in Beverly Hills, California. Dr. Boxer Wachler may be reached at (310) 860-1900; bbw@boxerwachler.com.



1. Wollensak G, Wilsch M, Spoerl E, Seiler T. Collagen fiber diameter in the rabbit cornea after collagen crosslinking by riboflavin/UVA. *Cornea*. 2004;23:503-507.
2. Wollensak G, Spoerl E, Seiler T. Stress-strain measurements of human and porcine corneas after riboflavin-ultraviolet-A-induced cross-linking. *J Cataract Refract Surg*. 2003;29:1780-1785.

A. John Kanellopoulos, MD, is a cornea and refractive surgery specialist. Dr. Kanellopoulos is Director of the Laservision.gr Eye Institute in Athens, Greece; an attending surgeon at the Department of Ophthalmology, Manhattan Eye, Ear, and Throat Hospital in New York; and Clinical Associate Professor of Ophthalmology at New York University Medical School in New York. He acknowledged no financial interest in any product or company mentioned herein. Dr. Kanellopoulos may be reached at +30 21 07 47 27 77; laservision@internet.gr.



3. Kanellopoulos AJ. Management of post-LASIK ectasia with UVA collagen cross-linking, followed by customized topography-guided PRK—an efficient approach to avoid corneal transplantation. *J Ophthalmol*. In press.
4. Hettlich HJ, Lucke K, Kreiner CR. Light induced endocapsular polymerization of injectable lens refilling materials. *Ger J Ophthalmol*. 1992;1:346-349.
5. Spoerl E, Huhle M, Seiler T. Induction of cross-links in corneal tissue. *Exp Eye Res*. 1998;66:97-103.
6. Wollensak G, Spoerl E, Seiler T. Stress-strain measurement of human and porcine corneas after riboflavin-ultraviolet-A-induced cross-linking. *J Cataract Refract Surg*. 2003;29:1780-1785.
7. Wollensak G, Spoerl E, Wilsch M, Seiler T. Endothelial cell damage after riboflavin-ultraviolet-A treatment in the rabbit. *J Cataract Refract Surg*. 2003;29:1786-1790.
8. Wollensak G, Spoerl E, Reber F, Seiler T. Keratocyte cytotoxicity of riboflavin/UVA treatment in vitro. *Eye*. 2004;18:718-722.
9. Wollensak G, Spoerl E, Wilsch M, Seiler T. Keratocyte apoptosis after corneal collagen crosslinking using riboflavin/ultraviolet-A treatment. *Cornea*. 2004;23:43-49.
10. Kanellopoulos AJ, Pe LH. Wavefront-guided enhancements using the Wavelight excimer laser in symptomatic eyes previously treated with LASIK. *J Refract Surg*. 2006;22:345-349.
11. Kanellopoulos AJ. Topography-guided Custom re-treatments in 27 symptomatic eyes. *J Refract Surg*. 2005;21:(supp)513-518.