

Thermo-Biomechanics for Treating Keratoconus and Refractive Errors

Surgeons say initial results for Keraflex and annular CXL are encouraging.

BY LAURA STRAUB, EDITOR-IN-CHIEF

Over the years, ophthalmic surgeons have introduced many innovations that either caught on like wildfire or crashed and burned before making it off the runway. Developing new technology to address pathologies or refractive errors takes much research and dedication. The most recent innovation Peter S. Hersh, MD, and John Marshall, PhD, FRCPATH, FRCOphth(Hon), have had the pleasure to investigate is Keraflex KXL (Avedro, Inc., Waltham, Massachusetts), a minimally invasive, two-step, nonincisional procedure with the potential for treating keratoconus and the refractive errors associated with it. It may also be used to treat other refractive errors such as myopia in the future. Dr. Hersh and Professor Marshall recently spoke with *CRST Europe* to discuss this novel thermo-biomechanics technique to reshape the cornea. No tissue is removed, and neither incision nor flap is created, thus preserving biomechanical integrity and corneal anatomy.

Initial results of a study conducted by Ömer Faruk Yilmaz, MD, of Beyoglu Eye Research and Training Hospital in Istanbul, Turkey, showed significant improvements in corneal flattening, smoothness, and regularity in the first seven eyes with keratoconus treated with the technique. The mean change in manifest refraction spherical equivalent was 4.39 D, with a range of 0.50 to 10.125 D, and the mean change in steepest keratometry was -6.00 D, according to Dr. Yilmaz's study results.

Although this is very early data and includes only a small number of patients, the results are nevertheless promising, Dr. Hersh and Professor Marshall said, with results even alluding to the possibility of correcting

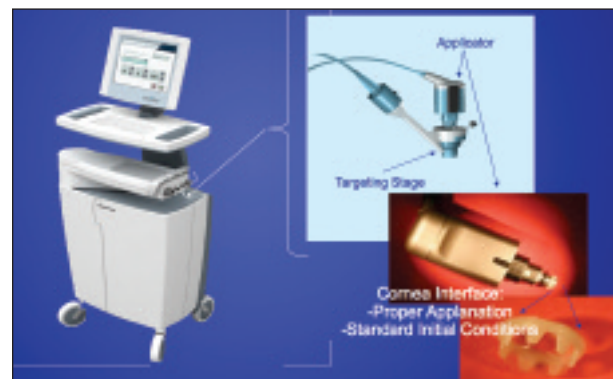


Figure 1. The Avedro Vadera Vision Correction System applies microwave energy in a toroidal pattern to the mid-periphery of the cornea.

refractive errors without inducing biomechanical weakening of the cornea. In fact, laboratory investigations not only showed improvement in corneal curvature but also indicated corneal strengthening, Dr. Hersh continued. Additional clinical trials are now under way in Europe to confirm the safety and effectiveness of Keraflex for the treatment of keratoconus and to potentially expand its indications to the correction of low and moderate myopia.

PROCEDURE

According to company literature, Keraflex KXL is conducted in two steps that, when combined, provide both thermal and photopolymerization biomechanical modalities to achieve flattening of the cornea. In the first step, patients undergo Keraflex with the Avedro Vadera

REFRACTIVE SURGERY FEATURE STORY

Vision Correction System (Figure 1), which applies less than 1 second of microwave energy in a toroidal pattern to the mid-periphery of the cornea. The microwave energy is applied in either a 360° annulus or a 270° annulus to prevent direct application over the pupil in keratoconus patients with eccentric cones. This step stimulates reshaping of the collagen lamellae to induce central and peripheral flattening.

In the second step, the patient undergoes focal-patterned collagen crosslinking (CXL) to synergistically enhance outcomes including corneal flattening, corneal rigidity, and corneal stability. This step may be performed simultaneously or at any time after the microwave application. Riboflavin 0.1% drops saturate the annulus, and then focal CXL is applied.

CURRENT APPLICATIONS

Compared with invasive refractive techniques such as LASIK, Keraflex reportedly maintains biomechanical integrity and corneal geometry, leaving untouched the corneal nerves that can induce dry eye when severed in LASIK. Also, this procedure potentially may be performed on patients with thinner corneas who are contraindicated for LASIK. Lastly, there are no potential problems with corneal flaps. At this stage of research, Keraflex is under investigation for the indications of keratoconus and myopia.

Keratoconus. In this progressive disorder, abnormalities of the corneal collagen structure and anatomy result in changes to the cone of the cornea. The microwave energy applied during Keraflex penetrates approximately the superficial one-third of the cornea to change the tension within the collagen lamellae, which according to company literature results in corneal flattening, corneal strengthening, and a reduction in myopia.

When Keraflex is used in conjunction with CXL, Professor Marshall said that the treatment goal is twofold: (1) to improve refraction and (2) to stabilize the cornea. With the Keraflex step, the cone is first flattened, thus addressing the refractive error induced by this disease. Applying riboflavin and ultraviolet-A light during focal CXL then stabilizes the corrected cornea. Another hope, Professor Marshall said, is that the CXL will also further increase corneal rigidity. Incorporating CXL into the treatment increases the potential of the induced correction to remain stable for longer compared with the effect of Keraflex alone.

Keratoconus is a source of distress for refractive surgeons. Keraflex may allow surgeons to tackle the main concern with this disease: reshaping the cornea to a surface that is more amenable to contact-lens fitting as well as refractive correction and improved visual acuity and function. The potential for stabilization makes this proce-

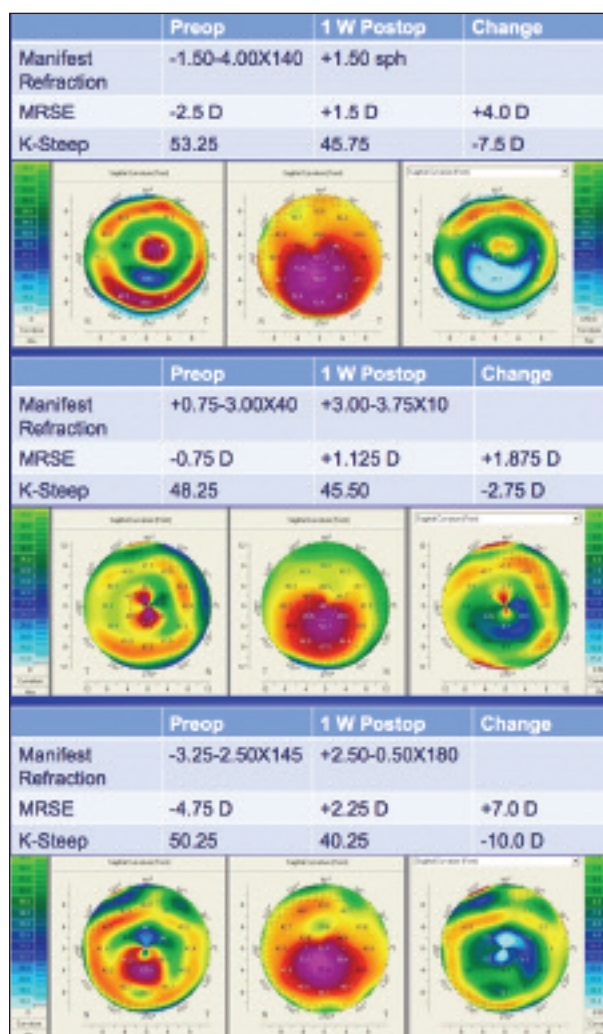


Figure 2. Case examples of three patients, (A) 33 years old, (B) 24 years old, and (C) 18 years old, who underwent Keraflex for the treatment of keratoconus.

sure of great interest to both corneal surgeons and patients with keratoconus. Figure 2 depicts three patients who underwent Keraflex for the correction of keratoconus.

Myopia. Approximately 30 million patients worldwide have undergone laser vision correction,¹ representing a mere 2% of the population eligible for refractive correction. Therefore, there is a large untapped market in which refractive surgery may be indicated, Professor Marshall said. First and foremost, the main reason patients avoid surgery is fear; the second is the lack of reversibility of such procedures. Because Keraflex is noninvasive, with no tissue removal or corneal weakening, and because of the transient nature of thermal procedures, Keraflex may be an attractive, patient-friendly treatment option. It will not replace but rather may

TAKE-HOME MESSAGE

- Keraflex is a minimally invasive procedure that uses thermo-biomechanics to reshape the cornea.
- Initial results in seven patients with keratoconus showed improvements in corneal flattening, smoothness, and regularity.

supplement current refractive surgery methods.

Laser vision correction is not a refractive solution often used in patients with low to moderate myopia. With Keraflex, there is potential to broaden the surgical vision correction market into this population.

CONCLUSION

To date, there is no concrete evidence on how long the cornea remains stable after the combined treatments of Keraflex and focal CXL. The first cohort of patients was treated in late November 2009, and stability data are not yet available. A larger cohort was treated in January 2010.

However, long-term data suggests that CXL alone effectively stabilizes the keratoconic cornea, as seen in multiple US and European clinical trials. In Dr. Hersh's experience, data extending to 2 years show good stability after CXL. According to Dr. Hersh, the hope is that adjunctive CXL will aid in stabilizing the Keraflex refractive effect as well as the keratoconic process itself.

Dr. Hersh and Professor Marshall both indicated that Keraflex has the potential to decrease the number of corneal transplants performed in patients with keratoconus who otherwise have no other alternative for treatment. Over the next few months, Avedro will be gathering data regarding the safety, efficacy, and stability of the procedure for keratoconus and myopia. Keraflex treatments for astigmatism are also being developed. ■

Peter S. Hersh, MD, is a Clinical Professor of Ophthalmology at New Jersey Medical School, a Visiting Researcher at Princeton University, and Director of the Cornea and Laser Eye Institute, CLEI Center for Keratoconus, New Jersey. Dr. Hersh states that he is a medical monitor for Avedro, Inc. He may be reached at e-mail: PHersh@Vision-Institute.com.

John Marshall, PhD, FMedSci, FRCPath, FRCOphth(Hon), is a Professor of Ophthalmology at the Institute of Ophthalmology, University College, London. Dr. Marshall states that he is a paid consultant for and shareholder in Avedro. He may be reached at e-mail: eye.marshall@googlemail.com.



1. Laser Eye Surgery News Web site. Available at: <http://lasereyeneews.blogspot.com>. Accessed February 17, 2010.