

Microwave Thermokeratoplasty: A Potential Treatment for Keratoconus

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A new thermokeratoplasty procedure holds promise for treating keratoconus.

While thermokeratoplasty has been used to reduce refractive error in the past, prior procedures have been plagued by problems with regression, lack of predictability, and competition from other options. With the development of a new thermokeratoplasty technology that delivers a precise, annular pulse of microwave energy, however, this concept is now being revived as a possible treatment for keratoconus and/or mild-to-moderate myopia. Still in the early testing phases, the Keraflex® procedure (Avedro, Inc.) is being evaluated both as a stand-alone procedure and for use in combination with collagen crosslinking.

Like other thermokeratoplasty procedures, Keraflex works by shrinking corneal collagen. In this case, the treatment involves applying microwave energy to an annulus of tissue in the corneal mid-periphery, thereby flattening the cornea. Unlike past procedures for hyperopia—for example, holmium laser thermokeratoplasty and conductive keratoplasty—which worked by applying focal spots in the periphery of the cornea, the size and shape of the Keraflex procedure is geometrically different. The choice of optical zone, diameter, and configuration determines the corneal shape change, thus allowing the Keraflex procedure to have a flattening effect. Depending on the intensity and configuration of the microwave energy, this procedure can yield corrections between roughly 1.00 D and 5.00 D.

The Surgical Procedure

Because success with Keraflex depends on centration, the first step in the procedure is to define the geometric center of the cornea. (I also like to note the first Purkinje image in order to locate the corneal apex.) The surgeon then marks the apex with a Sinsky hook and a gentian violet marking pen.

Next, the surgeon centers and locks the handheld targeting stage, which is very similar in its application to a standard microkeratome suction ring. X-Y dials are then used to center the device precisely over the centration mark, and the microwave handpiece is inserted into the targeting stage and engaged.

The interface on the handpiece then cools the cornea to a preset temperature—cooling sets standard baseline parameters and helps to make the procedure reproducible between patients—after which the circular electrode applies the microwave treatment energy. The electrode is computer controlled and automatically delivers the treatment to the right depth. Energy is applied in a ring that is approximately 4.5 mm in diameter and between 200 and 500 microns wide; the depth of the treatment is about 150 microns. The actual application of microwave energy takes less than a second, after which suction is disengaged and the instrument is removed.

Because this treatment affects the epithelium as well as the underlying stromal tissue, patients will have a small annular defect in the epithelium following the procedure. The epithelium typically heals within 24 hours, but non-preserved artificial tears and topical nonsteroidal antiinflammatory drugs (NSAIDs) may be used to ensure patient comfort during this period; a bandage contact lens may also be applied. Antibiotic drops are used to prevent infection.

Combining Keraflex and Collagen Crosslinking

Used alone, the Keraflex procedure should benefit keratoconus patients by flattening the cornea and possibly reducing corneal asymmetry. To achieve long-term improvement in vision, however, the eye must be stabilized so that further progression of the patient's keratoconus does not negate the effect of treatment. With this goal in mind, the Keraflex procedure is being tested in conjunction with collagen crosslinking, in the hope that together these procedures will be able to flatten the cone, regularize the corneal topography, and then stabilize the cornea in its new geometry.

Unlike a standard collagen crosslinking procedure (in which treatment is applied to the entire cornea), the collagen crosslinking procedure being developed for this application targets just the area of the corneal mid-periphery where the microwave treatment was performed (Figure 1). After completing the Keraflex procedure as described above, the surgeon uses a dry sponge to debride the residual epithelial cells overlying the treatment zone. An ultraviolet-blocking mask is then applied to protect the untreated central and peripheral cornea,

KERAFLEX® PROCEDURE	
✓	Uses microwave energy to perform thermokeratoplasty
✓	Being tested as a treatment for keratoconus
	— Can yield approximately 1 D to 5 D of flattening
	— May improve corneal regularity
✓	Could be combined with collagen crosslinking
	— Goal: To stabilize refractive change and halt keratoconus progression
	— Collagen crosslinking targets only corneal mid-periphery
✓	May also treat mild to moderate myopia and astigmatism



FIGURE 1 When performed in conjunction with a Keraflex® procedure, collagen crosslinking is performed only in the narrow region of the corneal mid-periphery underlying the Keraflex treatment.

leaving just the microwave-treated area of the corneal mid-periphery exposed. Finally, riboflavin drops are administered to the annulus of exposed stroma every 2 minutes for 30 minutes, after which ultraviolet light is applied to the area for 30 minutes.

In addition, adjunctive use of the standard pan-corneal crosslinking technique is being investigated.

Early Results

More research is needed to evaluate the efficacy of this combined procedure, but my hope is that the Keraflex procedure and collagen crosslinking will work synergistically. Laboratory studies have shown that collagen crosslinking increases the rigidity of corneal tissue, and work by John Marshall has shown that the Keraflex procedure also increases corneal rigidity.¹ As a result, use of both procedures together may be able to further slow or halt disease progression, as well as reduce the myopia and astigmatism already produced by the disease.

While the Keraflex procedure has only been tested in a handful of patients to date, early results appear promising. In a series of seven patients who were treated in Turkey and followed for 2 months, investigators found that the Keraflex/collagen crosslinking combined procedure achieved an average of 6.0 D of corneal flattening and a mean change in manifest refraction spherical equivalent (MRSE) of 4.39 D. No data is available regarding possible astigmatic corrections, but regularity of the corneal topography appears to be improved in some cases (Figure 2). Also, while additional follow-up will be needed to assess long-term changes in refraction, topographies and visual acuity appear stable so far.

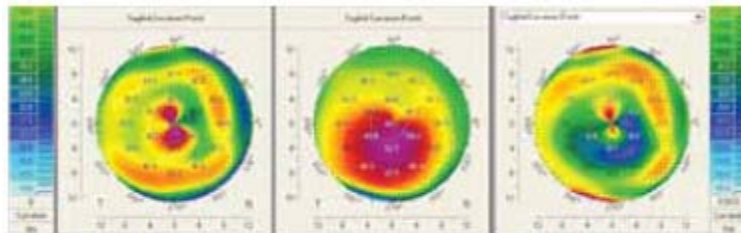


FIGURE 2 Corneal topography 1 month after Keraflex and collagen crosslinking (left) shows a significant change compared to preoperative topography (center). Specifically, the difference map (right) shows flattening of the cone and regularization of topography.

Keys to Success

Like any procedure, Keraflex requires proper patient selection to achieve optimal outcomes. Currently, the Keraflex procedure is being evaluated in keratoconus patients who have a potential for good visual acuity but are experiencing some optical problems that cannot be easily corrected with glasses or contact lenses. Patients with corneal scars are not good candidates for Keraflex, as they are likely to need a penetrating or lamellar keratoplasty to achieve good vision, and patients with thin corneas in the area of microwave application (midperipheral thickness < 400 microns) are also unsuitable for the procedure, since treating these eyes could result in complications or unpredictable refractive changes.

The Keraflex procedure should have a good safety profile, but there are still a few risks that must be considered. The procedure affects only a small area of corneal epithelium, so the risk of complications related to the epithelial defect is modest; nonetheless, care should be taken with patients who are at high risk of infection or delayed epithelial healing. Also, any change in corneal conformation presents a risk of optical side effects—such as glare, halo, or diplopia—so patients need to be educated about this possibility. While the goal of the Keraflex procedure is to reduce the incidence of such symptoms, there is always the possibility that patients may develop new dysphotopsias.

Finally, while the Keraflex procedure is currently being evaluated only for the treatment of keratoconus, future applications may include treatment of myopia and/or astigmatism. As with keratoconus, treatment of spherical myopia would involve uniform flattening of the cornea. To treat astigmatism, however, different treatment patterns would be needed.

The Bottom Line

Keraflex is a new thermokeratoplasty procedure being tested for the treatment of keratoconus. The Keraflex procedure uses microwave energy delivered in a small annulus to the corneal mid-periphery. This procedure can flatten the cone and may also help to regularize the cornea. By combining the procedure with a modified collagen crosslinking procedure, investigators hope to improve the stability of the eye as well as regularize its geometry. While still in clinical trials outside of the United States, early results with this technology appear promising.

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References

1. John Marshall, personal communication. May, 2010