Promoting Corneal Wound Healing

A new, proprietary amniotic membrane replaces passive wound healing for corneal and limbal regeneration.

BY WILLIAM B. TRATTLER, MD

Wound healing mechanisms in the cornea and limbus typically rely on the body's natural ability to promote cellular mediators. Under ideal conditions, the development of a corneal wound would incite cellular mediators to trigger the healing process. Not all eyes respond as desired or expected, however, and it is possible for the healing response to incite an immune reaction that leads to sustained inflammation, uncontrolled angiogenesis, fibrotic tissue formation, and disorganized scar tissue.

Use of an amniotic membrane may help initiate an active healing process that selectively triggers the immune system to suppress inflammation. The Prokera device (Bio-Tissue; Figure 1) is manufactured with a proprietary process that maintains many of the crucial components of the extracellular matrix that aid in tissue regeneration.

The Prokera amniotic membrane graft is approved by the FDA for use as an in-office treatment for corneal and limbal defects and scarring due to various etiologies. Several studies demonstrate that it is a safe and effective method for promoting healing of the corneal surface with minimal side effects. The device is easy to incorporate into practice, and it offers ophthalmologists an element of control over the sometimes unpredictable corneal healing process.

"BIOLOGICAL SCAFFOLDING" FOR ACTIVE WOUND HEALING

The Prokera graft is cryopreserved using the proprietary CryoTek method, which protects key components of the extracellular matrix and thereby promotes the regenerative tissue process.[1-3] The process is supported by over 300 peer-reviewed articles, and more than 100,000 safe and effective CryoTek grafts have been performed worldwide.

The CryoTek method used to make the Prokera membrane preserves heavy-chain hyaluronic acid, which has been found to directly inhibit proinflammatory cells,[4,5] suppress T-cell activation, and inhibit giant cell formation. Other key components of the preserved extracellular matrix include proteoglycans and growth factors that are important in regenerative healing.[6] Collagens, fibronectin, and lamilin are also present in the Prokera device and serve as biological scaffolding for tissue regeneration.

Figure 1. The Prokera amniotic membrane graft is a cryopreserved membrane attached to a 16-mm-diameter thermoplastic ring.

IN-OFFICE THERAPY

The Prokera graft is FDA-approved as a wound-healing,[7-10] antiangiogenic,[7] anti-inflammatory,[8,11,12] anti-scarring,[7] and protective[7,13] device that actively promotes wound healing without scarring. The simple device, designed to be used in the office setting, is an amniotic graft held in place by a 16-mm thermoplastic ring that is placed inside the eye (beneath the upper and lower lids; Figure 2) and allows the amniotic membrane direct contact with the affected area on the cornea. I have had success with this technology in treating neurotrophic persistent corneal epithelial defects, postinfectious

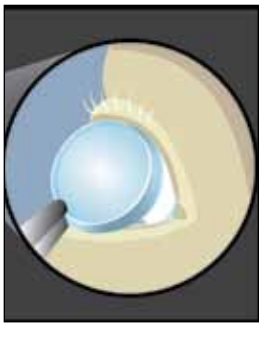

Figure 2. To insert the Prokera device, the surgeon prepares the eye with topical anesthesia, rinses the graft with sterile saline solution, and instructs the patient to look down while inserting the Prokera graft into the upper cul-de-sac first. The patient then looks up while the surgeon fits the ring into the lower cul-de-sac.

THE PROKERA DEVICE HELPS TO DELIVER THE PREMIUM CLINICAL EXPERIENCE

BY NEEL R. DESAI, MD

So much of the work we do as anterior segment surgeons is affected by postoperative inflammation and scarring. We do everything we can to modify pre-, intra-, and postoperative regimens, surgical techniques, and technologies in an effort to reduce ocular inflammation and the resulting scar tissue. The goal of reducing inflammation, particularly in ocular surface diseases and corneal transplant treatments, often is a matter of speed—how quickly we can reduce the inflammation and thus prevent scar tissue from forming. These are the cases in which an amniotic membrane graft is invaluable.

THE CRYOPRESERVED DIFFERENCE

I have had the opportunity to use both dehydrated and cryopreserved amniotic membranes in a variety of settings over the last several years. The difference between these two types of amniotic membranes is the difference between passive and active agents. Dehydrated amniotic membrane products are passive dressings[1] that in many cases work no better than a bandage contact lens. A cryopreserved amniotic membrane, like Bio-Tissue's Prokera, however, retains the cytokines, high-molecular-weight proteins, and other active properties of the tissue that serve a variety of functions,[2,3] from antiangiogenesis to antiinflammatory to anti-scarring. These active complements also help expand the existing population of limbal stem cells and therefore rapidly promote the re-epithelialization of the corneal surface.[4-7] Plus, because the Prokera device is mounted on a symblepharon ring that takes seconds to insert, its application is an in-office procedure, rather than a surgical one, which therefore allows immediate treatment upon diagnosis.

I have used the cryopreserved amniotic membrane grafts for a variety of indications, from the treatment of pterygia, conjunctivochalasis, and other conditions requiring ocular surface reconstruction where controlling inflammation and its sequellae is critical. The Prokera device now allows me to add this powerful tool to my in-office armamentarium for a variety of indications as an anterior segment and refractive-cataract surgeon.

CASE: PREMIUM IOL IMPLANTATION IN AN EYE WITH SALZMANN DEGENERATION

A recent case beautifully illustrates the value of a bioactive amniotic membrane graft. A patient presented to my office for cataract surgery because I had successfully implanted several of her friends with premium IOLs. She requested a particular IOL by name, but when I examined her corneas, she had one of the worse cases of bilateral Salzmann nodular degeneration I had ever seen (Figure 1A). I felt that my staff and I would be lucky to obtain accurate biometry on the eye preoperatively for standard cataract surgery, let alone able to achieve a precise refractive target for presbyopia and astigmatism correction.

Because I had recently been testing the Prokera amniotic membrane graft, I did not immediately dismiss this patient as a poor candidate for her desired premium IOL. Ordinarily, I would have scheduled her for an OR visit, sutured a dehydrated amniotic membrane to the eye, waited a week, removed the sutures, placed a bandage

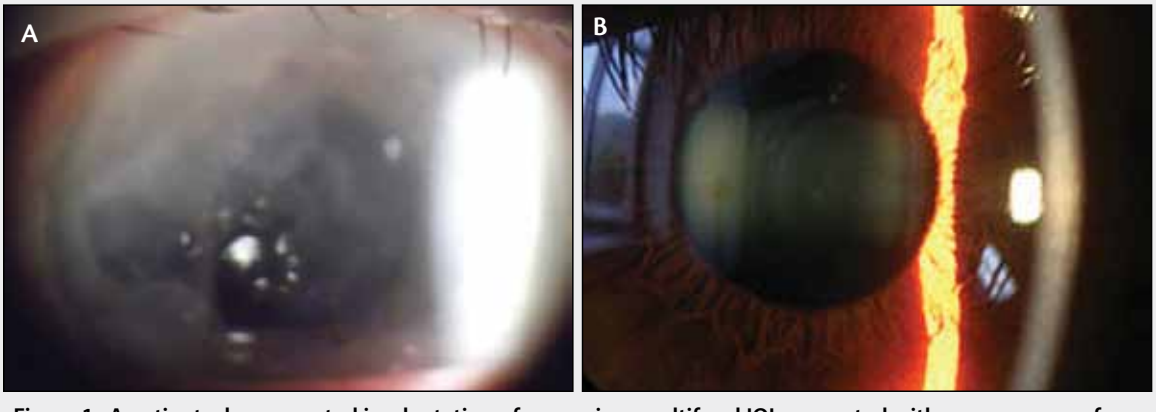

Figure 1. A patient who requested implantation of a premium multifocal IOL presented with a severe case of Salzmann nodular degeneration (A). After a superficial keratectomy and placement of a Prokera amniotic membrane graft for 4 days, the eye had improved significantly (B) and was able to undergo biometry for the lenticular surgery 2 weeks later.

THE PROKERA DEVICE HELPS TO DELIVER THE PREMIUM CLINICAL EXPERIENCE (CONTINUED)

contact lens, let the eye heal for perhaps 4 more weeks, and then tried to perform biometry on it. Instead, I performed a superficial keratectomy in the office and placed a Prokera graft, all within a couple minutes, and the eye was re-epithelialized within 4 days (Figure 1B). I scheduled this patient to undergo biometry 2 weeks later, and I was able to give her an accommodating presbyopia-correcting IOL (although not the IOL she'd requested). The patient's preoperative BCVA was 20/80 in both eyes, and her UCVA was 20/400. After treatment with the Prokera device, her eye showed no scar tissue or haze, and her postoperative UCVA was 20/20 and J2 in both eyes.

In summary, the Prokera device has helped me provide the kind of immediate in-office treatment critical to quelling the inflammatory, angiogenic, and scarring processes common to a variety disease states, including the management of ocular surface disease, prior to refractive cataract surgery.

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THE PROKERA GRAFT PROVIDES OPTIMAL CORNEAL HEALING

BY MARY DAVIDIAN, MD

Some of the cases in which I commonly use the Prokera device are infectious keratitis, persistent herpes zoster pseudodendrite, recurrent corneal erosions, filamentary keratitis, vernal shield ulcers, and high-risk surgical cases (such as rheumatoid melt). One of the important features of this amniotic membrane is that it does not act as a barrier against antibiotics. To the contrary, it acts as a delivery vehicle or a sponge to retain antibiotics and allow them to be constantly emitted on the surface of the eye, which assists with healing and further promotes the membrane's anti-inflammatory effects.

CASE EXAMPLE: PSEUDODENDRITE

A 23-year-old female presented with pain in the right eye after undergoing sinus surgery. She suspected the eye was accidentally splashed with disinfecting solution during the preparation for the sinus surgery. She first presented with a large corneal abrasion that had a pH of 7. My team and I irrigated the eye and treated it with topical antibiotics and artificial tears. At first, the abrasion appeared to be healing, although the surface showed delayed re-epithelialization. Three weeks later, however, the patient presented with a pseudodendrite on that same cornea (Figure 1) and a refraction of 20/50. I started her

Figure 1. A pseudodendrite that appeared after a corneal abrasion was treated with topical antibiotics.

on ganciclovir ophthalmic gel 0.15% (Zirgan; Baush + Lomb) five times per day as well as oral Valtrex (GlaxoSmithKline Pharmaceuticals) at 1 gram three times per day, and I subsequently added some mild antibiotic-steroid, tobramycin/dexamethasone ophthalmic suspension 0.3%/0.05% (Tobradex ST; Alcon Laboratories, Inc.), once per day. The eye still did not improve after 3 weeks of this treatment regimen, so I debrided the pseudodendrite from the corneal surface with a Paton spatula (Katena Products, Inc.), and I placed a Prokera ring on the eye. I had the patient continue using Zirgan five times a day, Besivance (Bausch + Lomb) three times a day, and Valtrex 1g po three times per day. After 2 weeks, the Prokera

THE PROKERA GRAFT PROVIDES OPTIMAL CORNEAL HEALING (CONTINUED)

graft melted, and I removed the ring. The eye looked significantly better: the pseudodendrite had resolved, and the epithelium was flat, with some very mild residual haze (Figure 2). Her postoperative refraction in that eye was 20/25- UCVA.

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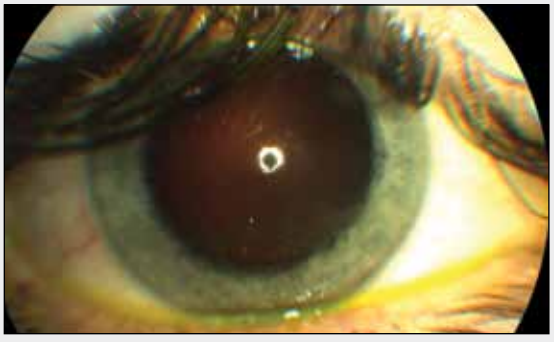

Figure 2. After 2 weeks under a Prokera graft, the epithelium was flat with only mild residual haze.

recalcitrant corneal inflammation, and active corneal ulcers (in combination with topical antibiotics).

Other products used for promoting healing such as a bandage contact lens, therapeutic eye drops, steroids, dry amniotic membrane, and collagen matrix materials are mostly protective in nature. In contrast, Prokera combines the functionality of a symblepharon ring with the biologic actions of a cryopreserved amniotic membrane to create a unique, active treatment option for corneal and limbal wound healing.

In clinical studies, Prokera has proven to be a safe and effective method to promote healing of the corneal surface with minimal side effects,[8] while also inhibiting angiogenic processes and inflammation, thus promoting healing.[7-12,14] It also stimulates healthy re-epithelialization of the corneal wound without sutures.[8-12,15] Prokera can relieve pain and reduce corneal haze in some cases, which may result in improved visual acuity of up to 2.5 Snellen lines.[10,11]

CONCLUSION

For patients experiencing conditions that can lead to corneal haze or scarring, such as persistent epithelial defects, neurotrophic corneal ulcers, or infectious keratitis, it is important to consider therapies that can limit inflammation, which can lead to corneal opacity and vision loss. The use of the Prokera amniotic membrane in select patients to actively engage the regenerative tissue process may help shorten healing times and overcome recalcitrant corneal epithelial defects and scarring. The device's use is supported by a number of clinical studies, and it is applicable in a variety of settings. Lastly, the Prokera device is easy to incorporate into the clinical setting with a fairly short learning curve. ■

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