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Corneal scarring from laser in situ keratomileusis after epikeratoplasty: Clinical and histopathologic analysis

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Abstract

A 47-year-old woman required penetrating keratoplasty in the right eye after developing delayed visually significant corneal scarring bilaterally after laser in situ keratomileusis (LASIK) in 1997 following epikeratoplasty in 1987. Spectral domain ocular coherence tomography of the left cornea showed a 100 μ m lenticule with a LASIK flap posterior to the host Bowman layer at 250 μ m. Histopathology and electron microscopy of the right corneal button showed a 120 μ m lenticule with a LASIK flap within the lenticule at 100 μ m. Clinically significant scarring was present within the LASIK flap interface, within the lenticule stroma, and within the area of the underlying host Bowman layer. There were keratocytes at the junction between the LASIK flap and lenticule stromal bed. Although epikeratoplasty is no longer practiced, post-epikeratoplasty patients may present for refractive surgical options and LASIK carries significant risks for corneal scarring in these individuals, especially when using flap-creating devices that may create thin LASIK flaps.

Epikeratoplasty is a corneal refractive procedure that involves placement of a donor lenticule onto a host stroma to correct aphakia, keratoconus, hyperopia, and high myopia.^{1–3} The procedure was primarily used in the 1980s, with purported reversibility and lack of the immune reactions seen in penetrating keratoplasty (PKP). However, longer follow-up revealed refractive complications of this surgery and the procedure became obsolete as laser refractive surgery advanced.⁴

Although some refractive complications from epikeratoplasty can be treated by lenticule removal, there have been several reports of treating residual refractive error with photorefractive keratectomy (PRK) and/or laser in situ keratomileusis (LASIK), usually with good results.^{5–7} In all these cases, follow-up has been limited. We report a case of LASIK after epikeratoplasty with more than 10 years of follow-up. Corneal scarring developed, requiring PKP for visual rehabilitation.

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CASE REPORT

A 47-year-old white woman was evaluated in January 2011 for progressive decreased visual acuity, right eye worse than the left eye, and difficulty driving due to blurriness, glare, and halos in both eyes. Bilateral epikeratoplasty for myopia was performed in 1987; no preoperative information was available. Following the surgery, the patient reported seeing well without glasses for 1 year but then required glasses again for progressively increasing myopia. In 1997, LASIK was performed in both eyes; no preoperative data were available. Following LASIK, the patient reported some visual improvement but noted progressive bilateral visual deterioration, worse over the past 3 years, not correctable with glasses or contact lenses and not sufficient for her activities of daily living.

On examination in our clinic, the corrected distance visual acuity (CDVA) was 20/50 in the right eye and 20/40 in the left eye, with manifest refractions of $-7.50 +2.00 \times 40$ and $-0.75 + 0.50 \times 165$, respectively; there was no improvement in either eye with rigid gaspermeable contact lens over-refraction. Slitlamp examination revealed bilateral intact epikeratoplasty grafts in position with bilateral central anterior stromal haze, worse in the right eye (Figure 1). Spectral domain optical coherence tomography (Optovue, Inc.) performed in the left eye demonstrated a distinct lenticule anterior to Bowman layer, with overall corneal thickness of 735 μm and lenticule thickness of 105 μm centrally (Figure 2). A LASIK flap measuring 238 to 255 μm in thickness across the flap was visible posterior to Bowman layer in the stroma. Topography revealed a relatively well-centered optical zone with irregular astigmatism greater in the left eye than in the right eye. Ultrasound pachymetry revealed central corneal thickness greater than 800 μm in both eyes.

Because the patient's acuity was limited by irregular myopic astigmatism and visually significant corneal haze that could not be corrected with contact lenses, the decision was made to perform full-thickness PKP in the right eye. Surgery was uneventful, and the corneal button was sent for histopathologic evaluation.

Histopathologic examination revealed an intact epithelium with an epikeratoplasty lenticule measuring 120 μm in thickness (Figure 3). There was focal disruption in Bowman layer overlying the lenticule. A LASIK flap measuring 100 μm , including 50 μm of epithelium and 50 μm of combined Bowman and stroma, was present within the lenticule. Scarring was present at the interface of the flap and within the remaining lenticule stroma. There was scarring in the area of the underlying host Bowman layer and the interface between the lenticule and host stroma (Figure 3). Electron microscopy revealed migrating keratocytes at the junction between the LASIK flap and the lenticule stromal bed with transection of collagen lamellae at the interface between lenticule and host stroma (Figure 4).

After 6 months, the CDVA improved to 20/30 in the right eye and the patient reported significant improvement in her visual symptoms. The left eye remained stable, and to date the patient has not pursued surgery in that eye.

DISCUSSION

Laser in situ keratomileusis after epikeratoplasty has been reported with good early outcomes^{6,7}; however, significant long-term follow-up has not, to our knowledge, been reported. This case demonstrates the potential for visually significant corneal haze and scarring after LASIK within the epikeratoplasty lenticule induced by LASIK flap creation, excimer laser ablation, or both. In this patient, scarring required full-thickness PKP in 1 eye for visual rehabilitation and acuity remains limited in the unoperated eye.

As epikeratoplasty was heralded as a reversible procedure, it appeared that few patients should require more than simple removal of the lenticule if ametropia or complications arose postoperatively. However, in previous cases of lenticule removal, certain histopathologic findings were noted, including thickened epithelium, collagenous subepithelial fibrocellular tissue, disrupted Bowman layer, and a scarred and edematous stroma, with keratocytes surrounding Bowman layer.⁸ Electron microscopy has shown irregularities and duplications in basement membrane as well as reduction in hemidesmosomes.⁹ Cases of recipient corneal scarring that did not improve after removal of the graft have also been reported.¹⁰ Rodrigues et al.¹¹ report breaks in host Bowman layer with irregular collagen, focal posterior stromal fibrosis, persistent Descemet folds, and focal endothelial degeneration. Other cases have shown decreased lenticular keratocytes, fibrogranular material, and recipient keratocyte migration into the lenticule.¹²

We found evidence of disruption in Bowman layer in the lenticule and the host; in addition, there was scarring at the host lenticule interface. Electron microscopy showed migration of keratocytes at the LASIK flap and lenticule junction. This has been reported in a series of epikeratoplasty grafts showing migration of keratocytes from the periphery to the center of the lenticule¹³ and recipient keratocyte migration into the lenticule.¹² However, migration has not been shown in the setting of LASIK after epikeratoplasty.

The decision to perform LASIK after epikeratoplasty carries risks in addition to scarring and keratocyte migration. Using a mechanical microkeratome over a lenticule poses a risk for lenticule dislocation or damage. Lee and Mannis⁷ describe the creation of a buttonhole in an epikeratoplasty button with the keratome due to steep keratometry readings. Kim et al.¹⁴ describe detachment of the lenticule during microkeratome in situ keratomileusis without suture in several patients that was difficult to replace and caused epithelial ingrowth. Damage from the microkeratome may contribute to scarring of donor or lenticule tissue.⁸ The safety and efficacy of femtosecond LASIK with epikeratoplasty has yet to be determined. There is concern that a femtosecond laser could also potentially create an ultrathin flap,¹⁵ which may lead to postoperative haze, reported in ultrathin flaps¹⁶ with an outcome similar to that in our patient. If femtosecond LASIK is performed, targeting a thicker than usual flap may be a better option to avoid the lenticule altogether; however, as seen in this case in the patient's left eye, even a thick LASIK flap into host stroma can result in visually significant scarring.

Surface ablation may be a better option than LASIK to avoid these risks and may also be used to treat anterior scarring on the lenticule in select cases¹⁷; however, haze has occurred

after most cases of PRK after epikeratoplasty reported in the literature.^{17,18} Mitomycin-C (MMC) was not used in these reports, and its use may mitigate this haze formation. A recent case series of 10 patients reported improvement in astigmatism and visual acuity with topography-guided laser-assisted subepithelial keratectomy with 6 months follow-up.¹⁹ As seen in our patient, however, longer follow-up is necessary to determine whether surface ablation will be an appropriate procedure for patients with epikeratoplasty.

In summary, LASIK after epikeratoplasty can result in visually significant corneal haze and scarring requiring corneal transplantation for visual rehabilitation. Although epikeratoplasty is no longer practiced, patients with a history of epikeratoplasty may present looking for surgical alternatives to visual correction. In these individuals, we recommend considering surface ablation procedures with MMC use and avoiding the use of a mechanical microkeratome if LASIK treatment is planned.

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Figure 1. Slitlamp photograph of the right eye (A) in sclerotic scatter illumination highlights the epikeratoplasty graft with irregular edges and significant central scarring, while the left eye (B) in broad-beam tangential illumination demonstrates the epikeratoplasty graft with less central haze.

Figure 2.

A: Spectral domain optical coherence tomography image of the left eye demonstrates a distinct lenticule anterior to Bowman membrane in cross section. B: The pachymetry map shows central corneal thickness of 735 μm , which increases to almost 800 μm paracentrally within the central 6 mm.

Figure 3.

Periodic acid-Schiff stain of the right corneal button submitted after PKP. *A:* At $\times 25$ magnification, the epikeratoplasty lenticule (*L*), measuring 120 μm thick, is identifiable between the lenticule Bowman layer (*arrows pointing upward*) and the recipient Bowman layer (*asterisk*) above the recipient stroma (*RS*). The LASIK flap interface is identifiable within the epikeratoplasty lenticule (*arrowheads pointing downward*). *B:* Higher magnification ($\times 100$) shows the lenticule Bowman layer (*small arrows pointing upward and downward*), recipient Bowman layer (*asterisk*), and fibrocytes (*arrowheads pointing upward and downward*) in the LASIK interface within the epikeratoplasty lenticule (*L*).

Figure 4.

Electron microscopy of the corneal button demonstrates the following: A: Epithelium (*E*) overlying the epikeratoplasty lenticule (*L*) and Bowman layer (*B*), which is focally disrupted (*arrow*). There are activated keratocytes present (*K*). B: Keratocytes are present (*asterisk*) at the interface between the LASIK flap (*between arrowheads*) and underlying recipient stroma (*RS*) within the epikeratoplasty lenticule (*L*). C: An activated keratocyte (*arrowhead*) is seen migrating from the recipient stroma into the lenticule stroma at the lenticule–recipient interface.