The feasibility of managing ectasia after small-incision lenticule extraction (SMILE) using tissue addition and pocket corneal crosslinking (CXL) is described. Four eyes of 3 patients (mean age 25.7 years) developed features of keratoectasia at a mean period of 3 years after SMILE for myopia. All cases were managed with insertion of heterologous SMILE lenticules in the previously created pocket, followed by simultaneous accelerated CXL. At a mean follow-up of 7.67 months, there was improvement in corrected distance visual acuity and reduction in keratometry and higher-order aberrations in all eyes. The visual, refractive, and topographic parameters remained stable at the last visit compared with the 2-week follow-up visit. No eye developed haze, infection, or rejection requiring tissue explanation. Early experience showed tissue addition with simultaneous pocket CXL to be a feasible approach for managing ectasia after SMILE. However, further follow-up is required to establish the long-term safety and effects on corneal stabilization.

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TECHNIQUE

Management of small-incision lenticule extraction ectasia using tissue addition and pocket crosslinking

Sri Ganesh, MS, DNB, Sheetal Brar, MS, Rohan Bowry, MS

Tissue addition is emerging as a new paradigm in corneal and refractive surgery in which corneal allogenic tissue has been shown to be successfully used for potential management of hyperopia and keratoconus. The first such case of endokeratophakia was reported by Pradhan et al., wherein the authors used a donor lenticule from a patient who had undergone small-incision lenticule extraction (SMILE) for myopia and implanted it into a recipient cornea to correct aphakia. In 2015, our group showed the feasibility using SMILE lenticule for the potential treatment of hyperopia and, in 2016, for keratoconus. In the 6 eyes treated with this technique, a tissue addition procedure called femtosecond intrastromal lenticule implantation (FILI) using donor SMILE lenticules combined with accelerated corneal crosslinking (CXL) in pocket, it was found that the technique was safe and effective in managing mild to moderate keratoconus through a follow-up of 6 months. Because ectasia might be considered as keratoconus developing in a postrefractive surgery eye, the feasibility and safety of this technique in post-SMILE ectasia was evaluated. We report 4 eyes with post-SMILE ectasia (3 operated at our center and 1 operated elsewhere) and explore the feasibility of tissue addition using SMILE lenticules combined with accelerated CXL for potential management.

SURGICAL TECHNIQUE

Written informed consent was obtained both from the SMILE donors regarding the use of their lenticule for this purpose and from the recipients regarding the nature of the procedure. However, ethics committee approval was not deemed necessary, because we already had approval for this technique to treat keratoconus and had already published the safety profile in keratoconic eyes. As per our standard protocol, both the donor and recipients underwent serology for HIV, HBsAg, VDRL, and syphilis. In all cases, both the donor procedure and the FILI procedure were planned for the same day, after receiving the serology report. The power of the lenticule to be implanted was based on the spherical equivalent of the recipient eye that had signs of ectasia. Exclusion criteria were advanced ectasia with significant decentration, thinnest pachymetry less than 400 μm, maximum keratometry more than 55 diopter (D), central scarring, or corrected distance visual acuity (CDVA) less than 6/36.

After extraction from the donor eye, the SMILE lenticule was thoroughly rinsed 3 times in a balanced salt solution to remove any debris, tear secretions, or metallic particles that might have attached to the lenticule surface during dissection, extraction, and examination of the lenticule on the corneal surface. The washed lenticule was then placed on a
Table 1. Preoperative and 1-year postoperative visual and refractive outcomes of eyes treated for ectasia (n = 5).

<table>
<thead>
<tr>
<th>S. No.</th>
<th>Eye Operated</th>
<th>UDVA (Snellen)</th>
<th>Sph (D)</th>
<th>Cyl (D)</th>
<th>Axis (degree)</th>
<th>UDVA (Snellen)</th>
<th>Sph (D)</th>
<th>Cyl (D)</th>
<th>Axis (degree)</th>
</tr>
</thead>
<tbody>
<tr>
<td>Patient 1</td>
<td>Left eye</td>
<td>6/6</td>
<td>0.00</td>
<td>0.00</td>
<td>0</td>
<td>6/6</td>
<td>0.00</td>
<td>0.00</td>
<td>0</td>
</tr>
<tr>
<td>Patient 2</td>
<td>Left eye</td>
<td>6/6</td>
<td>0.00</td>
<td>−6.00</td>
<td>40</td>
<td>6/18</td>
<td>1.00</td>
<td>−2.50</td>
<td>100</td>
</tr>
<tr>
<td>Patient 3</td>
<td>Right eye</td>
<td>6/18</td>
<td>−1.00</td>
<td>−2.50</td>
<td>170</td>
<td>6/12</td>
<td>1.00</td>
<td>−2.50</td>
<td>100</td>
</tr>
<tr>
<td>Patient 4</td>
<td>Left eye</td>
<td>6/24</td>
<td>−1.00</td>
<td>−2.75</td>
<td>170</td>
<td>6/12</td>
<td>1.00</td>
<td>−2.50</td>
<td>100</td>
</tr>
<tr>
<td>Patient 5</td>
<td>Left eye</td>
<td>6/36</td>
<td>−4.50</td>
<td>−1.75</td>
<td>120</td>
<td>6/12</td>
<td>1.00</td>
<td>−2.50</td>
<td>100</td>
</tr>
</tbody>
</table>

CDVA = corrected distance visual acuity; FILI = femtosecond intrastromal lenticule implantation; UDVA = uncorrected distance visual acuity

Table 2. Details of SMILE lenticule donor tissues that were used for femtosecond intrastromal lenticule implantation for management of post-SMILE ectasia (n = 4).

<table>
<thead>
<tr>
<th>S. No.</th>
<th>Eye Operated</th>
<th>Recipient Eye SE (D)</th>
<th>Donor Eye SE (D)</th>
<th>Central Lenticule Thickness (μm)</th>
<th>Optical Zone (mm)</th>
</tr>
</thead>
<tbody>
<tr>
<td>Patient 1</td>
<td>Left eye</td>
<td>−3.00</td>
<td>−3.00</td>
<td>103</td>
<td>6.0</td>
</tr>
<tr>
<td>Patient 2</td>
<td>Right eye</td>
<td>−2.25</td>
<td>−2.92</td>
<td>70</td>
<td>6.5</td>
</tr>
<tr>
<td>Patient 3</td>
<td>Left eye</td>
<td>−2.37</td>
<td>−3.27</td>
<td>91</td>
<td>6.5</td>
</tr>
<tr>
<td>Patient 4</td>
<td>Left eye</td>
<td>−5.37</td>
<td>−4.95</td>
<td>94</td>
<td>6.5</td>
</tr>
</tbody>
</table>

SE = spherical equivalent; SMILE = small-incision lenticule extraction

Teflon block and stained with 0.23% riboflavin solution (Peschke L) to enhance its visibility. A 3.0 mm trephine was used to punch the center of the lenticule to create a doughnut-shaped lenticule tissue.

In the recipient eye, the old SMILE incision was opened using the Sinskey side of the Reinstein dissector (Duckworth & Kent Ltd.), followed by dissection of the pocket using the blunt side of the same instrument. This allowed access to the interface, into which 0.23% riboflavin dye was then injected. The dye was allowed to soak for 60 seconds, after which the interface was washed with a balanced salt solution. Following this, the doughnut-shaped lenticule was held with lenticule holding forceps and inserted into the pocket using a T-shaped inserter. The lenticule was then adjusted and centered to the first Purkinje image/corneal vertex (Supplemental Digital Content 5, Video 1, available at http://links.lww.com/JRS/A140). The eye was finally exposed to ultraviolet (UV) A radiation using a power of 18 mW/cm² for a period of 5.8 minutes with an accelerated system (Avedro, Inc.), delivering a total energy of 6.3 J.

Postoperatively, topical steroid in the form of 1% prednisolone (Predforte, Allergan, Inc.) was prescribed for a period of 3 months in tapering dosage, along with 0.5% moxifloxacin antibiotic eyedrops (Vigamox 0.5%, Allergan, Inc.) 4 times a day for 2 weeks. Lubricants were prescribed for 4 times a day for 1 month and as needed thereafter. All cases were uneventful intraoperatively, and there was no incidence of lenticule or incision tear while handling and inserting the lenticule into the recipient eye.

RESULTS

Four ectasia eyes of 3 post-SMILE patients with a mean age of 25.7 years were treated with FILI combined with simultaneous accelerated CXL in pocket. Patients 1 and 3 had unilateral ectasia, whereas patient 2 had bilateral ectasia. The fellow eye of patient 3 was treated with accelerated CXL in pocket alone, using the same energy parameters as for the combined procedure. Table 1 summarizes the preoperative and postoperative data of the 4 eyes treated with FILI plus CXL, along with data of the fellow eye that had pocket CXL alone. Table 2 describes details of the donor lenticules that were used to perform FILI. Patient 2 completed 6 months follow-up, whereas patients 1 and 3 completed 8 and 9 months of follow-up, respectively.

Patient 1 was a 24-year-old woman with pre-SMILE refractive of −4.75 −1.50 ×10 and −4 −2 ×165 in the right and left eyes, respectively, with both eyes improving to 6/4.5. Preoperative topography showed borderline corneas with abnormal Belin/Ambrosio Enhanced Ectasia Display (BAD) scores in both eyes (Supplemental Digital Content 1, Figure 1, available at http://links.lww.com/JRS/A136). Her post-SMILE uncorrected distance visual acuity (UDVA) in both eyes was 6/6. Three years and 3 months later, she developed features of ectasia in her left eye, with reduction in CDVA to 6/18, with manifest refraction of 0.

Her ectatic eye (left eye) received FILI plus CXL, using donor tissue of spherical equivalent −3.00 D. For the fellow eye, an option of doing prophylactic CXL or observation with repeat topography was offered to the patient. The patient chose to be observed because her UDVA was maintained at 6/6 in the right eye.

Figure 1 shows the difference map of 2 weeks vs 8 months for anterior keratometry in the left and the right eyes, respectively. There was flattening of 4.5 D in the steep keratometry observed in the left eye, whereas the right eye...
remained stable without any features of ectasia. The CDVA in the left eye improved from 6/18 to 6/9 with reduction in refractive cylinder from −6.00 to −2.50 D, whereas the right eye maintained UDVA of 6/6. Figures 2, A and 3, A show the anterior segment optical coherence tomography (AS-OCT) and clinical picture of the left eye at 8 months, respectively, showing the doughnut-shaped lenticule in situ.

Patient 2 was a 23-year-old man with preoperative refraction of −3.00 −1.65 × 165 and −6.65 −0.75 × 170 in the right and left eyes, respectively. At 2 weeks after SMILE, his UDVA was 6/6 in each eye, after which the patient did not return for follow-up. Three years later, he presented with complaints of difficulty in focusing while working on a computer, but there were no obvious complaints of decreased vision. On examination, his UDVA in the right eye was 6/18, which could be improved to 6/12 with refraction of −1.00 −2.50 × 170. UDVA in the left eye was 6/24, which improved to 6/12 with refraction of −1.00 −2.75 × 170. His preoperative Pentacam tomography showed normal quad maps and BAD in both eyes, except 1 borderline parameter (Supplemental Digital Content 2, Figure 2, available at http://links.lww.com/JRS/A137). FILI plus CXL was performed in both eyes. Figure 4 shows the difference map of 2 weeks vs 12 months for anterior keratometry for eyes. There was flattening of 6.2 D and 5.0 D in the steep keratometry in the right and left eyes, respectively. Both eyes showed improvement in CDVA from 6/12 to 6/9, with corresponding reduction in refractive cylinder (Table 1). AS-OCT at 6 months for both eyes showed the lenticule in the corneal pocket, with a central demarcation line at 224 and 219 μm in the right and left eyes, respectively (Figure 2, B and C).

Patient 3 was a 28-year-old woman who sought a second opinion regarding blurred vision 2.5 years post-SMILE performed elsewhere. Her case was published as having bilaterally asymmetrical SMILE ectasia, where deficiency of lysyl oxidase (LOX) enzyme was determined to be the cause of post-SMILE kerectasia.4 Her pre-SMILE refraction was −9.2 D in and −10 D in the right and left eyes, respectively.4 Preoperative topography as reported was within normal limits in both eyes.

Twelve months post-SMILE, her topography showed features of frank ectasia in her left eye (Supplemental Digital Content 3, Figure 3, available at http://links.lww.com/JRS/A138) with CDVA of 6/12 and refraction improved to −4.5 −1.75 × 120. The right eye CDVA was 6/6 with refraction of −1.00 −1.00 × 95. The topography, however, seemed to favor diagnosis of regression rather than ectasia (Supplemental Digital Content 3, Figure 3, available at http://links.lww.com/JRS/A138). FILI plus CXL was performed in the left eye and prophylactic pocket CXL in the right eye. Figure 5 shows the difference maps of anterior keratometry in both eyes; the left eye shows marked reduction in steep keratometry, with no significant difference in the right eye. After FILI plus CXL, her UDVA improved to 6/6p and CDVA improved to 6/6 with a minimum acceptance of −0.50. The CDVA in her right eye did not show any change (Table 1). The AS-OCT and clinical picture of the left eye shows the doughnut lenticule in the pocket, with mild hyperreflectivity in the anterior
layers of the cornea because of accelerated CXL in pocket (Figures 2, D and 3, B). Similar findings were observed in the fellow eye AS-OCT in which pocket alone was performed; the mean depth of demarcation line was observed at 23 μm (Supplemental Digital Content 4, Figure 4, available at http://links.lww.com/JRS/A139).

All 4 eyes treated with FILI plus CXL also showed reduction in higher-order aberrations and Q values, as summarized in Table 3. A detailed analysis and comparison of various topographic parameters, such as change in mean keratometry, anterior and posterior elevation, central pachymetry, anterior chamber depth, and Q value, is tabulated in Table 4. None of the ectasia eyes treated with FILI plus CXL or with pocket CXL only had any incidence of postoperative infection, visually significant haze, or progression of ectasia at the end of the last follow-up.

**DISCUSSION**

Despite the various potential advantages of SMILE, chiefly its flapless nature, less postoperative dry eye, less induced aberrations, faster rehabilitation, and minimum postoperative discomfort, keraectasia after SMILE remains a matter of concern because the biomechanical stability of the procedure has not yet been established. Few cases of ectasia reported after SMILE had topography suggestive of early or forme fruste keratoconus; however, ectasia has been also reported after SMILE in eyes with normal preoperative topography. Recently, Shetty et al. reported a case of post-SMILE ectasia in a young patient with high myopia; the cause of ectasia being implicated as reduced preexisting LOX and collagen levels in the extracted lenticule.

The second patient developed bilateral ectasia and normal topographic indices, including the BAD overall scores, except for 1 parameter that was at borderline in the left eye. This patient, however, reported frequent eye rubbing after relocating to a foreign place. A similar case of post-SMILE ectasia was recently reported, where frequent eye rubbing was the cause of ectasia. This reemphasizes the importance of strict preoperative screening protocols for refractive surgery and prevention of avoidable risk factors, such as eye rubbing, as suggested by previous reports on LASIK.

The previously reported cases of SMILE ectasia were managed using the conventional epithelium-off CXL alone or combined with phototherapeutic keratectomy, which was found to be safe and effective for stabilization of ectasia. In this case series, we used the tissue addition technique, FILI, with simultaneous accelerated CXL, as previously reported for management of keratoconus. Because the technique involves positioning of a doughnut-shaped lenticule around the most protruded part of the ectatic cornea, it is expected to result in better outcomes in early cases, where the protrusion is still central. As suggested earlier, our technique might not be suitable for decentered or advanced ectasia; hence, this case series only included eyes with central and relatively regular forms of post-SMILE ectasia.

Regarding the accelerated pocket CXL that was combined with tissue addition, we observed good stability of keratometry and pachymetry at the last follow-up in all 4 eyes treated, with no eye progressing to ectasia. The mean depth of demarcation line was observed at approximately 210.2 μm, which was comparable with that found in various other studies on accelerated CXL. Because there is no deepithelialization and intact epithelium might interfere with the absorption of riboflavin and UV radiation, the efficacy of pocket CXL still needs to be verified and compared with the gold standard.

![Figure 3](http://links.lww.com/JRS/A139)

*Figure 3.* Clinical pictures of patients 1 and 4, taken in retro-illumination showing the doughnut-shaped donor lenticule in situ (A: Patient 1 left eye; B: Patient 3 left eye).

![Figure 4](http://links.lww.com/JRS/A139)

*Figure 4.* Both eyes anterior keratometry difference maps of 2 weeks vs 12 months after femtosecond intrastromal lenticule implantation + CXL for patient 2 (CXL = corneal crosslinking).
We performed pocket CXL because it was reported to show good safety and efficacy in stabilizing keratoconus by Kanellopoulos and, in our personal experience, in treating keratoconus with FILI plus CXL. Furthermore, it was shown by Bottos et al. that, using immunofluorescence microscopy in porcine corneas, the corneal epithelium reduces the effectiveness of CXL by preventing the penetration of the drug and not by limiting the UVA transmittance. It was also preferred because patients have better postoperative comfort and, theoretically, less risk of developing infection compared with conventional epithelium-off CXL.

Patient 3 was thought to have developed ectasia because of corneal stromal weakening due to reduced preexisting LOX levels and collagen, showed evidence of stability in both the eyes at 9 months. The effect of LOX on the behavior of CXL on ectatic corneas thus remains to be elucidated, and as suggested by the authors, further studies are required to establish a concrete relationship between LOX and its role in ectasia development, and its effect on the outcomes of CXL.

Tissue addition is an emerging modality in management of various corneal and refractive conditions; however, achieving perfect refractive predictability might be challenging in the absence of nonavailability of suitable nomograms. However, the purpose of using this technique in this series of SMILE ectasia was purely therapeutic, with the aim of improving CDVA, reducing higher-order aberrations, and improving quality of vision.

Table 3. Change in HOAs and Q value post-FILI + CXL in the 4 eyes treated for SMILE ectasia.

<table>
<thead>
<tr>
<th>S. No.</th>
<th>Eye</th>
<th>Pre-FILI + CXL</th>
<th>Post-FILI + CXL</th>
</tr>
</thead>
<tbody>
<tr>
<td></td>
<td></td>
<td>HOA (μm)</td>
<td>Coma (μm)</td>
</tr>
<tr>
<td>Patient 1</td>
<td>Left eye</td>
<td>4.44</td>
<td>1.69</td>
</tr>
<tr>
<td>Patient 2</td>
<td>Right eye</td>
<td>3.12</td>
<td>0.56</td>
</tr>
<tr>
<td>Patient 3</td>
<td>Left eye</td>
<td>5.63</td>
<td>2.39</td>
</tr>
<tr>
<td>Patient 3</td>
<td>Left eye</td>
<td>1.62</td>
<td>0.20</td>
</tr>
</tbody>
</table>

FILI = femtosecond intrastromal lenticule implantation; HOA = higher-order aberrations; CXL = corneal crosslinking

Table 4. Change in CCT, keratometry, elevation and ACD post-FILI + CXL in the 4 eyes treated for SMILE ectasia in the present series.

<table>
<thead>
<tr>
<th>Patient, Eye</th>
<th>CCT (μm)</th>
<th>Keratometry* (Front, D)</th>
<th>Keratometry* (Back, D)</th>
<th>Elevation (Front, μ)</th>
<th>Elevation (Back, μ)</th>
<th>ACD (mm)</th>
</tr>
</thead>
<tbody>
<tr>
<td></td>
<td>Preop</td>
<td>Postop</td>
<td>Preop</td>
<td>Postop</td>
<td>Preop</td>
<td>Postop</td>
</tr>
<tr>
<td>Patient 1, left eye</td>
<td>357</td>
<td>365</td>
<td>50.6</td>
<td>47.6</td>
<td>−8.3</td>
<td>−8.4</td>
</tr>
<tr>
<td>Patient 2, right eye</td>
<td>447</td>
<td>452</td>
<td>44.4</td>
<td>38.7</td>
<td>−7.3</td>
<td>−7.2</td>
</tr>
<tr>
<td>Patient 2, left eye</td>
<td>419</td>
<td>422</td>
<td>43.6</td>
<td>38.7</td>
<td>−7.4</td>
<td>−7.6</td>
</tr>
<tr>
<td>Patient 3, left eye</td>
<td>407</td>
<td>408</td>
<td>44.0</td>
<td>39.5</td>
<td>−7.2</td>
<td>−7.3</td>
</tr>
</tbody>
</table>

ACD = anterior chamber depth; CCT = central corneal thickness; CXL = corneal crosslinking; FILI = femtosecond intrastromal lenticule implantation; preop = preoperative; postop = postoperative; SMILE = small-incision lenticule extraction

Mean keratometry.
Nevertheless, to our knowledge, we report the first case series of post-SMILE ectasia managed using donor SMILE lenticules combined with accelerated CXL in pocket, showing satisfactory outcomes. Although it is too small number to derive any conclusion now, it shows that the technique is feasible, reproducible, and does not seem to cause a deleterious effect on the visual acuity. It is also a reversible procedure. Hence, should a potential allogenic rejection occur, the tissue can be easily explanted. However, more experience and further data are needed to establish the long-term safety, efficacy, and effects on corneal stabilization with this procedure for management of post-SMILE ectasia.

**WHAT WAS KNOWN**
- Conventional epithelium-off crosslinking alone or combined with phototherapeutic keratectomy has been found to be safe and effective in stabilizing ectasia after small-incision lenticule extraction (SMILE).

**WHAT THIS PAPER ADDS**
- Tissue addition combined with accelerated cross-linking, using SMILE-derived donor lenticule, might be a feasible option for management of SMILE ectasia, potentially reducing keratometry and higher-order aberrations.

**REFERENCES**

Disclosures: Dr. Ganesh and Dr. Brar are consultants to Carl Zeiss Meditec AG, outside the submitted work. None of the other author has a financial or proprietary interest in any material or method mentioned.