

EPITHELIAL INGROWTH AFTER LASER-ASSISTED LENTICULE EXTRACTION

Strategies by which to improve a patient's quality and quantity of vision.

BY SOOSAN JACOB, MS, FRCS, DNB; ROMESH ANGUNAWELA, BM, MD, FRCOPHTH, FRCS, CERTLRS; VARDHAMAN KANKARIYA, MD; AND DARSHAK PATEL, MBBS, MSc, FRCOPHTH, CERTLRS

CASE PRESENTATION

A 36-year-old woman is referred for an evaluation. Following childbirth 2 months ago, the patient noticed a white spot in her left eye. One month ago, the vision in that eye decreased and became blurry.

The patient underwent small-incision lenticule extraction (SMILE; Carl Zeiss Meditec) 1 year ago.

The procedure treated a refractive error of -6.25 D OU. Surgical notes are not available.

Upon examination, her uncorrected distance visual acuity (UDVA) is a blurry 20/30 OS. An autorefractor is +5.00 -5.75 x 66° OS. Her corrected distance visual acuity (CDVA) is 20/20 OS with a

manifest refraction of -0.75 x 55°. A slit-lamp examination finds a 3 x 2-mm area of epithelial ingrowth superiorly between the 12 and 1 clock positions that approaches the pupil (Figure 1). The SMILE incision has a normal appearance, and there are no signs of a torn cap. Fluorescein staining produces no staining or tracking of dye.

Anterior segment OCT (AS-OCT) confirms the presence of subcap epithelial ingrowth (Figure 2). Topography shows irregularity (Figure 1). A Zernike analysis through a 6-mm pupil finds root mean square higher-order aberrations (HOAs) of 3.408 μm, vertical coma of 2.263 μm, horizontal coma of 0.850 μm, and spherical aberration of 0.952 μm. Other HOAs have also increased (Figure 3).

How would you proceed?

—Case prepared by Soosan Jacob, MS, FRCS, DNB

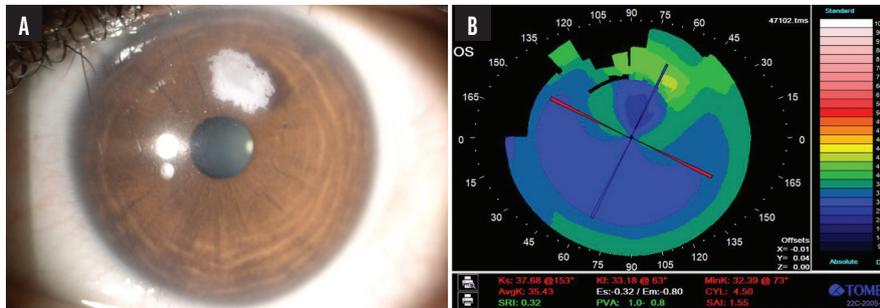


Figure 1. Slit-lamp photograph (A). Topography (B).

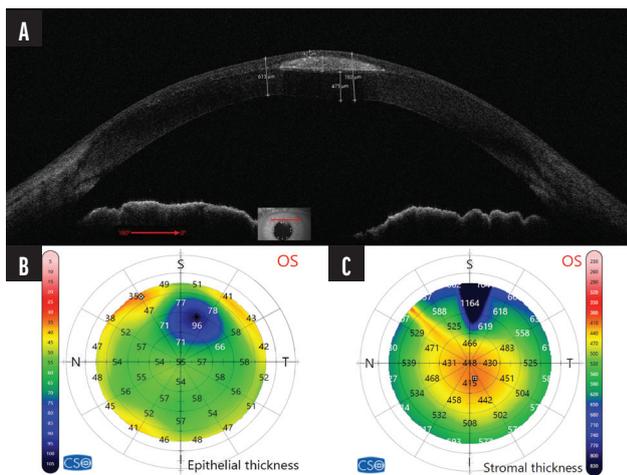


Figure 2. AS-OCT scan (A). Epithelial thickness (B). Stromal thickness (C).

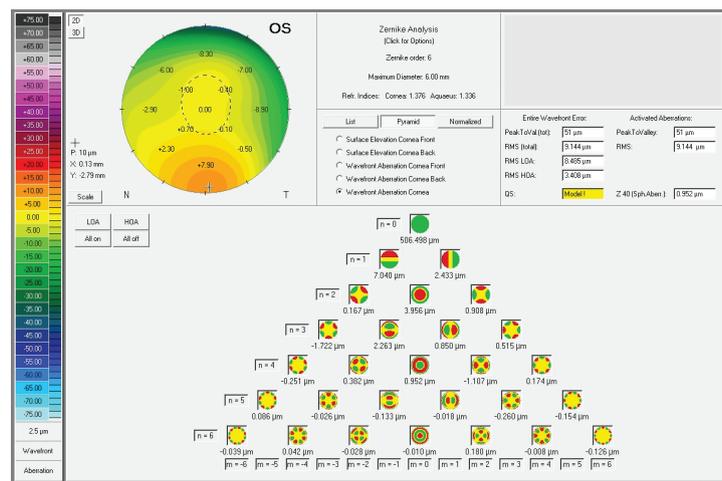


Figure 3. Aberrometry measurements.



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Management would be more straightforward if the patient had undergone LASIK: the flap would be lifted, the epithelial cell layer debrided, and the flap replaced with or without the application of fibrin glue to reduce recurrence. Because SMILE is flap-free, a cap-to-flap conversion is required using either the proprietary Circle software on the VisuMax laser (Carl Zeiss Meditec) or software on any femtosecond laser platform employing a side cut–only function.

Knowing the parameters of the original SMILE treatment would help guide the diameter and depth of the side cut, which should be smaller and 5 to 10 μm deeper than the original treatment diameter and cap thickness. The center of the cornea would be marked, and particular attention would be paid to treatment centration during the side cut. The position of the flap hinge could be altered to avoid the original entry incision to the lenticule plane. After the flap has been lifted, a blunt spatula would be used to debride the epithelium along the bed and the undersurface of the flap.

An alternative to surgery would be to perform an Nd:YAG laser treatment. Published case series have shown this method to be highly efficacious.¹ Energy levels of 0.3 to 0.6 nJ would be used to cause cavitation in the interlamellar space adjacent to the epithelial cell nests, resulting in their death. A light-touch approach would be required to avoid corneal melting by laser-mediated tissue destruction, and more than one treatment might be necessary.² An Nd:YAG laser treatment could be preferable to surgical intervention if the prior SMILE parameters are unknown or the patient does not wish to undergo additional surgery.

After treatment, she would be examined for recurrent ingrowth before discharge.



VARDHAMAN KANKARIYA, MD

Interface epithelial ingrowth is a known potential complication after SMILE.³ The cumulative risk of epithelial ingrowth after this procedure is 0.5% compared to a reported incidence of 0% to 3.9% after primary LASIK.⁴ In most instances, epithelial ingrowth after SMILE is nonprogressive and self-limiting, but a few cases of progressive proliferation requiring intervention have been reported.^{3,5,6}

The clinically significant epithelial ingrowth in the patient's left eye induced irregular astigmatism, leading to a decrease in her UDVA and CDVA and a significant increase in HOAs. The ingrowth was isolated, involving the visual axis without evidence of associated peripheral extension toward the small incision on fluorescein staining or AS-OCT. This suggests the ingrowth was caused by intraoperative epithelial implantation rather than a postoperative epithelial fistula at the small incision.

The management of epithelial ingrowth after SMILE is challenging because of the risk of incomplete removal if attempted through the small incision. My colleagues and I reported a novel therapeutic use of the Circle software for the management of visually significant isolated epithelial ingrowth following SMILE.⁷ All three cases were successfully managed by converting the SMILE cap into a flap, which provided full access to the original SMILE interface. Once the flap had been lifted, the epithelial ingrowth was completely debrided from the underlying stroma and undersurface of the flap, mitomycin C and absolute alcohol were

administered, and the interface was thoroughly washed. No recurrence was recorded in 5 years of follow-up.

Based on my experience, I would expect this approach to work well here. Because surgical data are not available, AS-OCT would be used to plan treatment with a D pattern and junctional cuts at the same depth as the previous SMILE interface. Care would be taken during planning to prevent the Circle side cuts from intersecting with the original small incision.



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The absence of incision tears or a fluorescein fistula and isolation from the incision suggest an epithelial implant rather than true ingrowth following SMILE. Risk factors for an epithelial implant include repeated reentry of the lenticule separator through the incision (which pushes epithelial cells into the interface) and anterior basement membrane dystrophy.

Topography shows flattening caused by the nest. The manifest cylinder axis is consistent with the nest's position. The irregularity is inducing significant HOAs, which are degrading the quality of vision despite the patient's 20/20 CDVA. Her symptoms, the clinical findings, and the risk of a cap melt necessitate intervention.

The options for managing an epithelial implant after SMILE include observation if the cells are in the periphery, because they generally resolve without intervention; Nd:YAG laser treatment; and interface scraping.⁸ Described by Ayala and colleagues,¹ Nd:YAG laser treatment for epithelial ingrowth involves delivering laser pulses of 0.3 to 0.6 mJ into the interface to cause cavitation of the cells. The resulting

debris is then cleared by macrophages. Two treatments are occasionally required for complete resolution. Complications after treatment include Bowman membrane fractures, scarring, anterior stromal defects, and flap melt.²

En bloc removal of an epithelial implant by scraping involves opening the small incision with a Sinsky hook, entering the eye with a flat-tipped flap separator, releasing the interface on the way to the implant, and scooping it out with the spatulated tip. The epithelial nest typically comes out in one piece and can be spread on the corneal surface to delineate the nest's size. A slit-lamp examination is performed to confirm that no cells have been left behind. The epithelium around the small incision is then recessed to permit edema-free wound apposition before epithelial closure.⁸

Given the lesion's proximity to the visual axis and its size (2.3 mm) on clinical examination and AS-OCT, a significant amount of Nd:YAG laser energy would be required, which could induce irregularity. En bloc removal of the implant would therefore be preferable to facilitate more rapid visual rehabilitation.



**WHAT I DID: SOOSAN JACOB, MS,
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A semicircle treatment using a large hinge was performed to open the cap and remove the epithelial ingrowth. The thickness of the cap was estimated with AS-OCT. Junction up and down mode of the Circle software was used with the following lamellar and side cut parameters: a diameter of 7.9 mm, a depth of 130 μm , a hinge angle of 190°, and a hinge width of 13 mm. The hinge's position was kept on the opposite side at 230°. The junction

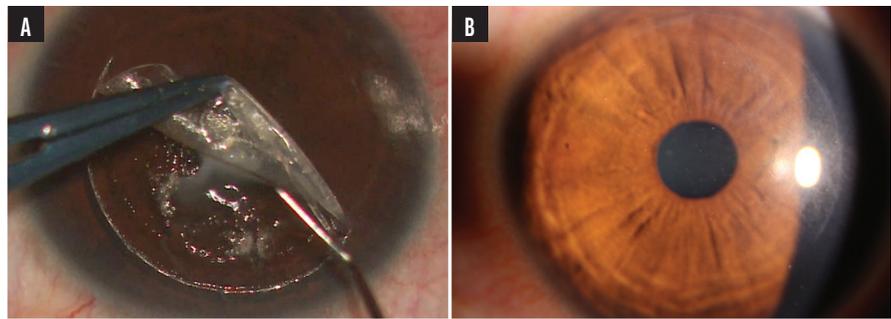


Figure 4. Epithelial ingrowth is removed after a semicircle treatment using a large hinge is performed. A slit-lamp image shows mild haze in the area of epithelial ingrowth (B).

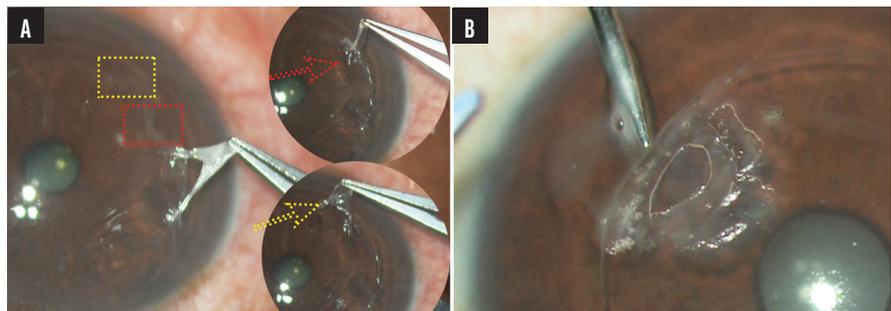


Figure 5. Piecemeal removal of an epithelial sheet. Rectangles indicate the inset areas of close-up, with each color-matched arrow showing incremental tissue removal (A). Epithelial cells are visible in necrotic liquid debris (B).

parameters were a diameter of 6.3 mm and lower and upper depths of 150 and 115 μm , respectively. These settings limited flap creation to the area of epithelial ingrowth while the rest of the cap remained uncut.

The flap was dissected from all sides, with the area of epithelial ingrowth addressed last to prevent the seeding of epithelial cells. The epithelial sheet was then peeled back. A No. 15 Bard-Parker blade was used to scrape the sheet and residual cells from the bed and the undersurface of the cap (Figure 4A). Next, 20% ethanol was applied to the bed and undersurface of the flap to kill any residual cells.

Thorough irrigation was performed. The flap was replaced and allowed to dry, and an absence of striae was confirmed. Fibrin glue was applied at the junction to decrease the risk of epithelial ingrowth. A bandage contact lens was placed.

Postoperatively, topography improved, and a reversal of the irregularity induced by the epithelial ingrowth was observed. The patient's UDVA, CDVA, and

subjective quality of vision improved. Root mean square HOAs, vertical coma, and horizontal coma were found to have decreased to 1.054 μm , 0.505 μm , and 0.391 μm , respectively. Vertical and oblique trefoil decreased from -1.722 μm and 0.515 μm to -0.468 μm and 0.115 μm , respectively.

AS-OCT and oblique illumination with a slit lamp revealed faint haze localized to the site of the previous epithelial ingrowth that did not involve the visual axis (Figure 4B). Topography and epithelial thickness maps with the MS-39 (CSO Italia) had become more regular. Autorefraction was +0.75 -1.00 x 65°, and the patient's UDVA was 6/6 OS.

My decision to scrape rather than sweep out the epithelial ingrowth after lifting the flap was prompted by my desire to avoid the risk of partial removal.⁶ Figure 5 shows how sweeping epithelial ingrowth out through the SMILE incision can result in incomplete removal. Removal through the small incision, moreover,

can send cells along the path. In my experience, partial treatment with the Circle software facilitates the complete removal of epithelial ingrowth, and the application of alcohol kills any residual cells. Taken together, these steps reduce the risk of recurrent epithelial ingrowth. ■

1. Ayala MJ, Alió JL, Mulet ME, De La Hoz F. Treatment of laser in situ keratomileusis interface epithelial ingrowth with neodymium:yttrium-aluminum-garnet laser. *Am J Ophthalmol*. 2008;145(4):630-634.
2. Kucukcilioglu M, Hurmeric V. Localized flap melt after Nd-YAG laser treatment in recurrent post-LASIK epithelial ingrowth. *Arq Bras Oftalmol*. 2015;78(4):250-251.
3. Thulasi P, Kim SW, Shetty R, Randleman JB. Recalcitrant epithelial ingrowth after SMILE treated with a hydrogel ocular sealant. *J Refract Surg*. 2015;31(12):847-850.
4. Krueger RR, Meister CS. A review of small incision lenticule extraction complications. *Curr Opin Ophthalmol*. 2018;29(4):292-298.
5. Sekundo W, Kunert KS, Blum M. Small incision corneal refractive surgery using the small incision lenticule extraction (SMILE) procedure for the correction of myopia and myopic astigmatism: results of a 6-month prospective study. *Br J*

Ophthalmol. 2011;95(3):335-339.

6. Ivarsen A, Asp S, Hjortdal J. Safety and complications of more than 1500 small-incision lenticule extraction procedures. *Ophthalmology*. 2014;121(4):822-828.

7. Kankariya VP, Gogri PY, Dube AB, Mohiuddin SM, Madia T, Vaddavalli PK. CIRCLE software for management of epithelial ingrowth after SMILE. *J Refract Surg*. 2021;37(11):776-780.

8. Piccinini P, Vida RS, Piccinini R, et al. Epithelial implantation treatment after small-incision lenticule extraction. *J Cataract Refract Surg*. 2020;46(4):636-640.

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