Treatment of Epithelial Ingrowth After Laser In Situ Keratomileusis With Mechanical Debridement and Flap Suturing

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Objective: To evaluate the efficacy and safety of mechanical debridement and suturing of the laser in situ keratomileusis (LASIK) flap in the treatment of clinically significant epithelial ingrowth after LASIK.

Methods: In a retrospective study, 20 eyes (n=19 patients) in which clinically significant epithelial ingrowth developed after LASIK were treated with lifting of the flap, scraping of the epithelial ingrowth, and flap suturing. Primary outcome measurements including recurrence of ingrowth, uncorrected visual acuity (VA), manifest refraction, best spectacle-corrected VA, and complications were evaluated at the last postoperative examination.

Results: At the last postoperative examination (mean±SD, 10.5±14.3 months; range, 1.5-64 months), 100% of eyes had no recurrence of clinically significant epithelial ingrowth. The uncorrected VA changed from 20/20 or better in 7 eyes (35%) and 20/40 or better in 15 eyes (75%) preoperatively to 20/20 or better in 9 eyes (45%) and 20/40 or better in 16 eyes (80%) at the last follow-up examination. There was no significant change in the mean logarithm of the minimum angle of resolution (logMAR) uncorrected VA before (mean±SD, 0.3±0.5; range, −0.1 to 1.7) and after surgery (mean±SD, 0.2±0.4; range, −0.1 to 1.7) (P=.40). Mean±SD spherical equivalent changed from −0.21±0.82 diopters (D) (range, −1.25 to 1.00 D) preoperatively to −0.53±0.89 D (range, −2.50 to 0.38 D) at last follow-up (P=.30). No eyes lost 2 or more lines of best spectacle-corrected VA, and there were no complications associated with the treatment.

Conclusions: Suturing the LASIK flap in addition to mechanical debridement of epithelial ingrowth is a safe and effective treatment for clinically significant epithelial ingrowth after LASIK.


Epithelial ingrowth after laser in situ keratomileusis (LASIK) has been reported to occur in 0% to 20% of cases, with a cumulative mean of 4.3% in a review of LASIK publications. Most cases are self-limited, occurring at the edge of the flap and extending inward less than 0.5 mm, and cause no adverse effect on the results of surgery. However, ingrowth becomes clinically significant and requires removal when it extends into the entrance pupil and decreases vision, approaches the edge of the pupil and reduces vision or induces night-time glare, causes keratolysis, induces astigmatism by raising an area of the flap, or causes epithelial irregularity with fluorescein staining at the edge of the flap and foreign-body sensation. Clinically significant ingrowth requiring removal has been reported in 0.92% to 3.2% of patients undergoing LASIK. Reported techniques for removing epithelial ingrowth include lifting the flap and scraping the epithelial ingrowth, with or without adjunctive treatments such as ethanol, mitomycin, phototherapeutic keratectomy, or suturing of the flap. The recurrence rate after scraping alone has been reported as 44%. Adjunctive treatments to lower this recurrence rate, however, may cause adverse effects. Treatments with ethanol and mitomycin have toxic effects, and phototherapeutic keratectomy can cause irregular astigmatism and unpredictable shifts in refraction. Suturing the flap to create a tight apposition between the flap and the stromal bed has been proposed to be effective at preventing the recurrence of ingrowth without the complications of other adjunctive treatments. This study evaluates the efficacy and safety of suturing the LASIK flap after removal of epithelial ingrowth in the treatment of clinically significant epithelial ingrowth after LASIK.

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A retrospective review was conducted of 20 eyes in 19 patients treated for clinically significant epithelial ingrowth after LASIK with lifting of the flap, scraping of the ingrowth, and suturing of the flap to the stromal bed. All eyes were diagnosed with clinically significant epithelial ingrowth after LASIK and were treated owing to evidence of progressive epithelial ingrowth, peripheral flap melting, topography changes, refractive changes, and/or chronic irritation. The preoperative LASIK examination, LASIK surgical report, postoperative course, epithelial ingrowth treatment report, and postepithelial ingrowth treatment examinations were reviewed.

Treatment of epithelial ingrowth was performed by a single surgeon (E.E.M.). After providing informed consent, patients were given topical 0.5% proparacaine hydrochloride (Ophthetin; Allergan Inc, Irvine, Calif), 0.1% diclofenac sodium (Voltaren; Ciba Vision Ophthalmics, Duluth, Ga), and 0.3% ciprofloxacin hydrochloride (Ciloxan; Alcon Laboratories Inc, Fort Worth, Tex) in the operated-on eye immediately before the procedure. Patients were taken to the laser and reclined in a supine position. A sterile drape and a wire lid speculum were placed in the operated-on eye. The flap was lifted using a LASIK spatula. The epithelial ingrowth was scraped from the posterior surface of the flap and from the keratectomy bed using a blunt photorefractive keratectomy spatula (AE-2767 Maloney spatula; ASICO, Westmont, Ill). After repositioning of the flap, the interface was irrigated with balanced saline solution. The flap was sutured into place with 10-0 nylon, using a total of 5 to 11 interrupted sutures. The eye was then irrigated with balanced salt solution, followed by 0.3% ciprofloxacin. Also administered were 0.1% diclofenac and 1% prednisolone acetate (Pred Forte; Allergan Inc), and a bandage contact lens was placed. Patients were treated postoperatively with 0.3% ciprofloxacin hydrochloride 4 times a day and 1% prednisolone acetate 4 times a day. Once the epithelium was healed, the bandage contact lens was removed, and 0.1% fluorometholone acetate (Flarex; Alcon Laboratories Inc) was given 2 times a day for 2 weeks.

Outcome measures included recurrence of epithelial ingrowth on slitlamp biomicroscopy results, uncorrected visual acuity (UCVA), manifest refraction, and best spectacle-corrected visual acuity (BSCVA). Postoperative examinations were performed at 1 day. The frequency of subsequent follow-up examinations varied according to the healing response and was determined by the surgeon. Statistical analysis was performed with the paired t test using Microsoft Excel 2000 (Microsoft Corp, Redmond, Wash). A P value of .05 was considered statistically significant. For statistical analysis of UCVA and BSCVA, Snellen visual acuity was converted to logarithm of the minimum angle of resolution (logMAR) notation. Unless otherwise indicated, data are expressed as mean±SD.

### RESULTS

Twenty eyes of 19 patients were treated for clinically significant epithelial ingrowth after LASIK with removal of the ingrowth and suturing of the LASIK flap (Table 1 and Table 2). Nine patients were men (10 eyes [50%]) and 10 were women (10 eyes [50%]). The mean age was 47.5±9.9 years (range, 30-60 years). All eyes underwent primary LASIK, and 13 eyes (65%) had a history of LASIK retreatment. All eyes received a diagnosis of clinically significant epithelial ingrowth (Figure 1). Six eyes (30%) had evidence of progressive, peripheral flap melting on examination. Ten eyes (50%) were referred from outside institutions for treatment.

Epithelial ingrowth was treated with mechanical debridement and suturing of the flap at a mean of 10.3±7.9 months (range, 3 weeks to 27 months) after the most recent LASIK procedure (Figure 2). All suture knots were buried at the time of surgery. Ten eyes (50%) had previous treatment before suturing of the flap was performed.
formed. Four eyes (20%) had more than 1 previous treatment. Previous treatments included lifting the flap and scraping the epithelial ingrowth in 10 eyes (50%), lifting the flap, scraping the ingrowth, and treating with alcohol in 3 eyes (15%), and lifting the flap, scraping the ingrowth, and suturing the flap down in 2 eyes (10%). The treatments of the 2 eyes that underwent previous suturing of the flap were performed at outside institutions. Sutures were removed at a mean of 1.9±0.6 weeks (range, 1-3 weeks). The mean last follow-up examination after treatment was 10.5±14.3 months (range, 1.5-64 months).

Table 2. Measurements of 20 Eyes With Clinically Significant Epithelial Ingrowth Before and After Treatment With Mechanical Debridement and Apposition of the Flap With Sutures

<table>
<thead>
<tr>
<th>Patient No.</th>
<th>Preoperative Measurements</th>
<th>Postoperative Measurements</th>
<th>Outcome at Last Follow-up, (Follow-up, mo)</th>
</tr>
</thead>
<tbody>
<tr>
<td>UCVA</td>
<td>Refraction, D</td>
<td>BSCVA</td>
<td>UCVA</td>
</tr>
<tr>
<td>1</td>
<td>20/25 PI + 0.75 × 25</td>
<td>20/15</td>
<td>20/20</td>
</tr>
<tr>
<td>2</td>
<td>CF</td>
<td>NR</td>
<td>NR</td>
</tr>
<tr>
<td>3</td>
<td>20/25 NR</td>
<td>NR</td>
<td>20/20</td>
</tr>
<tr>
<td>4</td>
<td>20/30 −2.25 + 2.00 × 65</td>
<td>20/20</td>
<td>20/40</td>
</tr>
<tr>
<td>5</td>
<td>20/30 NR</td>
<td>NR</td>
<td>20/25</td>
</tr>
<tr>
<td>6</td>
<td>20/20 +1.00 Sphere</td>
<td>20/15</td>
<td>20/15</td>
</tr>
<tr>
<td>7</td>
<td>20/30 −1.00 Sphere</td>
<td>20/20</td>
<td>20/20</td>
</tr>
<tr>
<td>8</td>
<td>20/30 NR</td>
<td>NR</td>
<td>20/25</td>
</tr>
<tr>
<td>9</td>
<td>20/25 −1.00 Sphere</td>
<td>20/25</td>
<td>20/25</td>
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<tr>
<td>10</td>
<td>20/20 NR</td>
<td>NR</td>
<td>20/20</td>
</tr>
<tr>
<td>11</td>
<td>20/50 +0.50 + 0.25 × 123</td>
<td>20/40</td>
<td>20/200</td>
</tr>
<tr>
<td>12</td>
<td>20/40 +0.50 + 0.75 × 125</td>
<td>20/20</td>
<td>20/50</td>
</tr>
<tr>
<td>13</td>
<td>CF</td>
<td>NR</td>
<td>NR</td>
</tr>
<tr>
<td>14</td>
<td>20/20 PI + 0.50 × 105</td>
<td>20/15</td>
<td>20/15</td>
</tr>
<tr>
<td>15</td>
<td>20/20 PI + 0.50 × 52</td>
<td>20/20</td>
<td>20/20</td>
</tr>
<tr>
<td>16</td>
<td>20/20 NR</td>
<td>NR</td>
<td>20/25</td>
</tr>
<tr>
<td>17</td>
<td>20/60 −2.50 + 0.75 × 124</td>
<td>20/20</td>
<td>20/100</td>
</tr>
<tr>
<td>18</td>
<td>20/60 −0.75 + 0.50 × 75</td>
<td>20/60</td>
<td>20/25</td>
</tr>
<tr>
<td>19</td>
<td>20/15 NR</td>
<td>NR</td>
<td>20/15</td>
</tr>
<tr>
<td>20</td>
<td>20/20 −0.25 Sphere</td>
<td>20/15</td>
<td>20/200</td>
</tr>
</tbody>
</table>

Abbreviations: BSCVA, best spectacle-corrected visual acuity; CF, counting fingers; D, diopters; NR, not reported; PI, plano; RGP, rigid gas-permeable contact lens; UCVA, uncorrected visual acuity.

Figure 1. Slitlamp photograph of a study eye with clinically significant epithelial ingrowth.

Figure 2. Slitlamp photograph of the same eye in Figure 1 after epithelial ingrowth treatment with mechanical debridement and suturing of the flap. All suture knots are buried.

RECURRENTWE OF EPITHELIAL INGROWTH

After treatment, there was no recurrence of clinically significant epithelial ingrowth (Figure 3). One eye had recurrence of ingrowth at the flap margin that was not considered clinically significant, did not progress, and did not require further removal.

VISUAL ACUITY

The UCVA changed from 20/20 or better in 7 eyes (35%) and 20/40 or better in 15 eyes (75%) preoperatively to
20/20 or better in 9 eyes (45%) and 20/40 or better in 16 eyes (80%) at the last postoperative examination. There was no significant change in the mean logMAR UCVA before (0.3 ± 0.5; range, −0.1 to 1.7) and after (0.2 ± 0.4; range, −0.1 to 1.7) (P = .40) surgery. No eyes lost 2 or more lines of BSCVA. For eyes with documented BSCVA before and after treatment (n = 10), mean logMAR BSCVA before treatment was 0.0 ± 0.1 (range, −0.1 to 0.3) and after treatment was 0.0 ± 0.1 (range, −0.1 to 0.1) (P = .60).

REFRACTION

For eyes that had documented manifest refractions before and after treatment (n = 10), mean spherical equivalent changed from −0.21 ± 0.82 diopters (D) (range, −1.25 to 1.00 D) before treatment to −0.53 ± 0.89 D (range, −2.50 to 0.38 D) at last follow-up (P = .30). The mean refractive shift was −0.31 ± 0.98 D (range, −1.75 to 1.25 D). Three eyes had hyperopic shifts (range, 0.13–1.25 D), 6 eyes had myopic shifts (range, −0.25 to −1.75 D), and 1 eye had no change in spherical equivalent.

COMPLICATIONS

There were no intraoperative or postoperative complications related to the epithelial ingrowth debridement and suturing of the flap. Specifically, there was no evidence of flap striae or diffuse lamellar keratitis as a result of lifting the flap, scraping the keratectomy bed, and suturing the keratectomy flap. Three eyes had sequelae resulting from the epithelial ingrowth. One eye with preoperative flap melting and irregular astigmatism had postoperative irregular astigmatism and also had minimal stromal edema associated with cornea guttata. The UCVA was 20/200 and corrected to 20/25 with a rigid gas-permeable contact lens at 21 months after treatment for clinically significant epithelial ingrowth. One eye with preoperative flap melting had slight haze in the interface postoperatively with a UCVA of 20/25. One eye had a history of a segmented flap from multiple microkeratome cuts that resulted in central scarring and a BSCVA of 20/160. This eye was the eye that had a recurrence of clinically insignificant epithelial ingrowth that did not require treatment. Because of the central scarring from the segmented flap, this eye underwent penetrating keratoplasty 58 months after the epithelial ingrowth had been treated.

Most cases of epithelial ingrowth after LASIK are clinically benign, self-limited, and do not require treatment. Clinically significant epithelial ingrowth is an uncommon but serious complication that can result in loss of vision, astigmatism, and keratolysis if left untreated. With appropriate treatment, however, the final best-corrected visual acuity is usually not affected.11 This study suggests that sputtering the LASIK flap in addition to mechanical debridement of epithelial ingrowth is a safe treatment for clinically significant epithelial ingrowth after LASIK, and a treatment effective at preventing recurrence, loss of vision, and flap melting.

Two hypotheses exist on the pathogenesis of epithelial ingrowth after LASIK.12,11 The first suggests that epithelial cells are implanted in the lamellar interface by the microkeratome blade or during irrigation of the stromal bed. However, isolated epithelial cells do not appear to spread.11 The second hypothesis is that epithelial cells grow under the edge of the flap and progress into the interface. This ingrowth generally stops, forming a demarcation line of mild fibrosis, and causes remodeling of the adjacent stroma with melting of the flap edge.11

The continuity of the epithelial ingrowth with the surface epithelium makes the second hypothesis more likely.11,17 It has therefore been suggested that epithelial ingrowth consists of an epithelial fistula underneath the flap with a tract extending to the edge of the flap.11 A fistula may form owing to poor flap adhesion, which allows for surface epithelial cells to enter into the lamellar interface. Epithelial defects, basement membrane dystrophy, excessive hydration of the flap intraoperatively, or unrecognized factors may cause poor flap adhesion and predispose to fistula formation.11 Once the fistula forms, remodeling of the stroma along the tract causes keratolysis. It has been recommended to treat clinically significant epithelial ingrowth as early as possible to prevent maturation of the fistula.11

Based on the theory of ingrowth occurring in the form of a fistula extending from the edge of the LASIK flap, the fistula must be closed to prevent recurrence of the ingrowth. Scraping the epithelial ingrowth removes the contents of the fistula but does not close it, and recurrence of epithelial ingrowth after treatment suggests that the passive apposition of the LASIK flap to the stromal bed may not always be enough to close the fistula. Treatment by lifting the flap, scraping the posterior surface of the flap and the stromal bed, and replacing the flap with a bandage lens to encourage tight flap adhesion resulted in a 44% recurrence rate of epithelial ingrowth, which included ingrowth that was clinically significant (23%) and that which was not (21%).11

Adjuvant treatments including mitomycin, ethanolic, and phototherapeutic keratectomy have been suggested as ways to reduce the high recurrence rate after epithelial ingrowth removal. These treatments have po-
tential complications and also do not close the fistula. Mitomycin may inhibit corneal wound healing.\textsuperscript{16} Ethanol has been shown to have damaging effects on keratocytes\textsuperscript{19} and to cause diffuse lamellar keratitis,\textsuperscript{13} and it can result in total flap melting after application to the interface to treat recurrent epithelial ingrowth.\textsuperscript{15} Phototherapeutic keratectomy may shift the refraction and induce irregular astigmatism.\textsuperscript{12,16} The only adjunctive treatment that closes the fistula is the placement of sutures at the site of ingrowth.\textsuperscript{14,20}

Our study shows that suturing the LASIK flap is an effective and safe adjunct to epithelial ingrowth removal after LASIK. There were no recurrences of clinically significant epithelial ingrowth in the study eyes. One eye had a recurrence of ingrowth that did not become clinically significant, did not progress, and did not require further treatment. Suturing of the flap did not cause a significant change in the spherical equivalent manifest refraction at the last follow-up after the sutures had been removed. The treatment also showed no adverse effect on the final UCVA or BSCVA, and no eyes lost 2 or more lines of BSCVA. There were no complications resulting from the treatment.

Discussion has occurred about whether suturing is appropriate as a primary form of treatment.\textsuperscript{20} The 44% recurrence rate reported after epithelial ingrowth removal has been attributed to less aggressive treatment (treatment after ingrowth was present for 1 month), which allowed the fistula to become established.\textsuperscript{11,20} An earlier approach of treating clinically significant ingrowth if present at the 3-week examination after surgery has reduced the recurrence rate, and suturing has only been necessary in a limited number of cases out of several hundred eyes.\textsuperscript{20}

Further study is needed to investigate the results of suturing of the LASIK flap as an adjunct to removal of epithelial ingrowth. Comparison of suturing as a primary form of treatment with its use as treatment for recurrent cases may help define its role in the removal of clinically significant epithelial ingrowth. A larger sample size with longer postoperative follow-up would further characterize refractive changes, stability of postoperative refraction, and recurrence rates of epithelial ingrowth. This preliminary study suggests that suturing of the flap is a safe and effective treatment option for clinically significant epithelial ingrowth after LASIK, and prevents loss of BSCVA due to astigmatism and keratolysis that can be caused by progressive epithelial ingrowth.

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