Clinical Investigation of Off-Flap Epi-LASIK for Moderate to High Myopia

Qin-Mei Wang, Ai-Cun Fu, Ye Yu, Chen-Cben Xu, Xiao-Xing Wang, Shi-Hao Chen, and A-Yong Yu

PURPOSE. To compare the clinical outcome of on-flap and off-flap epi-LASIK for moderate to high myopia.

METHODS. This prospective, observer-masked, randomized study included 62 eyes of 31 patients with myopia who underwent off-flap epi-LASIK (epikeratome; Moria, Antony, France) in one eye (off-flap group) and on-flap epi-LASIK in the contralateral eye (on-flap group). Corneal ablation was performed with a commercially available laser (Mel80; Carl Zeiss Meditec, Oberkochen, Germany). Patients were seen at 3, 5, and 12 days and 1 and 3 months after surgery. Clinical outcomes were compared between groups.

RESULTS. No significant between-group differences in the mean preoperative spherical equivalent (\(-6.18 \pm 1.29 \) D vs. \(-6.47 \pm 1.70 \) D), the change in lines of best corrected visual acuity at 3 months after surgery, and postoperative pain were found. Compared with the on-flap group, outcomes of better uncorrected visual acuity at 3 and 5 days after surgery (P < 0.001), rapider reepithelialization (P < 0.001), and lower level of haze at 1 and 3 months after surgery (P = 0.04, 0.04) were found in the off-flap group. Three months after surgery, contrast sensitivity function (CSF), with and without glare, did not differ from before surgery in both groups (P > 0.05) except CSF at 18 cpd with glare increased significantly in the off-flap group 3 months after surgery (P = 0.04). Wavefront aberration increased significantly from baseline in both groups 3 months after surgery (P < 0.05). The on-flap group revealed greater but insignificant increasing amplitude in wavefront aberration compared with the off-flap group.

CONCLUSIONS. In comparison with on-flap epi-LASIK, off-flap epi-LASIK offers comparable postoperative pain, a lower level of haze formation, a rapider visual recovery, and better visual quality. Further investigations of a larger number of subjects and longer follow-up periods are warranted. (Invest Ophthalmol Vis Sci. 2008;49:2390–2394) DOI:10.1167/iovs.07-0827

Surface ablations have become popular for patients with moderate to high refractive error and thinner corneas, or corneal thickness in which conservation of tissue is a factor. \(^1\) \(^2\) Epi-LASIK as an alternative surface ablation procedure, however, has been reported to involve slower healing and visual recovery than that of traditional LASIK surgery. \(^3\) Off-flap epi-LASIK as a modified surface ablation completely removes the epithelial flap after laser ablation. To our knowledge, no study of off-flap epi-LASIK has been published. In the present study, we investigated the preliminary clinical outcomes of off-flap epi-LASIK on myopia, and compared them with those of on-flap epi-LASIK, to detect any differences between the two modalities.

METHODS

Patients

Thirty-one patients with myopia (9 men and 22 women) with a mean age of 28 ± 5 years (range, 22–43 years) were enrolled in this randomized prospective contralateral comparative study between September and December in 2006. All patients revealed no abnormal findings by a comprehensive ophthalmic screening examination performed before surgery. The preoperative examinations included manifest and cycloplegic refraction, uncorrected visual acuity (UCVA), best corrected visual acuity (BCVA), corneal topography, biomicroscopy, mepi-sopic pupil size measurement, applanation tonometry, contrast sensitivity function (CSF), CSF under glare conditions (GSF), wavefront aberration, and dilated funduscopy. Enrolled patients fulfilled the criteria, including age of at least 18 years, spherical equivalent (SE) of at least –4.00 D, or anatomic limitations to undergoing LASIK surgery (estimated residual stromal thickness under the flap of less than 280 \(\mu\)m), stable refraction, no ocular disease, and no previous refractive surgery or systemic disease likely to affect the epithelial healing. All patients had a minimum of 3 months’ follow-up after surgery.

The research protocol adhered to the tenets of the Declaration of Helsinki and was approved by the local ethics committee. All patients were fully informed about the details and possible risks inherent to the surgery and to this study. Written informed consent was obtained from all patients.

Surgery Procedure

All patients underwent simultaneous bilateral epi-LASIK. The operative eye was prepared with three drops of topical tetracaine hydrochloride 0.5% along with topical nonsteroidal anti-inflammatory drug (NSAID) and an antibiotic applied every 5 minutes before the procedure. The surrounding area of the eye was then sterilized and was covered with a sterile drape. A speculum held the eyelids apart. The cornea was irrigated with cool (4°C) physiologic salt solution (BSS; Alcon Ltd., Fort Worth, TX). The epikeratome’s (Moria, Antony, France) preassembled hand piece was applied to the operative eye with its central circular opening centered around the limbus, and suction was activated. The operative eye was irrigated with PSS during the epikeratome pass. Depressing a foot pedal caused the oscillating block to run parallel to the horizontal corneal plane, separating the epithelial sheet. Once the separator reached its final position, producing a flap of 9.0 mm diameter with a nasal hinge, a reverse movement was performed, the suction was released, and the device was removed from the eye. The flap was reflected nasally, to reveal the corneal stroma, to allow ablation. As the patient focused on a fixation light, the excimer laser energy (Mel80 excimer laser; Carl Zeiss Meditec, Oberkochen, Germany) was delivered to the cornea according to the coaxial sighted cornea reflex. A soaked sponge (6 mm in diameter) with 0.02% mitomycin C (MMC) was applied to the ablated stroma for 15 to 20 seconds.
seconds, then removed. The corneal surface and the entire conjunctival fornix were irrigated with cool PS solution to remove residual MMC. The epithelial flap was then repositioned in one eye (the on-flap epi-LASIK group) and was completely removed by a forceps in the contralateral eye (the off-flap epi-LASIK group). A bandage contact lens of −0.50 D (Acuvue 2; Johnson & Johnson Vision Care, Jacksonville, FL) was placed on both eyes at the end of the procedure. Subsequently, a topical corticosteroid, NSAID, and antibiotic were instilled. The eyelid speculum was then removed carefully. The patient was examined with slit lamp biomicroscopy before dismissal (Fig. 1). All the corrections were intended to achieve emmetropia except that in three elderly patients who retained slight myopia in the nondominant eye (two eyes in the off-flap epi-LASIK group: −0.25 D, −0.75 D; one eye in the on-flap epi-LASIK group: −0.50 D).

All operations were performed by the same surgeon (QW). The right eye was operated on first in every case. The assignment of which eye would receive off-flap epi-LASIK and which eye would receive on-flap epi-LASIK was determined randomly, with the assignment stored in a sealed envelope that was opened after the patient had consented to study participation. Patients were told that each eye would have different surface ablation laser refractive surgery but were not told which eye had off-flap epi-LASIK and which had on-flap epi-LASIK. Operating room staff recorded which eye received which treatment.

Postoperative Care

The bandage contact lens remained in place until the sign of complete reepithelialization was observed. The patient was given combined eye drops of tobramycin-dexamethasone (Tobradex; Alcon, Ltd.) and NSAID (Pranopulin; Alcon, Ltd.), to be used four times a day for the first four postoperative weeks and 0.1% fluorometholone (Flarex; Allergan, Irvine, CA) and topical NSAID used three times a day in the second postoperative month, two times a day in the third month, and once in the fourth month. They were also given artificial tears (sodium hyaluronate, Alcon, Ltd.) for use four times a day for maintenance of tear film and a regular ocular surface.

Follow-up Examination

Patients were followed up daily by an ophthalmologist who was not informed of the type of surface procedure performed in each eye until the epithelial healing was complete and the therapeutic contact lens was removed. Examinations during the early postoperative period included recording of visual acuity and biomicroscopy. Slit lamp examination allowed for the observation of epithelial healing without requiring the removal of the contact lens. Pain scores within 2 days after surgery were included in subjective evaluation forms that were completed by patients according to a predetermined scale ranging from 0 to 4 as follows: 0, no pain or discomfort; 1, mild pain; 2, obvious pain, does not require analgesics; 3, obvious pain, analgesics may relieve; and 4, obvious pain, analgesics may not relieve. The questionnaires were completed every day and collected during the visit on the second postoperative day.

Figure 1. (A) Slit lamp image of right eye 10 minutes after off-flap epi-LASIK. The contact lens was on the no-flap corneal surface. (B) Slit lamp image of left eye in the same patient 10 minutes after on-flap epi-LASIK. The white curve between contact lens and corneal stroma indicated the repositioned epithelial flap.

Off-Flap Epi-LASIK for Moderate to High Myopia

After the removal of the bandage contact lens, patients were followed up at 3-, 5-, and 12-day and 1- and 3-month postoperative intervals. Examinations included manifest refraction, biomicroscopy, applanation tonometry, corneal topography, CSF, GSF, and wavefront aberration. Corneal haze formation was subjectively evaluated according to the system reported by Fantes et al.: 0, completely clear; 0.5, trace haze seen with careful oblique illumination with slit lamp biomicroscopy; 1, more prominent haze not interfering with visibility of fine iris details; 2, mild obscuration of iris details; 3, moderate obscuration of the iris and lens; and 4, completely opacification of the stroma in the area of the ablation.

Mesopic CSF and GSF were performed by testing with a contrast sensitivity test (CSV-1000E test chart; VectorVision, Inc., Arcanum, OH) before surgery and 1 and 3 months after surgery. The system used provides a fluorescent luminance source that retroilluminates a translucent chart and automatically calibrates to 85 cd/m² without room lights. The test was performed unilaterally at 2.5 m. The vertical plane illumination of glare photosource was 40 lux which got from test distance (2.5 m). The spatial frequencies were 3, 6, 12, and 18 cpd.

Wavefront aberration was measured by using a visual function analyzer (itrace; Tracey Technologies, Houston, TX) before surgery and 3 months after surgery. The right eye, then the left eye, was measured three times and an average value was calculated for a 5.5-mm pupil.

Statistical Analysis

Data were collected on standardized case report forms and then entered into a central database for analysis. There were no missing data in the analysis. Statistical analysis was performed with commercial software (SPSS, ver. 13.0; SPSS, Chicago, IL). Measures were compared by using a paired t-test, χ² test, and one-way ANOVA. The level of significance was P < 0.05.

RESULTS

All patients underwent an uneventful surgery. There was no statistically significant difference in the mean preoperative SE between groups (−6.18 ± 1.29 D vs. −6.47 ± 1.70 D, t = 1.651, P = 0.11, paired t-test).

Safety

Figure 2 demonstrates no significant difference in the change in lines of BCVA in logarithm of the minimum angle of resolution (logMAR) between groups 3 months after surgery (u = 0.008, P = 0.99, χ² test). BCVA increased or remained unchanged in 96.8% of patients in the off-flap epi-LASIK group and in 93.5% of the on-flap epi-LASIK group.

Efficacy

As Figure 3 shows, the logMar UCVA in the off-flap epi-LASIK group was significantly better than that in the on-flap epi-LASIK
group at 3 and 5 days after surgery ($t = 4.32, 4.31; P < 0.001$, paired $t$-test). No significant difference was found between groups at 12 days and 1 and 3 months after surgery. In each group, $87.1\% (n = 27)$ of the eyes had a UCVA of 20/20 or better 3 months after surgery.

**Predictability**

Three months after surgery, all eyes were within $\pm 1.00$ D of the attempted correction, and $71\%$ in the off-flap epi-LASIK group, $58.1\%$ in on-flap epi-LASIK group, respectively, were within $\pm 0.50$ D of the attempted correction.

**Pain Scores**

Figure 4 showed that $38.7\%$ in both groups experienced pain within 2 days after surgery. No postoperative pain of grade 4 occurred. There was no significant difference in postoperative pain between groups ($U = 0.57, P = 0.57, \chi^2$ test).

**Epithelial Healing**

As Figures 5 and 6 show, the off-flap epi-LASIK group demonstrated significantly rapid reepithelialization than did the on-flap epi-LASIK group ($\chi^2 = 20.13, P < 0.001, \chi^2$ test). The mean reepithelialization times in the off-flap and on-flap epi-LASIK groups was $3.45 \pm 0.98$ (range, 3–5) and $4.90 \pm 1.37$ (range, 3–9) days, respectively. Epithelial raphe was observed in $8 (25.8\%)$ eyes in the on-flap epi-LASIK group, but in no eyes in the off-flap epi-LASIK group.

**Haze Scores**

Haze was found in five eyes (four eyes, grade 0.5; 1 eye, grade 1) in the off-flap epi-LASIK group and 12 eyes (8 eyes, grade 0.5; 4 eyes, grade 1) in the on-flap epi-LASIK group 1 month after surgery and in 5 eyes (grade 0.5) in the off-flap epi-LASIK group and in 11 eyes (10 eyes, grade 0.5; 1 eye, grade 1) in the on-flap epi-LASIK group 3 months after surgery, which was a significant difference between groups ($u = 2.027, P = 0.043; u = 2.016, P = 0.044, \chi^2$ test).

**Contrast Sensitivity**

There were no statistically significant differences in the CSF and GSF between groups (paired $t$-test). CSF (Table 1) and GSF (Table 2) did not differ from before surgery 1 and 3 months after surgery in both groups, except that the GSF at 18 cpd increased significantly in the off-flap epi-LASIK group 3 months after surgery ($P = 0.04$, one-way ANOVA).

**Wavefront Aberration**

Table 3 shows that higher order (HOA), coma, and spherical aberrations had increased significantly from baseline in both groups at 3 months after surgery (paired $t$-test). In comparison with the off-flap epi-LASIK group, the on-flap epi-LASIK group revealed greater but insignificant increasing amplitude in wavefront aberration (paired $t$-test).

**DISCUSSION**

Over the past few years, a tendency toward performing surface ablation procedures has emerged. Thin, steep, or flat corneas and deep-set eyes are preferably treated with surface ablation, so that the flap-related complications of LASIK can be avoided.
However, epi-LASIK has the disadvantages of postoperative pain and delayed visual recovery. Therefore, it is essential to improve visual recovery in the early postoperative period. To our knowledge, this is the first study to date to investigate the off-flap epi-LASIK for moderate to high myopia.3,7 The reepithelialization in off-flap epi-LASIK was found to occur more rapidly than on-flap epi-LASIK by 1.5 days.

Postoperative Pain

This study revealed no significant difference in the postoperative pain between two groups. However, it is not similar to those reported previously. O’Doherty et al.8 reported pain after on-flap epi-LASIK, PRK, or LASEK for myopia. Patients who underwent epi-LASIK were found to have significantly less pain in the first 2 hours, after which all patients had the same level of pain. Torres et al.9 found the postoperative pain after on-flap epi-LASIK and PRK to be similar on postoperative day 1, but epi-LASIK demonstrated significantly more pain than PRK on days 3 and 6. The explanations for the difference include: (1)

Refraction Outcomes

Off-flap epi-LASIK is a modified surface ablation technique that removes epithelial flap after ablation. It offers comparable visual and refractive outcomes to on-flap epi-LASIK with rapid recovery in the early postoperative period. The UCVA in off-flap epi-LASIK was significantly better than on-flap epi-LASIK on 3 and 5 days after surgery. The significant SE reduction between the pre- and postoperative periods in on-flap epi-LASIK in this study corroborates the efficacy of epi-LASIK for moderate to high myopia.3,7

### Table 1. Mesopic CSF without Glare

<table>
<thead>
<tr>
<th></th>
<th>3 cpd</th>
<th>6 cpd</th>
<th>12 cpd</th>
<th>18 cpd</th>
</tr>
</thead>
<tbody>
<tr>
<td></td>
<td>Off-Flap Group</td>
<td>On-Flap Group</td>
<td>Off-Flap Group</td>
<td>On-Flap Group</td>
</tr>
<tr>
<td>Preop</td>
<td>1.63 ± 0.19</td>
<td>1.66 ± 0.14</td>
<td>1.89 ± 0.21</td>
<td>1.92 ± 0.18</td>
</tr>
<tr>
<td>Postop 1 mo</td>
<td>1.64 ± 0.19</td>
<td>1.65 ± 0.16</td>
<td>1.82 ± 0.22</td>
<td>1.84 ± 0.18</td>
</tr>
<tr>
<td>Postop 3 mo</td>
<td>1.70 ± 0.12</td>
<td>1.71 ± 0.12</td>
<td>1.95 ± 0.14</td>
<td>1.95 ± 0.16</td>
</tr>
<tr>
<td>F</td>
<td>1.25</td>
<td>1.50</td>
<td>3.21</td>
<td>2.93</td>
</tr>
<tr>
<td>P</td>
<td>0.30</td>
<td>0.23</td>
<td>0.05</td>
<td>0.06</td>
</tr>
</tbody>
</table>

### Table 2. Mesopic GSF with Glare

<table>
<thead>
<tr>
<th></th>
<th>3 cpd</th>
<th>6 cpd</th>
<th>12 cpd</th>
<th>18 cpd</th>
</tr>
</thead>
<tbody>
<tr>
<td></td>
<td>Off-Flap Group</td>
<td>On-Flap Group</td>
<td>Off-Flap Group</td>
<td>On-Flap Group</td>
</tr>
<tr>
<td>Preop</td>
<td>1.60 ± 0.18</td>
<td>1.62 ± 0.14</td>
<td>1.84 ± 0.18</td>
<td>1.88 ± 0.17</td>
</tr>
<tr>
<td>Postop 1 mo</td>
<td>1.64 ± 0.19</td>
<td>1.65 ± 0.15</td>
<td>1.81 ± 0.19</td>
<td>1.83 ± 0.18</td>
</tr>
<tr>
<td>Postop 3 mo</td>
<td>1.66 ± 0.10</td>
<td>1.67 ± 0.11</td>
<td>1.89 ± 0.14</td>
<td>1.88 ± 0.17</td>
</tr>
<tr>
<td>F</td>
<td>0.79</td>
<td>0.85</td>
<td>1.53</td>
<td>0.79</td>
</tr>
<tr>
<td>P</td>
<td>0.46</td>
<td>0.43</td>
<td>0.22</td>
<td>0.46</td>
</tr>
</tbody>
</table>

### Table 3. Preoperative and Postoperative Wavefront Aberration RMS

<table>
<thead>
<tr>
<th></th>
<th>Higher-Order Aberration</th>
<th>Coma Aberration</th>
<th>Spherical Aberration</th>
</tr>
</thead>
<tbody>
<tr>
<td></td>
<td>Off-Flap Group</td>
<td>On-Flap Group</td>
<td>Off-Flap Group</td>
</tr>
<tr>
<td>Preop</td>
<td>0.32 ± 0.13</td>
<td>0.31 ± 0.11</td>
<td>0.21 ± 0.13</td>
</tr>
<tr>
<td>Postop 3 mo</td>
<td>0.49 ± 0.17</td>
<td>0.54 ± 0.22</td>
<td>0.54 ± 0.18</td>
</tr>
<tr>
<td>t</td>
<td>4.48</td>
<td>5.92</td>
<td>2.94</td>
</tr>
<tr>
<td>P</td>
<td>&lt;0.001</td>
<td>&lt;0.001</td>
<td>&lt;0.001</td>
</tr>
</tbody>
</table>
the pain questionnaire applied and time point are different in different researches; and (2) all eyes in this study were irrigated by cooled PSS that relieved pain.

Epithelial Healing
In comparison with the on-flap epi-LASIK group, in the off-flap epi-LASIK group, the cornea was revealed to have a rapid recovery with a more regular and smooth surface. On the day of reepithelialization, a central epithelial raphe was observed in the on-flap epi-LASIK eyes, which is consistent with results in an earlier report. The raphe was irregular and decreased visual acuity in the short term. It was not observed in the off-flap epi-LASIK group. This finding may be due to the removal of the epithelial flap, which triggers epithelium regrow process resulting in a smooth corneal surface, whereas the epithelium is remodeled in on-flap epi-LASIK. In addition, the healing response in off-flap epi-LASIK is not a duplication of what happens in PRK. In PRK, the surgeon removes the epithelium with a blade. Compared with PRK, the removal of the epithelial flap with the use of an epikeratome in off-flap epi-LASIK results in a smooth corneal surface with regular borders, offering advantages with respect to comfort visual recovery and haze formation.

Haze Formation
Off-flap epi-LASIK resulted in lower levels of haze than did on-flap epi-LASIK. Haze is one of the major obstacles that prevent widespread acceptance of surface ablation by patients and surgeons. It is mainly relative to the surface regularity of ablated stroma and ablation depth. MMC obviously reduces haze, although the concentration and time in using MMC vary in different researches; and (2) all eyes in this study were irrigated with a central epithelial raphe was observed in the on-flap epi-LASIK group. This finding may be due to the removal of the epithelial flap, which triggers epithelium regrow process resulting in a smooth corneal surface, whereas the epithelium is remodeled in on-flap epi-LASIK. In addition, the healing response in off-flap epi-LASIK is not a duplication of what happens in PRK. In PRK, the surgeon removes the epithelium with a blade. Compared with PRK, the removal of the epithelial flap with the use of an epikeratome in off-flap epi-LASIK results in a smooth corneal surface with regular borders, offering advantages with respect to comfort visual recovery and haze formation.

Visual Quality
In consideration of visual quality in patients after refractive surgery, further attention should be paid to the influence of surgery on CSF, GSF, and wavefront aberration in detail, rather than visual acuity alone. In this study, HOA, coma, and spherical aberration increased from baseline in both groups, and on-flap epi-LASIK caused greater but insignificantly increased amplitude in wavefront aberration. Nevertheless, CSF and GSF recovered to preoperative levels 1 month after surgery in both groups. At 3 months after surgery, GSF at 18 cpd was even better than before off-flap epi-LASIK, indicating that visual quality in off-flap LASIK is superior to that in on-flap epi-LASIK. This result may be explained by the corneal surface being more regular and smooth after surgery in off-flap LASIK than in on-flap epi-LASIK. It has been reported that visual quality after a corneal surface ablation procedure is superior to LASIK. Oshika et al. reported that the aberrations after LASIK increased more than after PRK. The corneal topography after LASEK is more regular than that after LASIK, resulting in better visual quality, because the corneal flap of LASIK may be asymmetrical and shift. In our study, we further compared two groups who underwent a different surface ablation procedure and demonstrated that visual quality was much better after off-flap epi-LASIK.

This study adds to our previous knowledge of surface ablation procedures. The preliminary results of off-flap epi-LASIK for treatment of moderate to high myopia are encouraging. In conclusion, analysis of clinical outcomes of off-flap and on-flap epi-LASIK revealed that off-flap epi-LASIK offers comparable postoperative pain, lower levels of haze formation, rapid visual recovery, and better visual quality. Further investigations with a larger number of subjects and longer follow-up periods are warranted.

References