Three-year results of small incision lenticule extraction and wavefront-guided femtosecond laser-assisted laser in situ keratomileusis for correction of high myopia and myopic astigmatism

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Abstract
● AIM: To compare and calculate the 3-year refractive results, higher-order aberrations (HOAs), contrast sensitivity (CS) and dry eye parameters after small incision lenticule extraction (SMILE) and wavefront-guided femtosecond laser-assisted laser in situ keratomileusis (FS-LASIK) for correction of high myopia and myopic astigmatism.
● METHODS: In this prospective, non-randomized comparative study, 78 eyes with spherical equivalent (SE) of -8.11±1.09 diopters (D) received a SMILE surgery, and 65 eyes with SE of -8.05±1.12 D received a wavefront-guided FS-LASIK surgery with the VisuMax femtosecond laser (Carl Zeiss Meditec, Jena, Germany) for flap cutting. Visual acuity, manifest refraction, CS, HOAs, ocular surface disease index (OSDI) and tear break-up time (TBUT) were evaluated during a 3-year follow-up.
● RESULTS: The difference of uncorrected distance visual acuity (UDVA) postoperatively was achieved at 1mo and at 3mo, whereas the difference of the mean UDVA between two groups at 3y were not statistically significant (t=-1.59, P=0.13). The postoperative change of SE was 0.89 D in the FS-LASIK group (t=5.76, P=0.00), and 0.14 D in the SMILE group (t=0.54, P=0.59) from 1mo to 3y after surgery. At 3-year postoperatively, both HOAs and spherical aberrations in the SMILE group were obviously less than those in the FS-LASIK group (P=0.00), but the coma root mean square (RMS) was higher in the SMILE group (0.59±0.26) than in the FS-LASIK group (0.29±0.14, P=0.00). The mesopic CS values between two groups were not statistically significant at 3y postoperatively. Compared with the FS-LASIK group, lower OSDI scores and longer TBUT values were found in the SMILE group at 1mo and 3mo postoperatively. With regard to safety, no eye lost any line of CDVA in both groups at 3y after surgery.
● CONCLUSION: Both SMILE and wavefront-guided FS-LASIK procedures provide good visual outcomes. Both procedures are effective and safe, but SMILE surgery achieve more stable long-term refractive outcome and better control of early postoperative dry eye as compared to FS-LASIK.
● KEYWORDS: small incision lenticule extraction; wavefront-guided femtosecond laser-assisted laser in situ keratomileusis; femtosecond laser; refractive surgery; visual outcome DOI:10.18240/ijo.2018.03.18

INTRODUCTION
Femtosecond laser-assisted laser in situ keratomileusis (FS-LASIK), which involves flap cutting and stromal ablation using femtosecond laser and excimer laser respectively, has been widely applied in myopia correction[1-2]. The wavefront-guided ablation profiles with the latest excimer laser platforms provide a guarantee for the excellent visual, refractive, and aberrometric outcomes of FS-LASIK[3-6]. However, FS-LASIK for correcting high myopia and astigmatism is challenging owing to the associated risk of treatment regression, corneal biomechanics changes, and flap complications[7]. The recently introduced small-incision lenticule extraction (SMILE) is an all-in-one procedure, in which a corneal intrastromal lenticule is fashioned using femtosecond laser and extracted manually through a small peripheral corneal incision[8-9]. The size and shape of the extracted lenticule are based on the patient’s refractive error[10]. The new technique, which no longer requires a flap, might reduce some flap-related side effects of FS-LASIK, such as flap dislocation and flap-
induced astigmatism\textsuperscript{9,11}. Although there is consistent scientific evidence supporting of the efficacy and safety of SMILE for the correction of myopia and astigmatism\textsuperscript{8,12}, the superiority of SMILE over wavefront-guided FS-LASIK in correcting high myopia and astigmatism have not been demonstrated conclusively. Especially, long-term comparative studies of SMILE versus FS-LASIK in high myopia and myopic astigmatism eyes are far from being established. This may be essential to relieve patients’ concerns about clinical risk following SMILE surgery. The objective of the study was to compare the long-term (3-year) correction of high myopia and myopic astigmatism between SMILE and FS-LASIK in terms of visual acuity, refractive results, aberrations, contrast sensitivity (CS) and dry eye.

SUBJECTS AND METHODS

Participants  The study was approved by the Ethics Committee of Shengjing Hospital and comply with the tenets of the Declaration of Helsinki regarding research involving human subjects. This study involved 78 eyes of 40 patients who underwent SMILE and 65 eyes of 33 patients who underwent wavefront-guided FS-LASIK during January 1, 2013 to July 31, 2013 at the Refractive Surgery Center of Shengjing Hospital, China Medical University, China. All patients participated in complete follow-up examinations for 3y after surgery. All patients received a comprehensive preoperative examination for corneal refractive surgery. Patients with normal corneal topography (based on evaluation of Pentacam HR tomographs), central corneal thickness ≥500 \( \mu \)m, and calculated residual corneal stromal bed thickness ≥280 \( \mu \)m were informed about the outcome of laser refractive procedures. All patients were informed of full descriptions of the SMILE and wavefront-guided FS-LASIK procedures, including the potential advantages, disadvantages, side effects and complications. The patients decided whichever to choose between the two surgical procedures, and signed the informed consent before treatment. The main inclusion criteria were as below: spherical myopia ranging from -6.0 to -10.0 diopters (D); with or without regular astigmatism up to -3.5 D; corrected distance visual acuity (CDVA) of 20/20 or better; stable refraction in the past 12mo (<0.50 D change of sphere or cylinder); not wearing soft lenses at least 14d before the preoperative evaluation; age between 18 and 40y; with the ability to participate in follow-up examinations for 3y after surgery.

FS-LASIK and SMILE Surgical Procedures  A single experienced surgeon performed all surgeries under topical anaesthesia using a standard surgical technique. For FS-LASIK group, superior-hinge flaps were created using a 500 kHz VisuMax femtosecond laser (Carl Zeiss Meditec AG, Germany) with 175 nJ of energy. Femtosecond laser flaps were programmed with 110 \( \mu \)m thickness and 7.9 \( \mu \)m diameter, and 90° side cut angles. Following the flap creation, the
**Statistical Analysis**

Statistical analysis was performed using SPSS 20.0 statistical analysis software (USA) and reported as mean±standard deviation (SD). Visual acuity outcomes were calculated in logMAR notation. We analyze the multiple difference by using the variance analysis of repeated measurement data. Comparison of continuous variable between the two groups were examined by independent samples t-test, and a Chi-square test was used for statistical analysis of categorical variable at the baseline. Furthermore, we used paired t-test to analyze the difference of spherical equivalent (SE) between 1-month and 3-year postoperatively in both group. Statistical significance level was set at 0.05.

**RESULTS**

**Patient Population**

The preoperative demographic data of both groups are shown in Table 1. There were no statistically significant differences in terms of the mean age, spherical error, astigmatism, SE, CDVA, central corneal thickness between the two groups. All surgeries were successfully completed without any intraoperative complications. None of the subjects dropped out during the 3-year follow-up period.

**Visual Acuity**

Figure 1 shows the changes of UDVA at 3-year follow-up visits for two groups. There were significant differences between the two groups postoperatively (variance analysis of repeated measurement data; \( F=42.512, P=0.00 \)). In the SMILE group, the best postoperative UDVA (-0.07 in logMAR) was achieved at 1mo after surgery, but decreased gradually to -0.03 logMAR at 3y postoperatively. However, there were no statistically significant difference of the mean UDVA between two groups at 3-year postoperatively (independent samples Student’s t-test; \( t=-1.59, P=0.13 \)). Figure 2 shows cumulative Snellen postoperative UDVA at 3-year in two groups. Seventy-two (92.3%) of 78 eyes in the SMILE group had an UDVA better than or equal to 20/20, and 78 eyes (100%) had an UDVA better than or equal to 20/25. In the FS-LASIK group, 59 (90.8%) of 65 eyes had an UDVA better than or equal to 20/20, 65 eyes (100%) had an UDVA better than or equal to 20/25. The changes of CDVA pre- to post-surgery for two groups were shown in Figure 3. At 3-year postoperatively, of the 78 eyes treated with SMILE, 7 eyes (9.0%) gained one line of CDVA, 1 eye (1.3%) gained two line of CDVA, and 89.7% (70 eyes) were unchanged postoperatively. Of the 65 eyes treated with FS-LASIK, 4 eyes (6.2%) gained one line of CDVA, 2 eyes (3.1%) gained two lines of CDVA, and 59 eyes (90.8%) were unchanged postoperatively. None of them lost ≥1 lines of CDVA in both groups. The results indicate that both the SMILE and the FS-LASIK were effective and safe to correct high myopia and myopic astigmatism.

**Refractive Outcome**

Mean preoperative SE were -8.11±1.09 and -8.05±1.12 D in SMILE group and FS-LASIK group, respectively. The difference of the mean preoperative SE between two groups were not statistically significant.

**Table 1 Preoperative demographic data of patients in SMILE and FS-LASIK groups**

<table>
<thead>
<tr>
<th>Groups</th>
<th>Eyes</th>
<th>Gender (M/F)</th>
<th>Age (y)</th>
<th>SE (D)</th>
<th>Sphere (D)</th>
<th>Cylinder (D)</th>
<th>CCT (µm)</th>
<th>CDVA (logMAR)</th>
</tr>
</thead>
<tbody>
<tr>
<td>SMILE</td>
<td>78</td>
<td>13/27</td>
<td>26.9±9.00 (18 to 40)</td>
<td>-8.11±1.09 (-6.0 to -12.0)</td>
<td>-7.61±1.02 (-6.0 to -10.0)</td>
<td>-0.92±0.91 (-0.5 to -3.5)</td>
<td>552.15±30.80 (500 to 650)</td>
<td>-0.07±0.18 (0.2 to -0.2)</td>
</tr>
<tr>
<td>FS-LASIK</td>
<td>65</td>
<td>10/23</td>
<td>27.1±9.40 (18 to 40)</td>
<td>-8.05±1.12 (-6.0 to -12.0)</td>
<td>-7.58±1.05 (-6.0 to -10.0)</td>
<td>-0.95±0.85 (-0.5 to -3.5)</td>
<td>548.61±29.19 (500 to 650)</td>
<td>-0.06±0.19 (0.2 to -0.2)</td>
</tr>
</tbody>
</table>

Data were given as mean±standard deviation with range in parenthesis. SMILE: Small-incision lenticule extraction; FS-LASIK: Femtosecond laser-assisted laser in situ keratomileusis; D: Dioptries; SE: Spherical equivalent; CCT: Central corneal thickness; CDVA: Corrected distance visual acuity; logMAR: Logarithm of the minimum angle of resolution.

Figure 1 Changes of mean UDVA in logMAR after SMILE and FS-LASIK

UDVA: Uncorrected distance visual acuity; SMILE: Small-incision lenticule extraction; FS-LASIK: Femtosecond laser-assisted LASIK.
Considering the changes of SE from 1 to 36 mo after surgery, we found significant differences between the two groups (variance analysis of repeated measurement data; F = 82.618, P = 0.00). The mean SE in the SMILE group changed from +0.13 ± 0.79 D to -0.01 ± 0.76 D, and the FS-LASIK group from +0.46 ± 0.95 D to -0.43 ± 0.82 D. The mean change was 0.14 D in the SMILE treated eyes (paired t-test; t = 0.546, P = 0.59), and 0.89 D in the FS-LASIK treated eyes (paired t-test; t = 5.765, P = 0.00). The results indicated that the postoperative refractive outcome in SMILE group was more stable than FS-LASIK group over the 3-year follow-up period (Figure 4).

### Higher-order Aberrations

Data was analyzed under a 6.0-mm pupil diameter. Preoperative root mean square (RMS) value of HOAs, spherical aberrations, and coma were not significantly different between the SMILE and FS-LASIK groups (P > 0.05; Table 2). At 3-year postoperatively, the mean HOAs RMS and spherical aberrations were 0.33 ± 0.10 μm, 0.26 ± 0.31 μm in the SMILE group, and 0.59 ± 0.26 μm, 0.35 ± 0.19 μm in the FS-LASIK group, respectively, for a 6.0 mm pupil. Both the postoperative HOAs and spherical aberrations in the SMILE treated eyes were apparently less than those in the FS-LASIK treated eyes (P = 0.00). However, the postoperative mean coma RMS was higher in the SMILE treated eyes (0.59 ± 0.26 μm) than in the FS-LASIK treated eyes (0.29 ± 0.14 μm, P = 0.00).

### Contrast Sensitivity Function

At night environment (under a 5 mm pupil size condition), the CS values between two groups at 1.5, 3, 6, 12, and 18 cycles per degree were not statistically significant (P > 0.05; Figure 5). At 3 y postoperatively, there also were no statistically significant differences found in SMILE and FS-LASIK surgeries at all spatial frequencies (P > 0.05; Figure 5).

### Ocular Surface Disease Index

In terms of OSDI, we found significant difference at different time points between the two groups postoperatively (variance analysis of repeated measurement data; F = 120.318, P = 0.00). Table 3 showed postoperative OSDI scores at each time point for two groups. Figure 6 summarizes mean preoperative and postoperative OSDI scores at each time point for two groups. Mean preoperative OSDI scores were 6.73 ± 3.25 in the SMILE group and 6.68 ± 3.11 in the FS-LASIK group, and there was no significant difference between the two groups (t = 0.432, P = 0.61). The mean OSDI scores in the FS-LASIK group were increased significantly at 1 mo (9.32 ± 4.51) and 3 mo (9.32 ± 4.18) postoperatively relative to preoperative scores (t = 3.081, P = 0.00). However, the postoperative significant increases of OSDI scores in the SMILE group were only found at 1 mo postoperatively (9.08 ± 3.88, P = 0.00). In addition, mean OSDI scores were significantly worse in the FS-LASIK treated eyes than in the SMILE treated eyes at 1 mo and 3 mo postoperatively (independent samples t-test; t = -11.831, -8.389, P = 0.00, 0.00). There were no significant difference in the mean OSDI scores between the two groups at other follow-up time (P > 0.05).

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**Table 2** The comparisons of the RMS values of different higher-order aberrations for a 6 mm pupil between the SMILE and FS-LASIK group

<table>
<thead>
<tr>
<th>Parameters (RMS, μm)</th>
<th>SMILE</th>
<th>FS-LASIK</th>
<th>t</th>
<th>P</th>
</tr>
</thead>
<tbody>
<tr>
<td>Pre-operation</td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Total HOAs</td>
<td>0.28 ± 0.09</td>
<td>0.27 ± 0.08</td>
<td>0.920</td>
<td>0.359</td>
</tr>
<tr>
<td>Spherical aberration</td>
<td>0.12 ± 0.16</td>
<td>0.13 ± 0.15</td>
<td>0.418</td>
<td>0.677</td>
</tr>
<tr>
<td>Coma</td>
<td>0.24 ± 0.11</td>
<td>0.25 ± 0.12</td>
<td>-0.586</td>
<td>0.559</td>
</tr>
<tr>
<td>3-year post-operation</td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Total HOAs</td>
<td>0.33 ± 0.10</td>
<td>0.42 ± 0.13</td>
<td>-4.286</td>
<td>0.000</td>
</tr>
<tr>
<td>Spherical aberration</td>
<td>0.26 ± 0.31</td>
<td>0.35 ± 0.19</td>
<td>3.192</td>
<td>0.002</td>
</tr>
<tr>
<td>Coma</td>
<td>0.59 ± 0.26</td>
<td>0.29 ± 0.14</td>
<td>3.614</td>
<td>0.000</td>
</tr>
</tbody>
</table>

SMILE: Small-incision lenticule extraction; FS-LASIK: Femtosecond laser-assisted LASIK; RMS: Root mean square; HOAs: Higher-order aberrations. *Significant differences between the SMILE and FS-LASIK group.
The mean TBUT in both groups were shorter significantly after surgery relative to their preoperative level, and we found significant difference at different time points between the two groups postoperatively (variance analysis of repeated measurement data; F=256.530, P=0.000). However, the mean TBUT returned to the preoperative TBUT values at the third month postoperatively in the SMILE treated eyes, whereas at the sixth month postoperatively in the FS-LASIK treated eyes. The result was shown in Table 4 below.

**DISCUSSION**

Femtosecond laser technology to create corneal flaps enables a large increase in the flap safety of LASIK\(^1\)\(^-\)\(^2\). Wavefront-guided FS-LASIK becomes the most common corneal refractive surgery because of its excellent refractive outcomes\(^6\). SMILE has gained widespread acceptance in corneal refractive surgery because it is flapless. In the current research, we not only compared the visual acuity, refractive results, but also analyzed HOAs, CS, and the dry eye parameters at 3-year after SMILE and FS-LASIK for the correction of high myopia and myopic astigmatism.

**Tear Break-up Time** The mean TBUT in both groups were shorter significantly after surgery relative to their preoperative level, and we found significant difference at different time points between the two groups postoperatively (variance analysis of repeated measurement data; F=256.530, P=0.000). However, the mean TBUT returned to the preoperative TBUT values at the third month postoperatively in the SMILE treated eyes, whereas at the sixth month postoperatively in the FS-LASIK treated eyes. The result was shown in Table 4 below. We found significant differences between the two groups postoperatively. That is to say, higher TBUT scores were found in the SMILE group than in the FS-LASIK group at postoperative 1mo and 3mo (P=0.00; Figure 7).

**Table 3** The comparisons of OSDI between the SMILE and FS-LASIK group postoperatively

<table>
<thead>
<tr>
<th>Time</th>
<th>n</th>
<th>SMILE</th>
<th>FS-LASIK</th>
<th>t</th>
<th>P</th>
<th>F</th>
<th>P</th>
</tr>
</thead>
<tbody>
<tr>
<td></td>
<td></td>
<td>1mo</td>
<td>3mo</td>
<td>6mo</td>
<td>1y</td>
<td>2y</td>
<td>3y</td>
</tr>
<tr>
<td></td>
<td>78</td>
<td>9.08±3.88</td>
<td>7.37±3.31</td>
<td>7.25±3.37</td>
<td>6.90±4.06</td>
<td>6.68±4.11</td>
<td>6.63±4.01</td>
</tr>
<tr>
<td></td>
<td>65</td>
<td>12.63±4.51</td>
<td>9.32±4.18</td>
<td>7.46±3.37</td>
<td>7.38±4.24</td>
<td>7.25±4.14</td>
<td>7.08±4.22</td>
</tr>
<tr>
<td>P</td>
<td></td>
<td>0.000</td>
<td>0.000</td>
<td>0.096</td>
<td>0.085</td>
<td>0.114</td>
<td>0.121</td>
</tr>
</tbody>
</table>

OSDI: Ocular surface disease index; SMILE: Small-incision lenticule extraction; FS-LASIK: Femtosecond laser-assisted LASIK.

**Figure 4** Changes of spherical equivalent from 1mo to 3y after SMILE and FS-LASIK

**Figure 5** Comparison of contrast sensitivity between SMILE and FS-LASIK

**Figure 6** Comparison of ocular surface disease index between the SMILE group and FS-LASIK group pre- and post-operatively
In this study, the best postoperative UDVA were achieved at 1mo after FS-LASIK, and at 3mo after SMILE. The reason for the delayed visual recovery after SMILE was probably due to the corneal edema and healing response after extracted the lenticule, which is different from the FS-LASIK procedure[8,14-15]. However, the values of UDVA at 3-year post-surgery between two groups were not statistically significant. At 3-year postoperatively, UDVA of 20/20 or better was achieved in 92.3% after SMILE and 90.8% after FS-LASIK, which is lower than the findings by Liu et al[15]. Liu et al[15] reported that 96% of treated eyes in SMILE group and 99% treated eyes in FS-LASIK group, respectively, achieved 20/20 or better UDVA at 6-month postoperatively. Possible reasons for the difference of UDVA between our report and that of Liu et al[15] could be a relatively lower preoperative level. Further investigations on regression following SMILE surgery are required[12].

It is well known that HOAs and especially spherical aberrations after LASIK are increased[22-23], with some increases in aberrations being produced by flap creation alone[24-25]. The increase of aberrations is the main factor affecting the visual quality after surgery[26]. In the current study, we used the Hartmann-Shack WASCA aberrometer to measures the whole-eye wavefront aberrations and compared HOAs after SMILE and FS-LASIK at the analysis diameter of 6 mm. We found
that the postoperative HOAs and spherical aberrations in the SMILE treated eyes were markedly less than those in the FS-LASIK treated eyes, but the postoperative mean coma RMS was higher in the SMILE treated eyes than in the FS-LASIK treated eyes at 3-year postoperatively. Several comparative studies of SMILE versus FS-LASIK by others[^11,15,17,27] also found that SMILE eyes had more coma postoperatively and FS-LASIK eyes had more spherical aberration postoperatively. The higher level of coma after SMILE was thought to be associated with the presence of mild levels of treatment decentration[^11,15,16]. The lower induction of spherical aberration after SMILE was thought to be related to the larger ablation zone and less changes in the corneal shape of the SMILE procedure[^14,28-29].

In our opinion, although HOAs reflect the objective quality of vision, CS reflects the subjective quality of vision from the patient’s perspective, which is a crucial parameter for patients’ satisfaction. In this study, although there were statistically significant differences in the characteristics of HOA induction between the SMILE and FS-LASIK groups, no significant differences in mesopic CS values for all spatial frequencies were found between two groups at 3y postoperatively. In another comparative analysis of CS after SMILE and FS-LASIK, both procedures yielded no statistically significant differences from baseline to 6mo after surgery[^30].

As we know, one of the most feared and common complications of traditional refractive surgeries is dry eye[^31-32]. Dry eye is not only a simple disease causing patients feel uncomfortable about the deterioration of quality of life, but also impairs visual function, CS and ocular HOAs[^33-34]. SMILE uses the femtosecond laser system as an all-in-one device for lenticule processing and replacement of small incised corneal flap. Therefore, the ocular surface of eyes treated with SMILE were healthier than those with FS-LASIK surgery. Li et al[^13] found that patients in the SMILE group had less corneal staining and greater central corneal sensitivity scores than patients in the FS-LASIK group. Consistent with their studies, our study demonstrated significantly lower OSDI scores and longer TBUT values in the SMILE group compared with the FS-LASIK group at 1mo and 3mo postoperatively. Our data also showed a faster recovery of ocular surface injury in SMILE group than in FS-LASIK group, which should be mainly attributed to the slight of corneal nerve damage and a more regular corneal surface during the new flapless technique of SMILE[^13,33].

In conclusion, both SMILE and wavefront-guided FS-LASIK provide good visual outcomes. Both SMILE and FS-LASIK demonstrated the similar effectiveness and security in correcting high myopia and myopic astigmatism. SMILE surgery achieved more stable refractive outcome and better control of early postoperative dry eye as compared to wavefront-guided FS-LASIK.

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Conflicts of Interest: Xia LK, None; Ma J, None; Liu HN, None; Shi C, None; Huang Q, None.

REFERENCES


