Three-Year Results of Small Incision Lenticule Extraction for High Myopia: Refractive Outcomes and Aberrations

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ABSTRACT

PURPOSE: To assess the 3-year refractive and visual outcomes after small incision lenticule extraction (SMILE) in patients with high myopia and to evaluate the optical changes from 3 months to 3 years after surgery.

METHODS: A total of 87 eyes (87 patients) undergoing SMILE for high myopia were included. Preoperative and 3-month and 3-year postoperative follow-up examinations included manifest refraction and uncorrected and corrected distance visual acuities. Pentacam HR (Ocu- lus Optikgeräte, Wetzlar, Germany) was used to evaluate the total corneal refractive power and the root mean square of spherical aberration, coma, and total higher-order aberrations. The paired t test and Wilcoxon signed rank test were used.

RESULTS: The preoperative spherical equivalent averaged -7.30 ± 1.40 diopters (D); no significant changes occurred between 3 months and 3 years after surgery (-0.30 ± 0.50 vs -0.40 ± 0.60 D, P = .071). Uncor- rected distance visual acuity was stable from 3 months to 3 years after SMILE (0.04 ± 0.17 vs 0.03 ± 0.19 logMAR; P = .28), whereas corrected distance visual acuity improved from -0.05 ± 0.15 to -0.08 ± 0.11 logMAR (P < .001). At 3 months, 82% and 93% of eyes were within ±0.50 and ±1.00 D, respectively. At 3 years, 78% and 90% were within ±1.00 D of the attempted refraction, respectively. Spherical and higher-order aberrations significantly decreased from 3 months to 3 years, whereas coma remained stable. A significant regression of 0.36 ± 0.29 D was seen in total corneal refractive power (P < .001).

CONCLUSIONS: The refractive and visual outcomes seemed stable years after SMILE. A minor myopic regression was observed in total corneal refractive power but not in subjective refraction. There seems to be a significant long-term improvement in higher-order aberrations after surgery.

technique could be avoided. All of the patients except two had SMILE performed on both eyes; the right and left eyes were alternately included from each treated patient. Re-treatment was performed in one eye of one patient. In this specific case, the opposite eye was included instead.

**Preoperative Measurements**

Preoperative examination was performed by trained optometrists and included uncorrected (UDVA) and corrected (CDVA) distance visual acuity, slit-lamp microscopy, fundus examination, CCT measurements by laser interferometry (Optical Low Coherence Reflectometry; Haag-Streit, Koeniz, Switzerland), and corneal tomography (Pentacam HR; Oculus Optikgeräte, Wetzlar, Germany). Patients undergoing SMILE were informed about the outcome and side effects and gave informed consent before surgery.

**Surgical Procedure**

Surgery was performed under topical anesthesia with two drops of oxybuprocaine 0.8% hydrochloride. One of three experienced surgeons performed the surgery using a 500-kHz VisuMax femtosecond laser (Carl Zeiss Meditec, Jena, Germany) as previously described.7 Two types of laser settings were used: setting 1 (80 eyes) with a laser cut energy index of 24 to 26 nJ and a spot spacing of 2.5 to 3.0 µm, and setting 2 (7 eyes) with a laser cut energy index of 34 nJ and a spot spacing of 4.5 µm. The patient fixated on a blinking light while suction was applied. A 6- to 6.5-mm diameter intrastromal lenticule was created under a 7.3-mm cap with a thickness of 110 to 120 µm and a peripheral lenticule thickness of 15 µm. Through a 30° to 60° peripheral incision, a blunt spatula was used to break the remaining tissue bridges, and the lenticule was removed with forceps. One drop each of chloramphenicol (Kloramfenicol; Takeda Pharma, Roskilde, Denmark) and diclofenac (Voltaren Ophtha; Novartis Healthcare, Copenhagen, Denmark) were applied immediately after surgery.

**Postoperative Treatment and Follow-up**

Patients received chloramphenicol and fluorometholone drops (Flurolon; Allergan Pharmaceuticals, County Mayo, Dublin, Ireland) four times daily for 1 week and tapered to twice daily for 1 week. A thorough follow-up examination was performed routinely 1 month, 3 months, and 3 years after surgery. Each examination included manifest refraction, UDVA, CDVA, and corneal tomography.

**Corneal Aberrations and TCRP**

Wavefront aberrations, CCT, and TCRP were obtained with Pentacam HR. Wavefront aberrations were evaluated under scotopic light settings for a central zone of 5 mm. A previous study performed in a large number of patients treated with SMILE suggested that TCRP accurately assessed the change in manifest refraction after surgery.8 Standard refractive indices were used: cornea = 1.376 and aqueous = 1.336. In this study, we focused on the root mean square (RMS) of spherical aberration (Z4), RMS of coma (Z3 and Z3−1), and RMS of total higher-order aberrations (HOAs) from the third to eighth order. TCRP was analyzed in an apex zone of 4 mm as described previously.9 Twenty-five picture scans with a quality specification of “OK” were chosen for analysis.

**Statistical Analysis and Outcome Parameters**

Patient data were compiled in Microsoft Excel (Microsoft Corporation, Redmond, WA) and standard graphs were generated in Graphpad Prism (Prism v6.0 for MAC OS X; Graphpad Inc., La Jolla, CA). Normal distribution was evaluated by a Shapiro–Wilk normality test. Changes from the 3-month and 3-year follow-up examinations were analyzed with a paired Student’s t test for normally distributed data and with the Wilcoxon signed rank test for non-normally distributed data. A P value less than .05 was considered statistically significant. Outcome parameters were:

1. Efficacy index: ratio of mean postoperative UDVA and mean preoperative CDVA.
2. Predictability: percentage of eyes within ±0.50 and ±1.00 D of the attempted refraction.
3. Safety index: ratio of mean postoperative CDVA and mean preoperative CDVA.
4. Change in corneal aberrations, TCRP, and SE from 3 months to 3 years.

**Ethics**

The study adhered to the tenets of the Declaration of Helsinki. The Ethics Committee of Central Denmark Region considered this a quality-control study; therefore, ethical approval was not needed.

**Results**

All of the 87 patients attended the 3-month and 3-year follow-up examinations. Preoperative characteristics are described in Table 1. Mean CCT increased significantly from 3 months (448 ± 32 µm) to 3 years (452 ± 33 µm) (P < .001).
**Efficacy**

Efficacy is illustrated in Figure 1A by cumulative percentage of preoperative CDVA and postoperative UDVA at the 3-month and 3-year follow-up. All of the eyes had preoperative UDVA worse than 20/500. In total, 58% (33 eyes) reached 20/20 or better at the 3-month follow-up and 72% (41 eyes) reached 20/20 or better at the 3-year follow-up (only emmetropic eyes).

Changes in logMAR UDVA are shown in Figure 1B. No significant change was observed in mean UDVA from 3 months (0.04 ± 0.17 logMAR) to 3 years (0.03 ± 0.19 logMAR) ($P = .28$).

Efficacy index was 0.87 at 3 months and 0.91 at 3 years ($n = 57$, $P = .10$).

**Predictability**

Predictability is illustrated in Figure 1C. At the 3-month follow-up, the average error in refraction (achieved minus attempted) was -0.21 ± 0.48 D, which was similar to the average of -0.29 ± 0.55 D after 3 years ($P = .07$). At the 3-month follow-up, 82% (71 eyes) and 93% (81 eyes) were within ±0.50 and ±1.00 D of the attempted refraction, respectively. At the 3-year follow-up, 78% (68 eyes) and 90% (78 eyes) were within ±0.50 and ±1.00 D of the attempted refraction, respectively. Figure 1D shows a scatterplot and linear regression analysis of attempted versus achieved SE refraction 3 years after surgery.

**Safety**

Safety is illustrated in Figure 1E. In one case, CDVA was 20/100 3 months after surgery due to interface haze, and inferior punctate keratopathy was observed the day after surgery. Surgery was experienced as difficult in both eyes of this patient. However, spontaneous improvement was seen for a period of time and at the 3-year follow-up the patient had CDVA of 20/25.

At the 3-month follow-up visit, loss in CDVA of one Snellen line was seen in 16% (14 eyes) of eyes, no change in 46% (40 eyes) of eyes, and 38% (33 eyes) of eyes gained one Snellen line or more. Similar results were seen after 3 years with loss of one Snellen line in 12% (10 eyes) of eyes, no change in 40% (35 eyes) of eyes, and the remaining 48% (42 eyes) of eyes had an improvement of one Snellen line or more.

The development in logMAR CDVA is shown in Figure 1B. Improvement was seen in logMAR CDVA from 3 months (-0.05 ± 0.15) to 3 years (-0.08 ± 0.11) ($P < .001$). The safety index was 1.05 at 3 months, significantly increasing to 1.13 at 3 years ($P = .03$).

**Stability and TCRP**

Stability is shown in Figure 1F. Mean preoperative SE went from -7.30 ± 1.45 to -0.31 ± 0.53 D after 3 months and -0.39 ± 0.61 D after 3 years. No difference was observed in SE from 3 months to 3 years ($P = .071$). Refractive astigmatism is shown in Figure 1G. Mean refractive astigmatism went from -0.72 ± 0.59 D before surgery to -0.50 ± 0.35 D 3 months and -0.48 ± 0.38 D 3 years after surgery. No significant change was observed from the 3-month to 3-year follow-up examination ($P = .66$). Significant myopic regression was seen in TCRP with an average of 0.36 ± 0.29 D from 3 months to 3 years ($P < .001$) (Table 1).

**Corneal Aberrations**

Table A (available in the online version of this article) shows the change in corneal aberrations after surgery. Between the 3-month and 3-year follow-up examinations, spherical aberration and HOAs significantly decreased in corneal anterior surface, corneal posterior surface, and for the total cornea. Coma did not change during this period.

**Discussion**

LASIK has been the leading laser refractive technique for correcting myopia worldwide for more than a decade, and has high efficacy, stability, and safety. However, the technique requires making a corneal flap and the use of a microkeratome or both femtosecond and excimer lasers. Recently, SMILE has been introduced as a new single laser procedure. SMILE leaves the cornea more stable because only a small incision is made, causing less damage to the corneal nerves.
reduced, and only the femtosecond laser is needed during the procedure. However, the SMILE procedure may be surgically more challenging and retreatment can be difficult.

SMILE has routinely been performed in patients with high myopia at Aarhus University Hospital since January 2011. Until now, only a few short-term studies have been published with up to 1 year of follow-up. In the current study, mean UDVA did not change 3 years after surgery, whereas CDVA improved significantly. However, there was a minor myopic regression in corneal power 3 years after SMILE.
Several studies have evaluated short-term outcome after SMILE and found high efficacy, predictability, stability, and safety. Furthermore, we previously evaluated the type and frequency of complications after SMILE and found that the safety of the technique overall is comparable to LASIK. Until now, the longest follow-up studies of SMILE were 1 year, performed in patients with low to moderate myopia. Reinstein et al. reported UDVA of 20/20 or better in 96% of treated eyes and 9% with loss in CDVA of one Snellen line or more after 1 year. Similar results were found by Sekundo et al. with UDVA of 20/20 or better in 88% of the treated eyes and 12% with loss of one Snellen line or more after 1 year. The current study was performed on patients with high myopia and with longer follow-up, but visual outcomes were comparable with UDVA of 20/20 or more in 72% of treated eyes, and 12% with loss of one Snellen line or more after 3 years. CDVA increased from 3 months to 3 years, which may be explained by corneal stromal remodeling and reduction in corneal haze. Furthermore, neural adaptation to corneal aberrations may occur for a longer period, as suggested in earlier studies.

It has been suggested that SMILE would leave the cornea more stable, with less refractive regression compared with flap-based LASIK. TCRP increased from 3 months to 3 years, suggesting a late corneal remodeling with significantly increased CCT years after SMILE occurred. However, when evaluating the change in subjective refractive SE from 3 months to 3 years, there was no significant myopic regression. It may be that the observed change in TCRP is minor and has no influence on the subjective refractive SE. In long-term studies of LASIK, Alió et al. reported a significant increase in corneal power the first year after surgery, but the observed increase in corneal power from 1 to 15 years was not statistically significant. However, Ivarsen and Hjortdal reported a significant increase in corneal power 7 years after LASIK.

HOAs contribute to several postoperative complications, such as glare, halos, reduced contrast sensitivity, and poor night vision. Therefore, attention should be paid to the development in HOAs for a period of time after surgery. Corneal aberrations were evaluated for a pupil diameter of 5 mm, and a decrease in HOAs and spherical aberrations was observed from 3 months to 3 years. This may be due to a long-term corneal remodeling years after SMILE is performed. However, this is in contrast to a study by Sekundo et al. that reported a slight increase in HOAs, spherical aberrations, and coma from 3 months to 1 year after SMILE in 54 eyes. In a previous study of LASIK from Aarhus University Hospital with comparable preoperative characteristics as in this study, there were no significant changes in spherical aberrations, coma, and HOAs from 1 month and 7 years after LASIK. However, the limited number of participants with a 3-year follow-up (n = 15) might be a possible reason why no changes were observed. Agca et al. found no significant differences in HOAs, coma, and spherical aberrations between SMILE and femtosecond lenticule extraction for a 4- and 6-mm pupil diameter. Kamiya et al. did find significantly fewer fourth-order aberrations after femtosecond lenticule extraction than after wavefront-guided LASIK, whereas no significant differences were found in third-order aberrations and total HOAs, evaluated on a 6-mm pupil.

Patients were invited for an additional 3-year examination, which was not a part of the standard postoperative regimen. Selection bias may be present if more patients with visual complaints would accept the additional examination than patients with no postoperative visual complaints.

SMILE seems to be satisfactory in terms of efficacy, predictability, and safety. No myopic regression was observed in subjective refraction, but TCRP increased during time. It may be that the minor change in TCRP has no influence in subjective refraction. HOAs, including spherical aberrations, seem to decrease and patients treated with SMILE might experience less postoperative complications, such as glare, haze, and contrast sensitivity in the long term. However, further long-term studies of SMILE are required to support this theory and the reported long-term visual and refractive outcomes.

AUTHOR CONTRIBUTIONS
Study concept and design (AI, JH); analysis and interpretation of data (IBP, JH); writing the manuscript (IBP); critical revision of the manuscript (AI, JH); administrative, technical, or material support (JH); supervision (JH).

REFERENCES
5. Vestergaard A, Ivarsen AR, Asp S, Hjortdal JØ. Small-incision


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SD = standard deviation; RMS = root mean square; HOAs = higher-order aberrations; D = diopters

*aP < .05.