

Five-year results of Small Incision Lenticule Extraction (ReLEx SMILE)

Marcus Blum,¹ Kathrin Täubig,¹ Christin Gruhn,¹ Walter Sekundo,² Kathleen S Kunert¹

¹Department of Ophthalmology, HELIOS Hospital Erfurt, Erfurt, Germany
²Department of Ophthalmology, Phillips University of Marburg, Marburg, Germany

Correspondence to
 Dr Kathleen S Kunert, Department of Ophthalmology, HELIOS Hospital Erfurt, Nordhäuser Strasse 74, Erfurt 99089, Germany; kathleen.kunert@helios-kliniken.de

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ABSTRACT

Background To evaluate the 5-year results of Refractive Lenticule Extraction (ReLEx) as Small Incision Lenticule Extraction (SMILE) technique for treatment of myopia and myopic astigmatism.

Methods In 2008/2009, the worldwide first 91 eyes were treated using a novel surgical technique (SMILE), where a refractive lenticule of intrastromal corneal tissue is removed through a small incision completely eliminating flap-cutting. 56 out of 91 eyes of the original treatment group volunteered for re-examination 5 years after surgery. Uncorrected distance visual acuity and corrected distance visual acuity after 5 years, objective and manifest refractions as well as evaluation of the interface and corneal surface by slit-lamp examination were documented. Late side effects like corneal scars, corneal ectasia, persistent dry eye symptoms or cataract were documented.

Results 5 years postoperatively, no significant change to the 6-month data was found. Spherical equivalent was -0.375 D and therefore close to target refraction (emmetropia). 32 of the 56 eyes had gained 1–2 Snellen lines. There was no loss of 2 or more lines over the 5-year period. Regression in the long term was 0.48 D.

Conclusions This first long-term study demonstrates SMILE to be an effective, stable and safe procedure for treatment of myopia and myopic astigmatism.

Clinical trial number DE/CA93/KP/07/001. Post-results.

INTRODUCTION

When femtosecond (fs) laser technology entered the field of refractive surgery a new procedure—which no longer required an excimer laser—was first reported by Sekundo and coworkers in 2008.^{1–3} This new procedure was called ‘Femtosecond Lenticule Extraction (FLEx)’ and still needed the lifting of a flap to remove tissue—the refractive lenticule—from the anterior part of the cornea. However, this technique soon developed further to a minimal invasive surgery.⁴ This minimal invasive approach was called ‘Small Incision Lenticule Extraction (SMILE)’, where the ‘cap’ and the refractive lenticule are created in a one-step procedure using a fs-laser and the lenticule is then removed through a small incision which no longer requires a flap.

Meanwhile, a larger number of peer reviewed publications and positive reports by several other investigators have been published.^{5–7} Continuous improvements in the surgical performance, energy settings and laser technology have reached the point that this procedure has gained acceptance worldwide.^{8–12}

Nevertheless, this new procedure has to prove long-term stability in the correction of the

refractive error. This follow-up study was designed to investigate the long-term results in the very first eyes treated with the SMILE procedure 5 years ago. To the best of our knowledge these are the first long-term results on this topic.

PATIENTS AND METHODS

All patients had been treated in the initial prospective study in 2008/2009 and had met the inclusion and exclusion criteria of this first study.⁴ They received a written invitation for re-evaluation after 5 years on a voluntary basis. An informed consent was obtained from each patient. A total of 60 eyes from 30 patients were recruited and re-evaluated. On average the age was 42 years, the youngest patient being 26 years and the oldest being 61 years old (as the minimum age in the original study was 21 years). In four patients one eye had been treated with the FLEx technique whereas the other eye had been treated with the SMILE technique. The FLEx eyes were excluded, therefore the 5-year results of $n=56$ eyes that had been part of the original study with $n=91$ eyes published in 2011 are reported herein.⁴

The Refractive Lenticule Extraction (ReLEx) SMILE procedure

The SMILE treatment in eyes of this follow-up study was described in detail in our first publication.⁴

The following parameters were obtained at the 5-year re-evaluation visit:

- ▶ Uncorrected distance visual acuity (UDVA) and corrected distance visual acuity (CDVA) using different ETDRS charts at each visit and for each eye
- ▶ Objective and manifest refraction
- ▶ Corneal topography (Atlas, CZM, Jena, Germany)
- ▶ Wave front measurements (WASCA, CZM, Jena, Germany)
- ▶ Pachymetry (AC Master, CZM, Jena, Germany)
- ▶ Goldmann’s applanation tonometry
- ▶ Slit lamp examination with inspection of the interface and corneal surface to record long-term side effects (eg, corneal scars, corneal ectasia, persistent dry eye symptoms, cataract formation) were recorded and other non-related ocular pathology excluded (glaucoma or macular disorders).

All measured data was collected on standardised study spreadsheets for descriptive statistics of all eyes. Values are presented as means and SD. Statistical analysis was performed using Excel for Windows 8.1 (Microsoft, USA). The Wilcoxon

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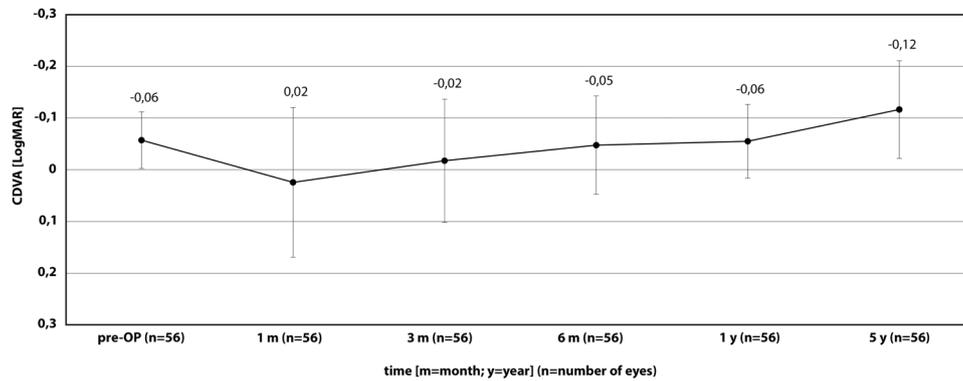


Figure 1 Corrected distance visual acuity (CDVA) 5 years after Small Incision Lenticule Extraction (SMILE) technique for myopia. Visual acuity is presented in logMAR (transverse axis). Examinations took place at 1 month, 3 months, 6 months and 1 year and 5 years after surgery (longitudinal axis).

signed rank test was used to compare data and p values less than 0.05 were considered statistically significant. The safety index (ratio between CDVA postoperatively and CDVA preoperatively) as well as the efficacy index (ratio between UDVA postoperatively and CDVA preoperatively) were performed.

RESULTS

Safety

The 5-year visit was accomplished by n=56 eyes. As shown in [figure 1](#), CDVA in logMar showed an improvement over time from 0.02 at 1 month after surgery to -0.12 after 5 years. However, statistical testing did not prove any significant changes ($p=0.186$). In 32 (58%) out of 56 eyes a gain of 1 or 2 lines was found after 5 years compared with the 6 months data. The change of lines of CDVA is shown in [figure 2](#). The safety index at the final follow-up was 1.2.

Efficacy

The efficacy of the 56 eyes is shown in [figure 3](#). UCVA remained stable during the 5 year postoperative period. The efficacy index at the 5 year follow-up was 0.9.

Predictability

In the eyes treated with this new refractive procedure the target was set at plano. Spherical equivalent (SEQ) after 5 years was -0.375 D. From target refraction, 48.2% of eyes were within 0.5 D, 78.6% were within 1.0 D. The data of the attempted versus achieved correction of n=56 eyes after 5 years is given in [figure 4](#).

Stability

The 5-year refraction in the group was -0.375 D. This corresponds to a regression of 0.48 D within the 5-year period (see [figure 5](#), solid line). We analysed individual eyes in more detail and found seven eyes being the main cause for this regression. One eye had a cap perforation with a resulting corneal scar that caused a central steepening of the cornea with myopisation. In six other eyes the regression might have been the result of long-term growth of the axial length (AL), as patients were 24 years and 25 years of age at time of surgery. If these seven eyes were excluded from the study n=49 eyes remained with a regression of 0.278 D (SEQ=-0.163 D) (see [figure 5](#), dotted line).

Two eyes developed cataract with presbyopia and increased hyperopia resulting in an overcorrection instead.

Side effects

All patients were routinely treated for dry eye symptoms within the first 3 months after SMILE—none of them needed further treatment after 3 months or reported any associated side effects at the 5 year follow-up. Furthermore, no signs of corneal ectasia, cataract formation or other ocular pathology were found in any of the eyes.

DISCUSSION

In this follow-up investigation of the initial prospective cohort of 56 eyes the results of the very first eyes treated with SMILE for myopia in 2008/2009 using the old 200 kHz VisuMax are presented. As the SMILE procedure was a novel surgical approach 5 years ago, the change in CDVA still represents the

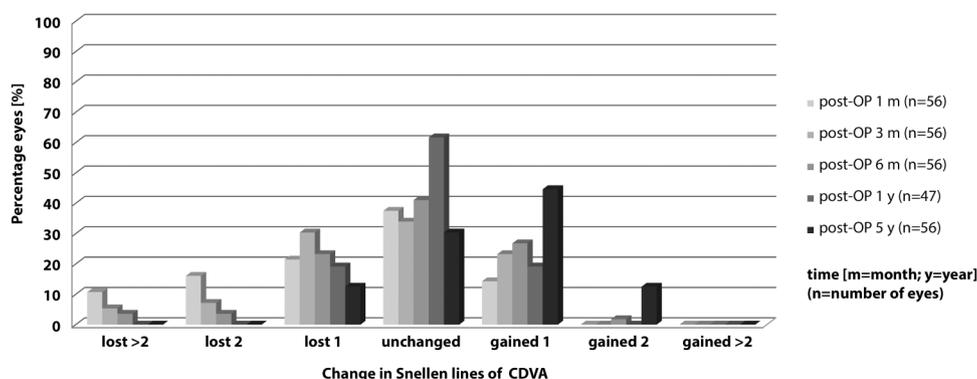


Figure 2 Safety of Small Incision Lenticule Extraction technique (SMILE) procedure shown as a loss/gain in Snellen lines of the corrected distance visual acuity (CDVA).

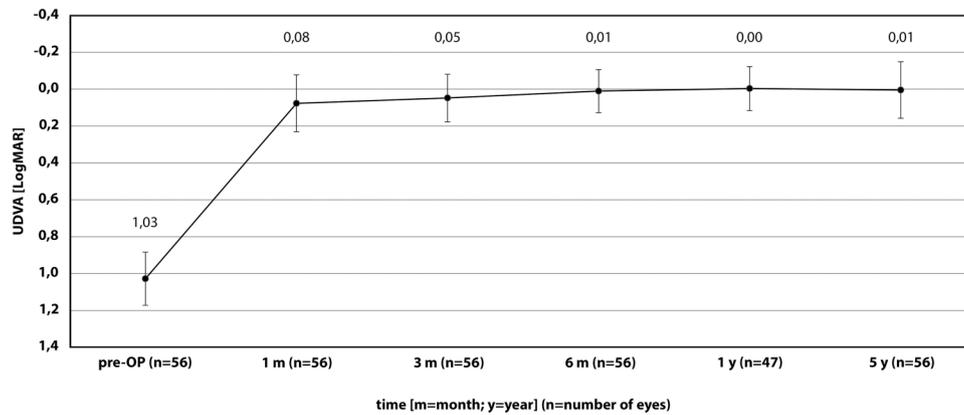


Figure 3 Uncorrected distance visual acuity (UDVA) 5 years after Small Incision Lenticule Extraction technique (SMILE) for myopia. Visual acuity is presented in logMAR (transverse axis). Examinations took place at 1 month, 3 months, 6 months and 1 year and 5 years after surgery (longitudinal axis).

most important value. The long-term safety index 5 years after surgery was excellent. However, comparison with other studies is not possible, since this is the first study presenting data over such a long period.

Besides safety of the surgery itself, two parameters are of prime importance for the patients: predictability and long-term stability. In LASIK approximately 50% of eyes remain within ± 1 D of the intended correction after 6–10 years largely correlated to the degree of correction.^{13–15} As a matter of fact, in the very first ReLEx flex eyes in 2006 where the flap was still present, predictability was not as good as with the LASIK procedure at the same time.^{2,3}

The efficacy index for this first SMILE cohort was 0.9 after 5 years being similar to, but not quite as good as expected in, LASIK today. Meanwhile advancements in laser technology, energy settings and laser scan patterns translated into better outcomes after SMILE. A 500 kHz VisuMax fs-laser is currently in use and less tissue damage and inflammation were reported in the animal studies supporting clinical impressions.¹⁰ In the last generation of studies SMILE delivers refractive outcomes superior to the first results with the 2008/2009 technology presented here and comparable with LASIK outcomes.^{7,16} Therefore, predictability is no longer a major concern.

However, once the nomograms are established, stability of the achieved correction seems to be one of the major advantages of

the ReLEx procedure. The increased biomechanical stability due to the absence of a flap and the diminished inflammatory response seem to be in part responsible for the long-term stability.

In LASIK a mean regression of 0.63–0.97 D is reported after 6–7 years.^{14,15} Other reports of PRK and LASIK even go as long as 15–18 years.^{17,18} In PRK a significant increase in SEQ is found specifically in patients younger than 40 years at time of surgery.¹⁷ In LASIK a regression rate of -0.12 ± 0.15 D per year with stabilisation from 2 years to 5 years in moderate myopia was reported.¹⁸ The data presented in this study 5 years after SMILE with a mean of -0.48 D regression over this period of time are at least as good as the data of other keratorefractive procedures. Moreover, our detailed analysis of the regression in the individual eyes revealed one intraoperative complication and six eyes of three younger individuals at the time of surgery. The latter aspect implies that the regression observed herein is likely due to an increase of the AL as a consequence of eye globe growth rather than a true regression at the corneal level. Nevertheless, as we did not measure the AL preoperatively, there is no hard proof for this assumption.

Similar to patients treated with LASIK, all FLEx and SMILE patients were treated for dry eye symptoms within the first 3 months after the procedure. No further treatment was required thereafter in the group presented here as well as in the

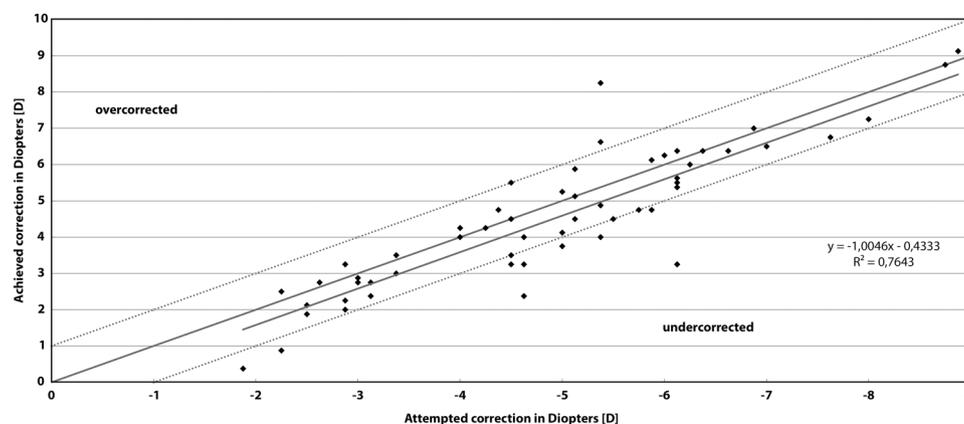


Figure 4 Attempted versus achieved refraction in dioptres 5 years after Small Incision Lenticule Extraction technique (SMILE) surgery. Please note that the dotted line is ± 1 D.

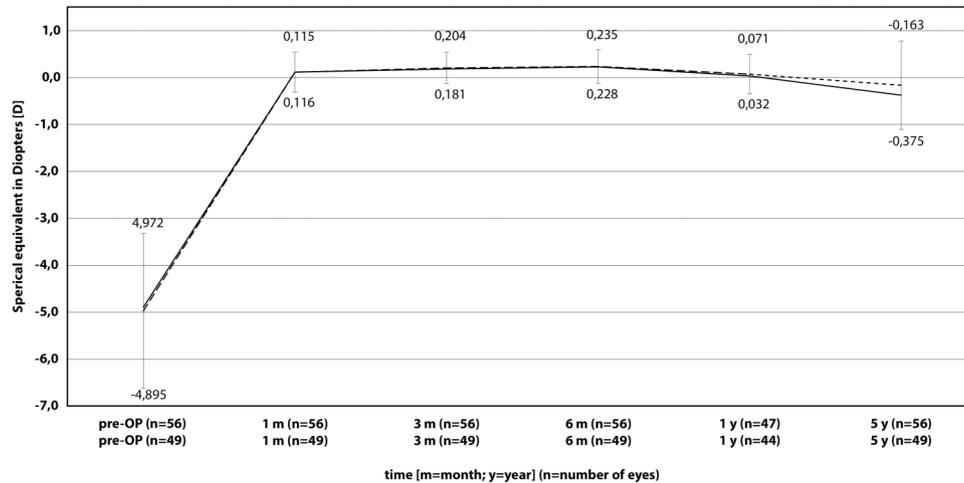


Figure 5 Stability of refractive outcome over the 5 year follow-up period (n=56)—solid line; excluding one eye with corneal scar and six eyes of younger patients with increase in axial length (n=49)—dotted line.

patients with FLEx.¹⁹ This is well in line with published data on corneal sensitivity: postoperative corneal sensitivity was less altered after SMILE surgery compared with fs-LASIK.^{11 20}

Furthermore, in LASIK postoperative flap-related complications can be sight-threatening and excessive photoablation might result in keratectasia. Clinical data as well theoretical models show less biomechanical effects on the cornea and the technique has the potential to leave the anterior stroma more stable.^{21 22} These late side effects do not seem to be a major problem and one of the advantages of the SMILE procedure might be the treatment of higher amounts of refractive error.

Another important and reassuring finding of this study is a continuing improvement of CDVA. Indeed, despite the early 200 kHz technology of the prototype laser used in our investigation, the CDVA was equal to the preoperative CDVA after 1 year and continued to improve over the 5 year follow-up period exceeding the preoperative levels.

In summary these first long-term outcomes of SMILE produced results that were stable and without any late complications. These long-term data might elevate remaining concerns among surgeons in terms of stability and late complications of this new treatment modality.

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Competing interests MB and WS are members of the Scientific Advisory Board of Carl Zeiss Meditec AG. Presented in part at the 112th meeting of the DOG in Berlin, 28th September 2014.

Ethics approval Ethics Committee of the Chamber of Physicians of Thuringia, Germany.

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