ASIK is a widely accepted method for correcting the refractive error, as evidenced by the number of publications in the peer-reviewed literature.\textsuperscript{1,2} We previously reported, in agreement with many others, on the safety and accuracy of flap making with mechanical keratomes for correction of myopia and myopic astigmatism\textsuperscript{3} and hyperopia.\textsuperscript{4}

In recent years, bladeless LASIK using a femtosecond laser for lamellar flap creation as an alternative option to the mechanical microkeratome has been studied.\textsuperscript{5,6} Greater predictability of flap depth and higher precision in planar flap thickness creation in long-term follow-up have already been reported.\textsuperscript{7-13} Meanwhile, current excimer laser platforms for LASIK have evolved to offer significantly more accurate centration, eye tracking, and cornea customization, which seems to increase the overall safety and efficacy of the procedure.\textsuperscript{14-17}

Small incision lenticule extraction (SMILE) is a new method of intrastromal keratomileusis that involves the creation of an intrastromal lenticule between two photodisruption planes that is mechanically removed through a small corneal incision tunnel without the use of an excimer laser. It was clinically introduced in 2006,\textsuperscript{18-24} and has recently received approval from the U.S. Food and Drug Administration for refractive correction of myopia and myopic astigmatism. This single laser “flapless” refractive procedure seems to be a viable alternative for refractive correction because numerous recent studies validate its safety and efficacy, even when compared to LASIK. This prospective, randomized study was designed to compare the safety and efficacy of topography-guided femtosecond laser–assisted LASIK to SMILE in the contralateral eye.
PATIENTS AND METHODS

This prospective, randomized clinical study received approval from the Ethics Committee of our institution and adhered to the tenets of the Declaration of Helsinki. Informed consent was provided and documented in writing from each patient prior to the time of the intervention. The study was conducted on patients in our clinical practice, during scheduled preoperative and postoperative procedure visits and unscheduled visits when necessary. The inclusion criteria were: age between 18 and 65 years, no previous ocular surgery, documented refractive stability for at least 3 years, and discontinuation of contact lens use for at least 2 weeks. Prior to intervention, a complete preoperative ophthalmologic evaluation ensured there was no current or past ocular pathology other than refractive error. Preoperative myopia was between -3.00 and -10.00 diopters (D), and up to -6.00 D of cylinder refractive error. According to the available and recommended treatment range of the SMILE technique, at that time within the European Union the sum of myopic plus astigmatic absolute numbers was up to -10.00 D. Finally, preoperative CDVA was least 20/30 in 22 patients studied. Exclusion criteria comprised history of corneal dystrophy and/or herpetic eye disease, topographic evidence of keratoconus as evidenced by Placido topography or Scheimpflug-based tomography, epithelial warpage from contact lens use, corneal scarring, glaucoma, severe dry eye, and collagen vascular disease.

Twenty-two patients with bilateral myopia or myopic astigmatism were enrolled in this study. One eye of each patient was randomly assigned (coin flip) to the topography-guided femtosecond laser–assisted LASIK group (LASIK group) and the fellow eye was then assigned to the SMILE group. Each patient was not aware which eye received LASIK or SMILE until the completion of the study. All surgeries were performed by the same surgeon (AJK).

The Alcon WaveLight Refractive Suite, specifically the FS200 femtosecond and EX500 excimer lasers (Alcon Laboratories, Inc., Fort Worth, TX), was employed for all femtosecond laser-assisted LASIK procedures. All cases had planned flap thickness of 110 µm and planned flap diameter of 8.5 mm. The 110-µm flap thickness was chosen in all LASIK cases because this has been optimal in our practice and has been used as the clinical standard during the past 10 years. Topographic data were imported by the Vario topolyzer (WaveLight, Erlagen, Germany) and corneal pachymetric data were imported by the Oculyzer II (WaveLight), a Scheimpflug-based tomography device associated with the Re refractive Suite, a diagnostic device that is essentially based on the Pentacam HD (Oculus Optikgeräte GmbH, Wetzlar, Germany). The cylindrical refraction was adjusted by the surgeon to match the amount and axis of the topographically measured cylinder and appropriate sphere adjustments were made to keep the same spherical equivalent (topography modified refraction).

All SMILE procedures were performed prior to the topography-guided LASIK procedure on a same-day basis using the VisuMax femtosecond laser (Carl Zeiss Meditec, Jena, Germany). The reason for this was the potential need for an excimer ablation in case the SMILE procedure ran into intraoperative complications that allowed conversion to LASIK (by converting the actual SMILE cap into a LASIK flap, and using an excimer laser to correct the refractive error). The intended thickness of the cap tissue was 130 µm because this was the optimal recommended by the Zeiss surgical application consultant and planned lenticule diameter was 6.5 mm.

All eyes were evaluated preoperatively and on each postoperative visit for corrected distance visual acuity (CDVA), uncorrected distance visual acuity (UDVA), and manifest spherical equivalent before and after cycloplegia with two drops of 1% tropicamide topical solution, autorefraction/keratometry with the Speedy-i-K model (Righton, Tokyo, Japan), slit-lamp biomicroscopy, dilated fundus examination including retinal periphery, and applanation tonometry. Additionally, several tests were completed at each preoperative and postoperative visit: Vario Placido-based topography, described above; Scheimpflug corneal tomography with the Oculyzer II, noted above; anterior segment optical coherence tomography (Avanti; Optovue, Fremont, CA); Objective Scatter Index using the HD analyzer model OQAS-HDA (Visiometrics, Barcelona, Spain); contrast sensitivity using the Functional Vision Analyzer (Stereo Optical Company, Inc., Chicago, IL) with the Eye View functional vision analysis software (Vision Sciences Research Corporation, Walnut Creek, CA); photopic, mesopic, and scotopic binocular pupillometry with the Pupillometer P3000 SA (Procyon Instruments limited, London, United Kingdom); and wavefront analysis with the Allegro II Tsern-type Wavefront analyzer (WaveLight), a device also part of the Refractive Suite operative network. Preoperative evaluations included wavefront analysis, pupillometry, keratometry and contrast sensitivity (Stereo Vision, Chicago, IL), and Objective Scatter Index (HD analyzer device; Visiometrics). Postoperative examinations included manifest and dilated refraction, slit-lamp microscopy, tonometry, and keratometry by means of corneal topography and tomography assessment.

Postoperative follow-up examinations were conducted at 1 day, 1 week, 1 month, and 3 months. All patients were postoperatively treated with moxifloxacin (Vigamox; Alcon Laboratories, Inc.) and 0.1%...
dexamethasone/chloramphenicol solution (Dispersa-dron C; Alcon Laboratories, Inc.) four times a day for both eye drops for 1 week in each eye and preservative-free artificial tears as needed. The frequency of artificial tear use was not monitored in this study, nor was corneal sensitivity.

All possible adverse effects or patient complaints were closely monitored. Preoperative refractive measurements were masked by default because eye allocation had not been held at the time. At each follow-up visit, the outcome assessors (eg, optometrists and research assistants) and the patients themselves remained masked to the assigned treatment to improve objectivity and minimize potential bias.

**RESULTS**

Of the 22 patients enrolled in this study, 13 were women and 9 men. The patient ages at the time of surgery ranged from 21 to 45 years (average: 29.5 years). Preoperative patient demographics are listed in Table 1.

Most patients responded that they found SMILE (95.4%; 21 of 22) more comfortable than LASIK (4.6%, 1 of 22). Preoperatively, UDVA was 0.02 ± 0.07 (range: 0.01 to 0.25) (there was no statistical difference between the preoperative UDVA for the LASIK group compared to the SMILE group), manifest spherical equivalent range was -3.125 to -10.00 D, and mean cylinder was -1.12 ± 0.99 D (range: 0.00 to -4.25 D).

**UDVA Outcomes and Stability**

At 3 months of follow-up, 86.4% of the LASIK group had UDVA of 20/20 (1.0 decimal) and 59.1% had UDVA of 20/16. In the SMILE group, 68.2% of the eyes had UDVA of 20/20 and 31.8% had UDVA of 20/16. The differences between the two groups at the 20/20 and the 20/16 levels were statistically significant ($P < .002$ for both comparisons) (Figure 1).
Effect of cDVA

The gain–loss data (preoperative CDVA versus postoperative UDVA, Figure 2) indicated that 9.1% of the eyes in the LASIK group and 4.5% of the eyes in the SMILE group gained two lines. These data were also statistically significant in comparison ($P < .02$).

Refractive Predictability and Accuracy

The residual manifest spherical equivalent between 0.00 and $+0.50$ D was achieved in 95.5% of the eyes in the LASIK group compared to 77.3% in the SMILE group ($P < .002$). Residual manifest refraction cylinder of less than $0.25$ D representing the accuracy of cylinder correction was achieved in 81.8% of the eyes in the LASIK group and 50% of the eyes in the SMILE group ($P < .001$) (Figures 4-5 and Figure A, available in the online version of this article).

Objective Scatter Index and Low Contrast Sensitivity Measurements

The average postoperative Objective Scatter Index (Figure B, available in the online version of this article) was 1.35 in the LASIK group (statistically better than preoperative mean value) and 1.42 in the SMILE group (not statistically different to preoperative values, but also not worse).

The average low contrast sensitivity at 6 cycles/degree postoperatively was in $7.2 \pm 1.01$ in the LASIK group, which constitutes an improvement in comparison to the preoperative measurements, and $6.20 \pm 1.52$ in the SMILE group (not statistically significantly different to preoperative measurements, but also not reduced at all). Figure C (available in the online version of this article) demonstrates the 1-month and 3-month data.
DISCUSSION

Both topography-guided LASIK and SMILE performed in contralateral eyes exhibited adequate stability and efficacy in terms of myopia and myopic astigmatic correction evaluated through the 3-month postoperative period. However, virtually all parameters studied rendered a statistical significance in favor of the topography-guided LASIK group.

The reason for this statistical difference of the topography-guided LASIK procedure’s efficacy should probably be attributed to its topography customization with additional centration and cyclorotation intraoperative compensation by the excimer laser. When comparing this well-established technique to an evolving procedure such as the current form of SMILE, in which centration is manually held by the surgeon, and where no tracking and/or cyclorotation adjustment is currently offered by the only femtosecond laser platform currently able to offer this procedure, these data should probably be anticipated. Admittedly initial studies report SMILE efficacy comparable to standard (wavefront-optimized) LASIK showing essentially “equal” postoperative results.\textsuperscript{15-22} Investigators recently reported comparable visual outcomes when comparing wavefront-optimized to topography-guided profiles in a contralateral eye study.\textsuperscript{26} However, this study did did not use topography-guided modification (TMR) of the clinical refraction in the respective treatments, something that was the backbone of the refractions used in our study herein and may explain the difference in outcomes.\textsuperscript{25}

To limit possible intersubject bias such as different healing properties, environmental, psychological, and compliance issues, we decided to use a contralateral eye study protocol.
We theorize that this treatment adjustment pre-emptively bypasses the bias of lenticular astigmatism, which is probably an issue in young myopic eyes and may compensate for some amount of corneal astigmatism and corneal coma generated by angle kappa. This theoretical lenticular astigmatism appears to be the factor that distorts the objective cylindrical refractive data, resulting in wavefront refractive data similar to the subjective refraction, and which seems to subside within days or months at the latest following the refractive surgery intervention.27 This concept has been adopted in modern refractive cataract surgery, with experience that the postoperative cylindrical refraction will depend mainly on the corneal astigmatism, but it is yet to be established in laser vision correction techniques applied on the cornea. The data provided by this contralateral eye study are compelling enough to encourage further study of this novel principle, which may ultimately increase our accuracy in refractions used for laser vision correction.

SMILE has undoubtedly constituted a promising method in our early clinical experience and possible future technological evolution enabling cyclorotation tracking and adjustment may offer improvement in refractive and quality of vision results. Additionally, possible future topographic data customization of SMILE-like procedures may also improve visual outcomes.

CONCLUSIONS

Topography-guided LASIK appears to offer improved outcomes in all parameters studied herein compared to the early clinical practice of SMILE for myopia and myopic astigmatism correction. The difference noted between the two techniques is likely to derive from the customization topography-guided excimer platform, offering automatic eye tracking with active centration control and cyclorotation compensation, aspects that may decisively affect refractive and visual performance outcomes.

AUTHOR CONTRIBUTIONS

Study concept and design (AJK); data collection (AJK); analysis and interpretation of data (AJK); writing the manuscript (AJK); critical revision of the manuscript (AJK); statistical expertise (AJK); administrative, technical, or material support (AJK); supervision (AJK)

REFERENCES


Figure A. Time course of manifest spherical equivalent refraction (SEQ) after (A) topography-guided LASIK and (B) small incision lenticule extraction (SMILE).

Figure B. Objective Scatter index (OSI) boxplots showing topography-guided LASIK versus small incision lenticule extraction (SMILE): the first boxplot represents the average for all, the second represents SMILE at 1 month, the third represents the LASIK at 1 month, the fourth the SMILE at 3 months and the fifth the LASIK at 3 months, respectively.

Figure C. Contrast sensitivity for postoperative month 1. The blue line represents the preoperative average for all, the red line the average small incision lenticule extraction (SMILE) data at 1 month, in all special frequencies, and the green line the respective topography-guided LASIK data at 1 month.