Femtosecond Lenticule Extraction (FLEX): Clinical Results, Interface Evaluation, and Intraocular Pressure Variation

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PURPOSE. To characterize the clinical profile of femtosecond lenticule extraction (FLEX) correlated with ultrastructural analysis of the corneal interface and in vivo real-time intraocular pressure (IOP).

METHODS. Prospective clinical case series with experimental studies; consecutive patients underwent FLEX at a single tertiary center over 10 months with posturgical follow-up of 3 months. The patients were divided into three groups according to spherical equivalence (SE) (A, < −5.0 diopters [D]; B, ≅ −5.0 D and < −9.0 D; and C, ≅ −9.0 D). Twelve human cadaveric eyes analyzed using scanning electron microscopy after receiving FLEX; 40 rabbit eyes received FLEX with in vivo IOP measurements. The main outcome measures were refractive outcomes from study subjects; with corneal interface and IOP in experimental studies.

RESULTS. Thirty-three subjects (22 females, 66.7%) underwent FLEX in both eyes (66 eyes). Mean age was 32 years (range, 21 to 46 years). Preoperative mean SE was −5.77 ± 2.04 D with astigmatism of −1.03 ± 0.72 D. There was a slight hyperopic shift (mean SE 0.14 ± 0.53 D); 94% achieved uncorrected visual acuity ≥20/25 3 months postoperatively. Refractive stability was achieved within 1 month (P < 0.001). Ultrastructurally, the smoothness of the corneal interface was independent of ablation depth (mean irregularity scores A, B, C = 8.8 ± 0.6, 10.3 ± 0.4, 8.7 ± 0.6, respectively; P = 0.88). The increase in IOP during FLEX was similar to that in femtosecond (FS)-LASIK, albeit a two-fold duration of raised IOP in FLEX (P < 0.001).

CONCLUSIONS. These results suggest that FLEX is predictable and effective in treating myopia and myopic astigmatism. Experimental studies support the early clinical results and safety of this procedure. (Invest Ophthalmol Vis Sci. 2012;53:1414–1421) DOI:10.1167/iovs.11-8808

The femtosecond (FS) laser is a near-infrared neodymium-doped yttrium aluminum garnet (ND:YAG) laser that photodisrupts the cornea with surgical precision through plasma cleavage of stromal lamellae.1 The first commercial ophthalmic FS laser was introduced into the market in 2001 for laser in situ keratomileusis (LASIK) flaps. Since then, significant improvements in laser energy profiles, spatial resolution, and faster laser speeds have occurred.2 FS lasers have thus made a significant impact on refractive surgery by enabling nonmechanical creation of a corneal flap during LASIK. The FS laser offers several advantages over manual microkeratomes including increased precision, reduced incidence of flap complications, and the ability to cut thinner flaps without the risk of buttonhole formation.3,4 Moreover, newer generation FS lasers have reduced problems such as transient light-sensitivity syndrome and interference by cavitation bubbles.5,6

In its current form, ‘bladeless’ LASIK requires the use of 2 lasers: the FS laser for flap creation and an excimer laser for ablative reshaping of the cornea. In 2006, a new FS laser-based vision correction method for myopic and myopic astigmatic correction was introduced using the VisuMax femtosecond system (Carl Zeiss Meditec, Jena, Germany). This method was initially introduced as femtosecond lenticule extraction (FLEX),7 and further developed into a small incision lenticule extraction (SMILE).8,9 Recently, these procedures have been renamed under the overall terminology as refractive lenticule extraction (ReLEx). In ReLEx, the FS laser cuts an intrastromal lenticule corresponding to the patients’ refractive correction, which is removed through a surface incision of varying size depending on whether the FLEX or SMILE procedure is being performed (specific techniques are discussed in detail in the Methods).10 In FLEX, the laser creates a flap (similar to LASIK), which is reflected, allowing lenticule removal. SMILE, a ‘flapless’ surgery, allows lenticule removal through a small 2 to 4 mm incision. FLEX offers the potential benefits of a reduced likelihood of flap-related complications and less compromise on biomechanical strength.9

Few studies are available to validate the outcome of the procedure, which has obtained CE Mark approval in 2009 but yet to be approved by the United States Food and Drug Administration.7-10 Initial clinical results have been promising, where postoperative refractive outcomes were comparable to standard LASIK with few complications.3,11,12 However, more studies are needed to assess the safety and efficacy of this new surgical procedure. Thus, we conducted a prospective clinical study of patients treated for myopia and myopic astigmatism using FLEX. In addition, we evaluated FLEX with respect to ultrastructural analysis of the flap and stromal bed interfaces and changes in vivo of real-time intraocular pressure (IOP) to further study the safety of this procedure.
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### Materials and Methods

**A Prospective Clinical Study**

We conducted a prospective, noncomparative clinical trial of FLEX at the Singapore National Eye Centre (SNEC) over a 10 month period in 2010. This study followed the principles of the Declaration of Helsinki, with ethics approval obtained from the SingHealth Institutional Review Board. Inclusion criteria for the study were as follows: spherical myopia between $-1.00$ diopters (D) and $-9.00$ D and myopic astigmatism less than $-3.00$ D; minimum age of 21 years, corneal thickness $>500 \mu m$ with calculated residual stromal bed after treatment $>300 \mu m$; stable refractive error for 12 months before surgery; normal peripheral retina or after prophylactic treatment with photocoagulation; with no previous ocular surgery, corneal diseases, glaucoma, or history of ocular trauma. Exclusion criteria were keratoconus or forme fruste keratoconus diagnosed on corneal topography; and active ocular or systemic diseases likely to affect corneal wound healing.

Preoperative evaluations with a topographer (Orbscan II; Bausch & Lomb, Orhtek Inc., Salt Lake City, UT) and ultrasound pachymetry (AC Master; Carl Zeiss Meditec AG) were performed to exclude forme fruste keratoconus and other topographic abnormalities. After FLEX, all patients underwent postoperative examinations at 1 day, 1 week, 1 month, and 3 months after the initial procedure. We evaluated both uncorrected and best-corrected visual acuity (UCVA and BCVA) using a standard Snellen acuity chart at 6 m; manifest refraction, slit-lamp biomicroscopy, fundoscopy, and cycloplegic refraction. Ocular wavefront analysis was performed pre- and postoperatively at 3 months using an aberrometer system (Technolas Zywave with Zywave software version 4.45, ZYOPTIX Diagnostic Workstation; Bausch & Lomb). Patients’ vision was evaluated by independent examiners at each follow-up.

We performed FLEX surgery on all patients using a previously described protocol. After application of topical anesthesia, standard sterile draping and insertion of the speculum, the patient’s eye was centered and docked with the curved interface cone before application of suction fixation. The laser treatment started with the posterior surface of the refractive lenticule (spiral in) before the lenticule border was created. A vertical $15 \mu m$ lenticule side cut at the outer border of lamellar dissection was then created to outline the edge of the lenticule. The anterior surface of the refractive lenticule (spiral out) was then formed which extended beyond the posterior lenticule diameter by $0.5 \mathrm{~mm}$ to form the anterior flap, followed by a surface rim cut. We used the following FS laser parameters: $120 \mu m$ flap thickness, $7.5 \mathrm{~mm}$ flap diameter, $6.5 \mathrm{~mm}$ optical zone of lenticule, $145 \mathrm{nJ}$ of power with side cut angles at $90^\circ$. A superior hinge, $50^\circ$ in cordal length, was made in all cases. The spot distance and tracking spacing were $3/3$ m for the flap, $2.5/2.5$ m for the lenticule side cut, $3/3$ m for the flap side cut. After the suction was released, a spatula (Seibel; Rhein Medical, Heidelberg, Germany) was inserted under the flap near the hinge before the flap was separated and reflected.

### Table 1. Preoperative and Postoperative Refraction

<table>
<thead>
<tr>
<th>Parameters</th>
<th>Mean ± SD</th>
<th>Range</th>
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</thead>
<tbody>
<tr>
<td><strong>Preoperative</strong></td>
<td></td>
<td></td>
</tr>
<tr>
<td>MR SE</td>
<td>$-5.77 \pm 2.04$ D</td>
<td>$-1.38 \text{ D to } -9.75$ D</td>
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<tr>
<td>MR sphere</td>
<td>$-5.28 \pm 2.05$ D</td>
<td>$-0.50 \text{ D to } -9.00$ D</td>
</tr>
<tr>
<td>MR cylinder</td>
<td>$-1.03 \pm 0.72$ D</td>
<td>Up to $-3.00$ D</td>
</tr>
<tr>
<td><strong>Postoperative 1 Month (n = 44 Eyes)</strong></td>
<td></td>
<td></td>
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<tr>
<td>MR SE</td>
<td>$0.19 \pm 0.64$ D</td>
<td>$1.75 \text{ D to } -1.63$ D</td>
</tr>
<tr>
<td>MR sphere</td>
<td>$0.39 \pm 0.57$ D</td>
<td>$2.00 \text{ D to } -0.50$ D</td>
</tr>
<tr>
<td>MR cylinder</td>
<td>$-0.41 \pm 0.45$ D</td>
<td>Up to $-2.25$ D</td>
</tr>
<tr>
<td><strong>Postoperative 3 Months (n = 40 Eyes)</strong></td>
<td></td>
<td></td>
</tr>
<tr>
<td>MR SE</td>
<td>$0.14 \pm 0.53$ D</td>
<td>$1.75 \text{ D to } -1.00$ D</td>
</tr>
<tr>
<td>MR sphere</td>
<td>$0.33 \pm 0.50$ D</td>
<td>$2.00 \text{ D to } -0.25$ D</td>
</tr>
<tr>
<td>MR cylinder</td>
<td>$-0.38 \pm 0.43$ D</td>
<td>Up to $-2.00$ D</td>
</tr>
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MR, manifest refraction.

**Figure 1.** Photomontage of the various stages of the FLEX procedure in a rabbit model showing (A) centerpetal progression of the posterior dissection plane of the lenticule, (B) centerfugal progression of the anterior dissection plane to create the anterior surface of the lenticule, (C) the flap side cut is created circumferentially with a spared area for the hinge, (D) the flap is lifted, and (E) manual extraction of the lenticule using forceps is possible after the posterior surface adhesions are separated after which the flap is repositioned (F).

**Figure 2.** Clinical results: predictability. Scatterplot of the attempted SE refractive change plotted against the achieved SE refractive change at 3 months (44 eyes).
The edge of the refractive lenticule was separated from the stromal bed with a sinsky hook and the posterior border of the lenticule gently separated with the spatula (Seibel; Rhein Medical). The lenticule was then grasped with nontoothed serrated forceps and removed, after which the flap was repositioned. One senior surgeon (DT) performed all surgeries. The postoperative regimen consisted of topical preservative-free dexamethasone and moxifloxacin, each four times a day for 1 week. Subsequently, only the lubricating drops were used up to 3 months as needed.

**In Vivo Real-Time IOP Study**

Forty female New Zealand White rabbits underwent FLEx procedure (40 eyes) and femtosecond flap creation (FS-LASIK) (40 eyes). We obtained approval from the SingHealth Institute Animal Care and Use Committee and all procedures were performed in accordance with the ARVO Statement for the Use of Animals in Ophthalmic and Vision Research. First, baseline IOP was measured using a calibrated tonometer (Tono-pen XL; Reichert Ophthalmic Instruments, Depew, NY). Rabbits were anesthetized with a combination of ketamine and xylazine (ketamine 40 mg/kg; xylazine 20 mg/kg, intramuscularly) and topical anesthesia (amethocaine 2.5%) was used during surgery. In vivo real-time IOP in the rabbit eyes was measured using a previously described and validated technique for each procedure (FLEx and FS-LASIK). The mean difference was calculated by subtracting the baseline IOP from the highest IOP in each phase and deriving the mean value.13

All procedures were performed by J.S.M. and R.I.A. with the 500 kHz VisuMax FS laser (Carl Zeiss Meditec). We performed the FLEx procedure on all rabbits using the technique described in Figure 1. The FLEx FS laser parameters were: 120 μm flap thickness, 7.5 mm flap diameter, 6.5 mm optical zone of lenticule, 145 nJ of power with side cut angles at 90°. The spot distances and tracking spacing were 3/3 μm for

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**Figure 3.** Preoperative (A), 1 week (B), 1 month (C), and 3 months postoperative (D) normalized double-angle minus-cylinder scatterplots.
the lenticule, 2.5/2.5 μm for the lenticule side cut, 3/3 μm for the flap, and 2/2 μm for the flap side cut. A bandage contact lens (Bausch & Lomb) was placed over the flap at the end of the procedure and the eyelid was closed with a temporary tarsorrhaphy using a 6 to 0 silk suture. FS-LASIK was performed according to a previously described protocol.\textsuperscript{13} The laser parameters for the FS-LASIK cuts were 110 μm flap thickness; 7.9 mm flap diameter, 170 nJ power, spot distance and tracking spacing of 4.8 μm/4.8 μm for the flap, and 2 μm/2 μm for side cuts, respectively.

**Ex Vivo Study of FLEX using Scanning Electron Microscopy (SEM)**

Human cadaveric corneas were used to study the ultrastructure of the corneal stromal bed and the posterior surface of the corneal flap. Human eyes stored in corneal storage medium (Optisol; Chiron Ophthalmics, Irvine, CA) were obtained from the Lions Eye Bank (Tampa, FL); mean age, 60 ± 10 years (range, 48 to 74 years); death to tissue harvest time, 1 day; mean death to experiment time, 10 ± 5 days (range, 5 to 17 days). We performed FLEX procedures on 12 human corneoscleral rims (JSM) using the VisuMax as described.\textsuperscript{14} Briefly, the corneoscleral buttons were mounted on an artificial anterior chamber (ACC; Coronet Network Medical Products, Yorkshire, UK) that was attached to an infusion bottle via a three-way tap to maintain physiological pressure. The VisuMax FS laser was programmed as follows: 130 nJ power, flap thickness 120 μm, 7.5 mm flap diameter, and 6.5 mm lenticule diameter, with side cut angles at 90° and a refractive correction of −3.0 to −9.0 D (three treatment groups: A, < −5.0 D; B, ≥ −5.0 D and < −9.0 D; C, ≥ −9.0 D). The spot distance and tracking spacing were as described earlier.

After lenticule extraction the residual stromal bed was immediately fixed overnight in a mixture of cold 2% glutaraldehyde, 2% paraformaldehyde, and 0.1 M sodium cacodylate buffer, pH 7.4 (Electron Microscopy Sciences, Fort Washington, PA) at 4°C. The tissues were then washed in buffer and secondarily fixed in 1% osmium tetroxide (Electron Microscopy Sciences) before being dehydrated, critical point dried, and mounted on SEM stubs. Specimens were sputter coated with 10 nm of gold and examined with a scanning electron microscope (JSM-5600; JEOL, Tokyo, Japan) at 10 kV.

We used an established scoring system to evaluate the surface morphology of the stromal bed and corneal flap.\textsuperscript{14} Essentially, this was based on four criteria to evaluate the surface relief (two points), regularity of the surface structure (three points), extent of surface irregularities (three points), and the position of the irregular area (three points). The total score was 11 points with a higher score indicating a smoother surface, and images were scored at magnification ×18 and ×50. To reduce subjectivity, two independent observers (MA, JSM) graded the images in a masked fashion.

**Statistical Analysis**

Statistical analysis included descriptive statistics. Mean and SD were calculated for continuous variables; while frequency distribution and percentages were used for categorical variables. Comparisons between categorical variables were conducted by Fisher’s exact tests. One-way ANOVA was used for means. We compared the IOP variations and surface irregularity indices from each group using the Student’s t test, and intra- and interclass correlation was used to compare interobserver agreement between graders. Alpha was set at a significance level of 5%. All analyses were performed using statistical software (STATA version 11; StataCorp LP, College Station, TX).

**RESULTS**

**Study Subjects: Refraction and Results at 1 and 3 Months**

We enrolled 22 female (67%) and 11 male patients (33%) that underwent FLEX in both eyes (total of 66 eyes). The mean age was 32 years (range, 21 to 46 years). Preoperative UCVA was 0.05 ± 0.01 with mean spherical equivalent (SE) of −5.77 ± 2.04 D, mean sphere −5.28 ± 2.05 D, and mean myopic astigmatism of −1.03 ± 0.72 D. Postoperative results at 1 and 3 months are described in Table 1.

**Predictability**

Predictability was high at 1 month postoperatively (Fig. 2). At the 3-month follow-up, 81.8% of eyes (36/44 eyes) were within ±0.5 D and 95.5% (42/44 eyes) within ±1.0 D of the attempted refractive correction 3 months postoperatively. There was a slight hyperopic shift in the eyes (mean SE 0.14 ± 0.53 D) at 3 months postoperatively, with mean sphere 0.33 ± 0.50 D. Mean induced myopic astigmatism was −0.38 ± 0.43 D at 3 months (Fig. 3).

**Stability**

On the first few postoperative days, the eyes were undercorrected. The refraction stabilized by the 1-week follow-up. The postoperative refraction appears to be stable within 1 week after surgery, as seen in the plot of the mean refraction (SE) and range of refraction against time (Fig. 4). There was no statistically significant difference in the SE refraction between 1 month and 3 months (P = 0.05, Wilcoxon test).

**Efficacy**

UCVA was ≥20/20 in 46%, 52%, and 65% of eyes at 1 week, 1 month, and 3 months postoperatively. BCVA was ≥20/20 in 88% and 94% of eyes at 1 month and 3 months postoperatively. UCVA was ≥20/25 in 88% and BCVA was ≥20/25 in 100% of eyes at 3 months postoperatively. Eighty-one percent of eyes were within ±0.50 D of intended refraction at 1 week and 85% at 1 month postoperatively, while 95% were within ±1.00 D of intended refractive target at 3 months postoperatively.

**Ocular Wavefront**

We compared aberration data in 50 eyes pre- and postoperatively at 3 months. The mean mesopic pupil diameter was 6.0 ± 0.8 mm. There was a significant increase in the root mean square (RMS) higher order aberrations (HOAs) of 0.26 ± 0.02 preoperatively compared with 0.38 ± 0.02 postoperatively (P < 0.001) (Table 2).

Safety and Complications

At 1 month postoperatively, 82% of eyes did not lose any lines of UCVA; increasing to 97% of eyes at 3 months postoperatively (Fig. 5). At 3-month follow-up, 3% of eyes lost 1 line of BCVA. There were no significant side effects such as diffuse lamellar keratitis, transient light sensitivity syndrome, subconjunctival hemorrhage, interface debris, or corneal ectasia in any of the cases during the period of the study. There was 1 case of suction loss during lenticule cutting where >10% was completed. We restarted and completed the procedure as recommended at the time, and the patient had a UCVA of 20/60 and BCVA of 20/25 with −2.0 D of induced astigmatism at 1 month postoperatively. Thus, this patient underwent subsequent enhancement with LASIK and the patient achieved UCVA of 20/25 on 1 day postoperatively and remained stable at 3 months postoperatively.

Results of Real-Time IOP during FLEx

We successfully measured real-time IOP in 78 eyes of 39 rabbits for both FLEx (n = 40) and FS-LASIK (n = 38) procedures. Incomplete data were obtained from one rabbit due to malfunction of the pressure transducer and was excluded from analysis. There were no significant differences between all baseline calibration IOP measurements with the tonometer (Tono-pen XL; Reichert Ophthalmic Instruments) and our device (8.56 ± 1.8 mm Hg vs. 9.14 ± 1.6 mm Hg; P = 0.190). No complications occurred during intraocular cannulation. We did not observe any procedural or postoperative complications. There was no significant difference between the mean baseline IOP in the rabbit eyes in the FS-LASIK group and the FLEx group (9.05 ± 2.1 mm Hg vs. 8.90 ± 2.4 mm Hg; P = 0.204). There was a significant increase in mean IOP in both FS-LASIK (mean increase in IOP: 26.8 ± 1.2 mm Hg; P < 0.001) and FLEx procedures (mean increase in IOP, 27.2 ± 1.5 mm Hg; P < 0.001) compared with the baseline IOP. However, there was no significant difference in mean increase in IOP between both procedures (P = 0.203); and mean difference between baseline and peak IOP (FS-LASIK 30.0 ± 1.6 mm Hg vs. FLEx 30.2 ± 1.4 mm Hg; P = 0.559).

We also compared real-time in vivo IOP measurements at specific stages of each procedure (Figs. 6A, 6B). We found no significant differences in mean IOP of the eyes undergoing the FLEx or FS-LASIK during the procedure comparing mean IOP for suction on (P = 0.803), cutting (P = 0.487) and suction off (P = 0.433) stages. Overall, the FLEx procedures took significantly longer to perform than the FS-LASIK procedures (mean overall duration of procedure: 46.1 ± 3.5 vs. 25.5 ± 2.7 seconds; P < 0.001), thereby subjecting each eye undergoing FLEX to a longer duration of increased IOP (Fig. 6C).

Ultra-Structural Analysis of FLEx

The human corneal flap beds analyzed with SEM appeared similar for both FS-LASIK (Fig. 7A) and FLEx (Figs. 7B, 7C) treated groups. There were minimal differences observed on high power images of the surfaces of the beds created by FS-LASIK (Fig. 7D) and prelenticule extraction FLEx (Fig. 7E). Cavitation bubbles generated by laser photodisruption in the prelenticule-extracted FLEx group can be easily seen demarcating a circumferential groove on the stromal surface before lenticule extraction (Figs. 7E, 7F). We used a previously described grading system with a maximal score of 11 (smoother) to grade the flap surfaces.14 There was good agreement between the independent, masked observers for each treatment group (intraclass coefficient, 0.8). We found no significant difference between the mean irregularity scores comparing treatment groups A, B, and C of the stromal bed after lenticule extraction (8.8 ± 0.6, 10.3 ± 0.4, and 8.7 ± 0.6, respectively; P = 0.88), which suggests that the smoothness of the stromal bed does not depend on the dioptric power of the lenticule extracted. There was also no significant difference in smoothness of the corneal flaps between all 3 groups (10.8 ± 0.8, 10.6 ± 0.4, and 9.8 ± 0.8, respectively; P = 0.33).
DISCUSSION

The clinical results of this prospective study of FLEX for the correction of myopia and myopic astigmatism reveal results that are comparable, in terms of safety, stability, predictability, as well as efficacy, to that reported in other studies of this technique. The experimental components of this study reveal comparable increase in IOP during FLEx and FS-LASIK using the VisuMax laser, which would be expected—and are considerably lower than reported in other femtosecond lasers and microkeratome LASIK. Eyes undergoing FLEX had almost twice the duration of exposure to suction and increased IOP compared with the eyes that underwent FS-LASIK, but given the relatively low pressures, this is unlikely to have clinical consequences. Finally, an objective grading system of flap and bed surfaces imaged with SEM for both FLEX and FS-LASIK revealed comparably smooth surfaces with both procedures. In the case of the FLEX stromal bed, morphology was independent of the attempted correction and depth of the FS laser ablation.

In FLEX, preparation of the superficial flap relies on a low-pressure (approximately 35 mm Hg) suction cone to stabilize the globe and a curved lens attached to the laser delivery system to grasp the cornea. Sufficient suction must be achieved to fixate the docking cone during the laser firing. The advantage of this FS laser system is that the resultant increase in IOP from the suction is low, as the suction is applied to the edge of the cornea and limbus. This reduces the likelihood of reported complications associated with the sudden increase in IOP during suction.
We found no significant differences in peak IOP increase for both procedures and the IOP level remained stable throughout the FLEX procedure, indicating no instability of the anterior chamber during the lenticule formation. However, eyes that underwent FLEX endured elevated IOP levels for a significantly longer time compared with FS-LASIK ($P < 0.001$). This might not be of significance, given the relatively low suction pressure with the VisuMax laser. However, there is potentially a higher risk of suction loss with the longer duration of the FLEX procedure at this low pressure. Although this occurred in one patient in our series, this has not been a clinically issue in other reported series. We have also previously shown that with the VisuMax laser, suction breaks can be immediately re-treated in the same sitting by reapplication of the interface cone and resuming laser ablation from the start, as the lamellar ablation did not involve the visual axis (Tan D. IOVS 2009;50:ARVO E-Abstract 595).

Scanning electron microscopy analysis demonstrated a few significant observations. First, a smooth corneal bed surface was observed in prelenticule-extracted (anterior lenticule surface) FLEX corneas, which were not discernibly different from those that underwent FS-LASIK. The surface quality of the anterior lenticule surface in our study for both FLEX and FS-LASIK were qualitatively comparable with a similar study by Kunert et al. Second, we observed that the anterior lenticule surface was qualitatively smoother compared with the stromal bed, after the lenticule was removed at all myopic corrections. This rougher surface (mean irregularity scores, range, 8.7 to 10.3) was likely the result of the deeper plane of posterior cut and the trauma from manual removal of the lenticule as it is peeled from the stromal bed, which emphasizes the need for gentle dissection. Third, we compared the smoothness of the stromal beds at different treatment depths (mean depth: A, 189 ± 7.5 μm; B, 205 ± 5.5 μm; C, 225 ± 3.5 μm) after lenticule removal and found that there was no significant, quantitative difference in stromal bed quality between the three refractive groups (mean surface irregularity scores in group A, 8.8 ± 0.6; B, 10.3 ± 0.4; and C, 8.7 ± 0.6; $P = 0.88$). This suggests that the smoothness of the lenticule extracted stromal bed is reliant on careful manual peeling of the lenticule, which was also suggested by a previous study. When we compared the visual recovery in our patients divided into the same myopic corrective treatment groups as our human cadaver eye study, we found no significant differences in percent eyes with UCVA ≥ 20/25 at 1 week between groups (A, 75% vs. B, 73% vs. C, 80%; $P = 0.55$) and 1 month (A, 82% vs. B, 75% vs. C, 87%; $P = 0.55$). As visual outcomes correlate with smooth optical sur-
faces,26 these clinical results taken in consideration with the SEM data suggest that the early visual outcomes for FLEx are independent of attempted correction and treatment depth and more dependent on careful lenticule extraction.

The results of FLEx from our clinical study are promising. UCVA ≥ 20/25 was achieved in 94% of eyes at 3 months postoperatively; and 81.8% were within ±0.5 D while 95.5% were within ±1.0 D of the intended refractive target. Refractive stability in our patients was achieved within 1 month (P < 0.001). In other similar studies on FLEx, 90% (7) and 98.1% (10) of eyes treated were within ±1.0 D, and 40% (7) and 74.8% of eyes were within ±0.5 D of the intended correction respectively. Overall, they showed that 97.1% of patients were satisfied with the visual result (10) and 90% of eyes had a UCVA of 20/40 or better. The progressively improving results with each published study suggest that there is a learning curve and an improvement in FLEx techniques. There have been minor complications previously reported including nonprogressive epithelial ingrowths, tears at the incision edge, epithelial defects, and incomplete incision opening for lenticule extraction.13 In our study, we did not observe any of these complications although one case experienced suction loss during the procedure where >10% of the lenticule cut was completed. In such cases, it was previously recommended to restart the entire procedure. However, we believe that by continuing the ablation this led to induced astigmatism (~2.0 D) due to laser misalignment; it is now recommended to abort the procedure and perform LASIK instead. Current recommendations for suction loss during each stage are now as follows: Stage 1 (lenticule cut <10%): re-start; Stage 2 (lenticule cut >10%): switch to LASIK; Stage 3 (lenticule side cut): repeat lenticule side with decreased size; Stage 4 (flap cut): repeat flap cut; and Stage 5 (flap side cut): repeat flap side cut with decreased size.27

The main limitation of our study is that ideally, the experimental studies such as SEM examination and in vivo IOP measurements should be made in our patients from the clinical study. However, these techniques are invasive and not possible to be performed on our patients. Therefore, we evaluated these parameters using the same technique in both a human cadaveric model and an animal model. We did not compare our SEM results from FLEx to a complete LASIK procedure (i.e., FS flap and excimer laser ablation). There have been several prior publications on this topic and the aim of our study was to examine the comparative effect of different ablations after FLEx.28

In summary, our study presents encouraging visual outcomes in patients that underwent FLEx. Our in vivo animal studies support the early clinical results and safety of this procedure; while in vitro human eye bank cornea revealed that stromal bed irregularity was independent of treatment and ablation depth.

References