Biomechanical changes after keratorefractive lenticule extraction with CLEAR and after femtosecond LASIK, correlated with optical coherence tomography findings

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ABSTRACT

The purpose of this retrospective, comparative, single-eye study was to evaluate the biomechanical changes that occurred after laser myopia correction using keratorefractive lenticule extraction (KLEX) and femtosecond LASIK (FS-LASIK), and to correlate them with stromal changes on anterior segment optical coherence tomography. Corneal biomechanical parameters were measured pre-operatively and one week after surgery using the high-speed Scheimpflug camera CorVis-ST (Oculus Optikgeräte GmbH): stiffness parameter at first applanation (SP-A1), stress-strain index (SSI), inverse integrated radius (IIR), and deformation amplitude ratio at 2 mm (DA ratio-2mm). A total of 79 eyes underwent KLEX (CLEAR, Ziemer Group), while 93 underwent FS-LASIK. After KLEX, the mean residual stromal bed (RSB) was 271.36±17.22 µm, while FS-LASIK resulted in 304.21±21.82 µm (p=0.00). Except for SSI after FS-LASIK (p=0.39), all parameters in both groups changed statistically significantly after surgery (p=0.00). The KLEX group showed significantly higher percentage changes in all parameters. Even in eyes with equal RSB (300±5 µm; 19 eyes post-KLEX, 26 eyes post-FS-LASIK), changes were significantly higher after KLEX (SP-A1: -35.9%; SSI: -6.7%) than after FS-LASIK (SP-A1: -29.6%; SSI: -3.8%) (p=0.02, p=0.00). In KLEX, stromal thickness reduction correlated weakly with SP-A1 reduction (r=0.39) and poorly with SSI reduction (r=0.26). In conclusion, stiffness parameters were significantly worse after KLEX compared to FS-LASIK, even in eyes with similar RSB. These results should be interpreted with caution, as the CorVis-ST may not detect all clinically significant alterations, particularly in the post-KLEX bi-layered cornea.

Key words: Keratorefractive lenticule extraction (KLEX), LASIK, myopia, biomechanics, optical coherence tomography (OCT).
Introduction

Keratorefractive corneal lenticule extraction (recently abbreviated as KLEx)\(^1\) corrects myopia and myopic astigmatism by removing an intrastromal disc of tissue through a small incision, leaving an intact stromal bed and avoiding the formation of a flap.\(^2\) These features have prompted the assumption that KLEx may induce less ocular biomechanical changes compared to LASIK, because the almost intact anterior stroma (cap) would provide a stiffer layer of tissue, forming, together with the residual stroma bed (RSB), the total uncut stroma.\(^3\)

Ocular biomechanics can be assessed by the CorVis-ST (Oculus Optikgeräte GmbH), a high-speed Scheimpflug video camera recording the corneal deformation in response to a puff of air.\(^4\) Despite the theoretical premises, the clinical in vivo studies with the CorVis-ST have shown inconsistent results, indicating greater biomechanical changes after KLEx,\(^5\) after LASIK,\(^6\) or similar changes.\(^7\) It has therefore been postulated that in KLEx, rather than by the total uncut stroma, the corneal stiffness is mostly determined by the RSB.\(^3\) However, RSB was not directly measured, but only calculated on pre-operative Scheimpflug pachymetry and presumed tissue removal based upon laser settings.\(^5-7\)

Anterior segment optical coherence tomography (AS-OCT) has shown excellent repeatability in measuring total corneal thickness, total stromal thickness, and RSB,\(^8,9\) and could be an ideal method to correlate biomechanical changes with stromal alterations.

All the previous studies on KLEx have been done after the SMILE (Carl Zeiss) procedure; newer KLEx platforms have not been assessed on biomechanical grounds. We have therefore evaluated the biomechanical changes occurring after KLEx with the novel CLEAR application (Ziemer Group),\(^10\) comparing it to femto-second LASIK (FS-LASIK) by the most recently implemented stiffness parameters of the CorVis-ST,\(^11,12\) and related them with the stromal modifications on pre- and post-operative AS-OCT.

Materials and Methods

A retrospective, comparative case series study was designed, including consecutive patients undergone KLEx or FS-LASIK in a single institute between February and June 2023. As in a previous study,\(^5\) the treatment was chosen based on the anticipated minimum stromal bed, ≥250 µm for KLEx and ≥290 µm for FS-LASIK. In patients receiving bilateral treatment, a single eye was randomized to be included. The Institutional Review Board provided approval on August 14, 2023. The research followed the tenets of the Declaration of Helsinki; patients provided a signed informed consent. The inclusion criteria for surgery were: i) myopia or compound myopic astigmatism with spherical equivalent (SE) -1 to -12 diopters (D), with at least 18 months of refractive stability, and refractive astigmatism ≤3 D; ii) age: between 25 and 50 years; iii) general health status: absence of collagen vascular disease, no pregnancy; iv) ocular disease: no previous surgery; absence of scars or epithelial irregularities; absence of macular or lens abnormality; no topical treatment for ocular hypertension; absence of dry eye symptoms, non-invasive tear film break-up time ≥10 seconds (MS-39, Costruzione Strumenti Oftalmici), lacrimal fluid osmolarity ≤300 mOsm/l (I-PEN, Imedpharma); v) corneal features on OCT and Placido topography: central pachymetry ≥480 µm; regular posterior elevation, anterior and posterior tangential topography; no signs of ectasia; vi) corrected distance visual acuity (CDVA) ≥20/40 Snellen; vii) minimum follow-up: 6 months from treatment.

The pre-operative assessment consisted of UDVA, CDVA, manifest and cycloplegic refraction (by tropicamide eye drops), undilated and dilated slit-lamp evaluation, Placido corneal topography, OCT tomography with epithelial and stromal thickness evaluation, computer-assisted scotopic pupillography, tonometry, tear function evaluation.

Conical biomechanical parameters were measured with the CorVis-ST between 10.00 and 13.00 a.m.; acquisitions with less than 93.0% data validity were repeated 1 hour later. Extracted biomechanical indices included those appearing in the Vinciguerra report: stiffness parameter at first applanation event (SP-A1), stress-strain index (SSI), inverse integrated radius (IIR), deformation amplitude ratio at 2 mm (DA ratio-2mm).

A spectral domain OCT MS-39 (Costruzione Strumenti Oftalmici, Firenze, Italy), using a S. Led at845nm source and providing an axial resolution >3.6µm (in tissue) was used for corneal sections, topography and tear film evaluation.

Soft contact lens use was interrupted 1 month before examination and surgery; rigid contact lens use was interrupted 3 months before examination and surgery. All
patients were informed about the surgical procedure and provided written consent. Being the biomechanical changes in the long term,\(^5\)\(^-\)\(^7\) and willing to avoid the early effects of edema and the late effects of tissue adhesion, the post-operative measures for the study were taken at day 7 and consisted of OCT tomography with evaluation of total stromal thickness and stromal bed thickness, and CorVis-ST evaluation.

**Surgical technique of KLEx**

Our technique for KLEx with the CLEAR application has been published.\(^10\)

Briefly, full manifest spherical and cylindrical corrections were planned. The optical zone was programmed to be the largest possible between 6 and 7 mm, depending on the amount of residual tissue resulting. The thickness of the cap (cornea anterior to the upper lenticule interface) was set between 135 and 120 µm, privileging the thickest possible cap, to preserve the anterior cornea for retreatments. In all cases, it was programmed to leave a stromal bed (tissue posterior to the lower lenticule interface) \(\geq 250\) µm and a total residual uncut stroma (stromal cap + residual stromal bed) \(\geq 320\) µm. A single supero-temporal 2.5 mm incision was programmed. The suction ring diameter was chosen according to white-to-white diameter measured by OCT: with diameters \(\geq 12\) mm, a 9.5 mm ring was used; with smaller diameters, a 9 mm ring. Femtosecond laser power and velocity were adjusted to obtain a uniform pattern of tiny, non-confluent plasma bubbles.

After topical anesthesia with oxybuprocaine, a drop of unpreserved 0.2% sodium hyaluronate was dripped on the cornea. The Ziemer Z8 handpiece was docked, and the patient was instructed to look into the red fixation light within the handpiece, suction was activated, and centration was accomplished. Once lenticule delineation was completed, the supero-temporal incision was scored and the lenticule separated with a Reinstein Lenticule Separator (Malosa MMSU1297S). Straight, fine-tip tying forceps (Malosa MMSU1414CS) were used to extract the lenticule.

Topical post-operative treatment consisted of dexamethasone 0.1% and netilmicin 0.3% eyedrops 5 times daily for 5 days and then 3 times daily for 5 days, and unpreserved 0.2% sodium hyaluronate as lubricant as needed.

**Technique of FS-LASIK**

Our technique for FS-LASIK has been described.\(^13\)

Briefly, full manifest spherical and cylindrical corrections were planned. The optical zone was programmed to be the largest possible between 6 and 7.5 mm, depending on the amount of residual tissue resulting. The thickness of the flap was set between 90 and 110 µm, calculated by adding 40 µm to the epithelial thickness as measured by OCT. In all cases, it was programmed to leave a stromal bed thick \(\geq 290\). The suction ring diameter was chosen as with KLEx. After topical anesthesia with oxybuprocaine, a drop of unpreserved 0.2% sodium hyaluronate was dripped on the cornea. An LDV femtosecond laser Z8 was used (Ziemer Group) to create the flap. After the completion of the femtosecond phase, the flap was separated and folded in a “taco” fashion with a flap spatula (MMSU1171, Malosa Surgical). After the refractive treatment with a Teneo 317 excimer laser (Bausch+Lomb) in Planoscan mode, the flap was repositioned, interface washed with BSS for 2 seconds through a single-use 25-G cannula, and the flap finally smoothed down with a wet microspunge. A drop of unpreserved netilmicin 0.3% + dexamethasone 0.1% was dripped on the cornea. Netilmicin and dexamethasone were continued 4 times daily for a week.

**Main outcome measures and statistical analysis**

In the CLEAR software calculations, the lenticule thickness is determined by the optical zone and by the sum of spherical and astigmatic correction; this is also true for the amount of tissue ablation with the Teneo 317 excimer laser. We, therefore, used in this study the sum of spherical and astigmatic correction (equaling to the correction on the steepest corneal meridian, or maximum myopic meridian\(^14\)) rather than the SE. Total stromal thickness, stromal bed thickness, SP-A1, SS1, IIR, and DA ratio-2mm were compared pre- and post-operatively and between the 2 treatment groups. Statistical analysis was performed with the SPS software, available online at www.statisticsfordataanalysis.com (accessed 28 November 2023). The mean±standard deviation was used to describe quantitative variables, and a \(p\)-value less than 0.05 is considered statistically significant. Student \(t\)-tests for paired data and a 95% confidence interval (95%CI) were used to compare pre-and post-operative data. Student \(t\)-tests for unpaired data and a 95% confidence interval (95%CI) were used to com-
pare data from lenticule extraction and LASIK. Pearson’s r coefficient was used to verify the correlation between reduction in stromal thickness and changes in SSI and SP-A1, considering values from 0.31 to 0.50 as weak, values from 0.51 to 0.70 as moderate, and values >0.70 as a strong correlation. ¹⁵

Results

A total of 79 eyes of 79 patients undergoing KLEx and 93 eyes of 93 patients undergoing FS-LASIK were finally included.

In the KLEx group, the female/male ratio was 48/31; the right/left eye ratio was 35/44, mean age of 37.2 years. In the FS-LASIK group, the female/male ratio was 51/42; the right/left eye ratio was 54/39, mean age of 38.8 years.

All pre-operative data and the comparison between the 2 groups appear in Table 1; the data in the 2 groups did not significantly differ in any parameter.

After surgery, the mean RSB in the KLEx group was 271.36 µm (SD 17.22); in the FS-LASIK group it was 304.21 µm (SD 21.82); the 2-tailed t-test score for unpaired data was 11.03, with p=0.00 (95% confidence interval for the difference between means: -38.78 to -26.32 µm).

The changes in total stromal thickness and biomechanical parameters are described in Table 2 for the KLEx group and Table 3 for the FS-LASIK group. All data

<table>
<thead>
<tr>
<th>Parameter</th>
<th>KLEX (79 eyes)</th>
<th>FS-LASIK (93 eyes)</th>
<th>p value</th>
<th>95% CI</th>
</tr>
</thead>
<tbody>
<tr>
<td>Maximum myopic meridian (D)</td>
<td>-5.85 (±2.79)</td>
<td>-5.71 (±2.52)</td>
<td>0.73</td>
<td>-0.67 to 0.95</td>
</tr>
<tr>
<td>Stromal pachymetry (µm)</td>
<td>462.88 (±26.01)</td>
<td>469 (±30.13)</td>
<td>0.27</td>
<td>-14.9 to 2.10</td>
</tr>
<tr>
<td>SP-A1</td>
<td>100.89 ±21.90</td>
<td>100.70 ±20.00</td>
<td>0.95</td>
<td>-6.22 to 6.60</td>
</tr>
<tr>
<td>Stress strain index (SSI)</td>
<td>0.84 (±0.13)</td>
<td>0.82 (±0.09)</td>
<td>0.50</td>
<td>-0.01 to 0.05</td>
</tr>
<tr>
<td>DA ratio-2 mm</td>
<td>4.71 (±0.43)</td>
<td>4.78 (±0.44)</td>
<td>0.43</td>
<td>-0.21 to 0.48</td>
</tr>
<tr>
<td>Inverse integrated radius (IIR)</td>
<td>9.71 (±1.18)</td>
<td>9.81 (±1.01)</td>
<td>0.55</td>
<td>-0.44 to 0.24</td>
</tr>
</tbody>
</table>

p value, p value at 2-tailed t-test for unpaired data; 95% CI, 95% confidence interval for the difference between means; SP-A1, stiffness parameter at first applanation event; DA ratio-2 mm, deformation amplitude ratio at 2 mm.

<table>
<thead>
<tr>
<th>Parameter</th>
<th>Value</th>
<th>Mean change</th>
<th>p value</th>
<th>95% CI</th>
</tr>
</thead>
<tbody>
<tr>
<td>Total stromal central pachymetry (µm)</td>
<td>357.09 (±38.56)</td>
<td>-105.19</td>
<td>0.00</td>
<td>-115.45 to -94.93</td>
</tr>
<tr>
<td>SP-A1</td>
<td>64.67 (±16.07)</td>
<td>-36.22</td>
<td>0.00</td>
<td>-42.21 to -30.33</td>
</tr>
<tr>
<td>Stress strain index (SSI)</td>
<td>0.76 (±0.09)</td>
<td>-0.08</td>
<td>0.00</td>
<td>-0.11 to 0.05</td>
</tr>
<tr>
<td>DA ratio-2 mm</td>
<td>6.09 (±0.58)</td>
<td>1.38</td>
<td>0.00</td>
<td>1.22 to 1.54</td>
</tr>
<tr>
<td>Inverse integrated radius (IIR)</td>
<td>12.88 (±1.54)</td>
<td>3.17</td>
<td>0.00</td>
<td>2.74 to 3.60</td>
</tr>
</tbody>
</table>

p value, p value at 2-tailed t-test for unpaired data; 95% CI, 95% confidence interval for the difference between means; SP-A1, stiffness parameter at first applanation event; DA ratio-2 mm, deformation amplitude ratio at 2 mm.

<table>
<thead>
<tr>
<th>Parameter</th>
<th>Value</th>
<th>Mean change</th>
<th>p value</th>
<th>95% CI</th>
</tr>
</thead>
<tbody>
<tr>
<td>Total stromal central pachymetry (µm)</td>
<td>347.25 (±29.27)</td>
<td>-122.05</td>
<td>0.00</td>
<td>-130.59 to -113.51</td>
</tr>
<tr>
<td>SP-A1</td>
<td>68.53 (±16.76)</td>
<td>-32.17</td>
<td>0.00</td>
<td>-37.47 to -26.87</td>
</tr>
<tr>
<td>Stress strain index (SSI)</td>
<td>0.80 (±0.12)</td>
<td>-0.02</td>
<td>0.39</td>
<td>-0.01 to 0.05</td>
</tr>
<tr>
<td>DA ratio-2 mm</td>
<td>5.83 (±0.58)</td>
<td>1.05</td>
<td>0.00</td>
<td>-1.19 to 0.91</td>
</tr>
<tr>
<td>Inverse integrated radius (IIR)</td>
<td>11.96 (±1.54)</td>
<td>2.15</td>
<td>0.00</td>
<td>1.80 to 2.50</td>
</tr>
</tbody>
</table>

p value, p value at t-test for paired data; 95% CI, 95% confidence interval for the difference between means; SP-A1, stiffness parameter at first applanation event; DA ratio-2 mm, deformation amplitude ratio at 2 mm.
showed a statistically significant change, except for the SSI after FS-LASIK.

The percent changes in all biomechanical parameters were in all cases significantly higher in the KLEx group than in the FS-LASIK group (Table 4).

To overcome the factor of different RSB, eyes with RSB 300±5 µm were isolated and compared, with a post-KLEx subgroup (19 eyes) versus a post-FS-LASIK subgroup (26 eyes). In the KLEx subgroup, SP-A1 changed from 99.37 (SD 19.73) to 63.74 (SD 12.83), and SSI changed from 0.90 (SD 0.14) to 0.84 (SD 0.15). In the FS-LASIK subgroup, SP-A1 changed from 100.19 (SD 18.17) to 70.49 (SD 15.48), and SSI changed from 0.80 (SD 0.08) to 0.77 (SD 0.09). The comparison of percent changes is shown in Table 5, with a significant reduction of stiffness in the KLEx group.

In the KLEx group, the reduction in stromal thickness had a weak correlation with the reduction in SP-A1 (\(r\) coefficient 0.39) (Figure 1) and a poor correlation with the reduction in SSI (\(r\) coefficient 0.26) (Figure 2).

Discussion

Main findings

Our data show a significant change in all biomechanical parameters measured with the CorVis-ST after KLEx and after FS-LASIK, except SSI in the latter; the changes were more pronounced after KLEx, including in subgroups with the same RSB. In the KLEx group, a weak correlation was found between a reduction in stromal thickness (equivalent to lenticule thickness) and a reduction in SP-A1.

Table 4. Percent change in biomechanical parameters in 79 eyes undergone keratorefractive lenticule extraction (KLEx) and 93 eyes undergone femtosecond-LASIK (FS-LASIK). Means (± standard deviation).

<table>
<thead>
<tr>
<th>Parameter</th>
<th>KLEx</th>
<th>FS-LASIK</th>
<th>p value</th>
<th>95% CI</th>
</tr>
</thead>
<tbody>
<tr>
<td>SP-A1</td>
<td>-35.9% (±8.8)</td>
<td>-31.9% (±7.4)</td>
<td>0.00</td>
<td>-6.5 to -1.5</td>
</tr>
<tr>
<td>Stress strain index (SSI)</td>
<td>-9.50% (±1.9)</td>
<td>-2.41% (±1.1)</td>
<td>0.00</td>
<td>-7.6 to -6.6</td>
</tr>
<tr>
<td>DA ratio-2 mm</td>
<td>29.3% (±1.8)</td>
<td>22.0% (±2.0)</td>
<td>0.00</td>
<td>6.7 to 7.9</td>
</tr>
<tr>
<td>Inverse integrated radius (IIR)</td>
<td>32.6% (±4.6)</td>
<td>21.9% (±3.9)</td>
<td>0.00</td>
<td>9.4 to 12.0</td>
</tr>
</tbody>
</table>

\(p\) value, \(p\) value at 2-tailed t-test for unpaired data; 95% CI, 95% confidence interval for the difference between means; SP-A1, stiffness parameter at first applanation event; DA ratio-2 mm, deformation amplitude ratio at 2 mm.

Table 5. Percent change in biomechanical parameters in 19 eyes with residual stromal bed 300±5 µm undergone keratorefractive lenticule extraction (KLEx) and 26 eyes undergone femtosecond-LASIK (FS-LASIK). Means (± standard deviation).

<table>
<thead>
<tr>
<th>Parameter</th>
<th>KLEx</th>
<th>FS-LASIK</th>
<th>p value</th>
<th>95% CI</th>
</tr>
</thead>
<tbody>
<tr>
<td>SP-A1</td>
<td>-35.9% (±7.7)</td>
<td>-29.6% (±8.5)</td>
<td>0.02</td>
<td>-11.3 to -1.3</td>
</tr>
<tr>
<td>Stress strain index (SSI)</td>
<td>-6.7% (±2.7)</td>
<td>-3.8% (±1.4)</td>
<td>0.00</td>
<td>-4.3 to -1.5</td>
</tr>
</tbody>
</table>

\(p\) value, \(p\) value at 2-tailed t-test for unpaired data; 95% CI, 95% confidence interval for the difference between means; SP-A1, stiffness parameter at first applanation event.

Discussion

Main findings

Our data show a significant change in all biomechanical parameters measured with the CorVis-ST after KLEx and after FS-LASIK, except SSI in the latter; the changes were more pronounced after KLEx, including in subgroups with the same RSB. In the KLEx group, a weak correlation was found between a reduction in stromal thickness (equivalent to lenticule thickness) and a reduction in SP-A1.
Comparison with previous literature

A balance with previous literature comparing KLEx with FS-LASIK by CorVis-ST must consider the use of different parameters. Among the studies using the recent and more appropriate parameters to assess corneal stiffness,\(^1^1,1^2\) Hashemi et al.,\(^5\) like us, observed a significant alteration in SSI, SP-A1, IIR, and DA ratio-2 mm after both techniques, more evident after KLEx: Xin et al.,\(^6\) He et al.,\(^1^6\) and Abd El-Fattah,\(^1^7\) on the contrary, observed less biomechanical changes after KLEx; Cao et al.,\(^1^8\) finally, found no difference. Studies using older parameters influenced by intraocular pressure and corneal thickness found fewer biomechanical changes after KLEx,\(^1^9\) with a meta-analysis substantially concluding no significant differences.\(^2^0\) It would appear that no definitive conclusion can be based on the published studies.

To explain the higher biomechanical impairment after KLEx, Hashemi et al. postulated that corneal stiffness was mainly determined by the RSB thickness, and that the preserved anterior cornea was not contributing to it, or, at least, that its contribution could not be measured by current parameters because of the 2 layers of tissue experiencing different stress.\(^5\) This concept is supported by a report indicating that a thinner cap provided more stiffness\(^1^9\) and contradicted by another study with opposite results.\(^2^1\) Within the limitations of the CorVis-ST evaluation, our findings in eyes ending with the same RSB indicate that the cap does not improve the stiffness provided by the RSB itself.

The biomechanical changes after laser vision correction have been correlated with the thickness of anticipated RSB,\(^5^,-7\) which was not however directly measured post-operatively. AS-OCT is the most commonly available tool to measure the corneal thickness and the RSB.\(^8^,9\) In our study, the first correlating OCT measures with biomechanical alterations, the changes in total stromal thickness in the KLEx group were only weakly correlated with the reduction in SP-A1. The clinical meaning of these findings is uncertain: it cannot be excluded that, given the profound difference in corneal architecture after the 2 procedures, the CorVis ST may not capture the true alterations subsequently leading to ectasia.

Study limitations

Our study has several limitations. The study is retrospective, and the treatment was not randomized. The optical zone was not uniform all over the series. Parameters were only measured at 1 week; our approach is however justified by previous studies demonstrating non-significant changes over time.\(^5^,-7\)

Conclusions

When measured with the CorVis ST, a high-speed Scheimpflug video camera recording the corneal deformation, the stiffness parameters were significantly more altered after KLEx than after FS-LASIK, even in eyes with the same RSB. The reduction in stromal thickness in KLEx is weakly correlated with the reduction in SP-A1. The clinical meaning of these findings is uncertain: it cannot be excluded that, given the profound difference in corneal architecture after the 2 procedures, the CorVis ST may not capture the true alterations subsequently leading to ectasia.

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Contributions

AL and SVF contributed to the conception, drafting, final approval, and agreement to be accountable for all aspects of the work. GDB and MP contributed to the analysis of data, revising, final approval, and agreement to be accountable for all aspects of the work. CC and AM contributed to the conception, analysis of data, final approval, and agreement to be accountable for all aspects of the work.

Conflict of interest

The authors have no conflicts of interest to declare.

Ethics approval and consent to participate

The study has been granted an exemption from requiring ethics approval by the Institutional Review Board at Siena Eye Laser. Ethical approval is not required for this study in accordance with national guidelines.

Availability of data and materials

All data generated or analyzed during the study are available upon request.

References


