Biological lenticule implantation for correction of hyperopia: an ex-vivo study in human corneas

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Biological Lenticule Implantation - Possibilities

- Precise cutting of stromal lenticules is today possible with the VISUMAX femto-second laser and lenticule implantation may enable:

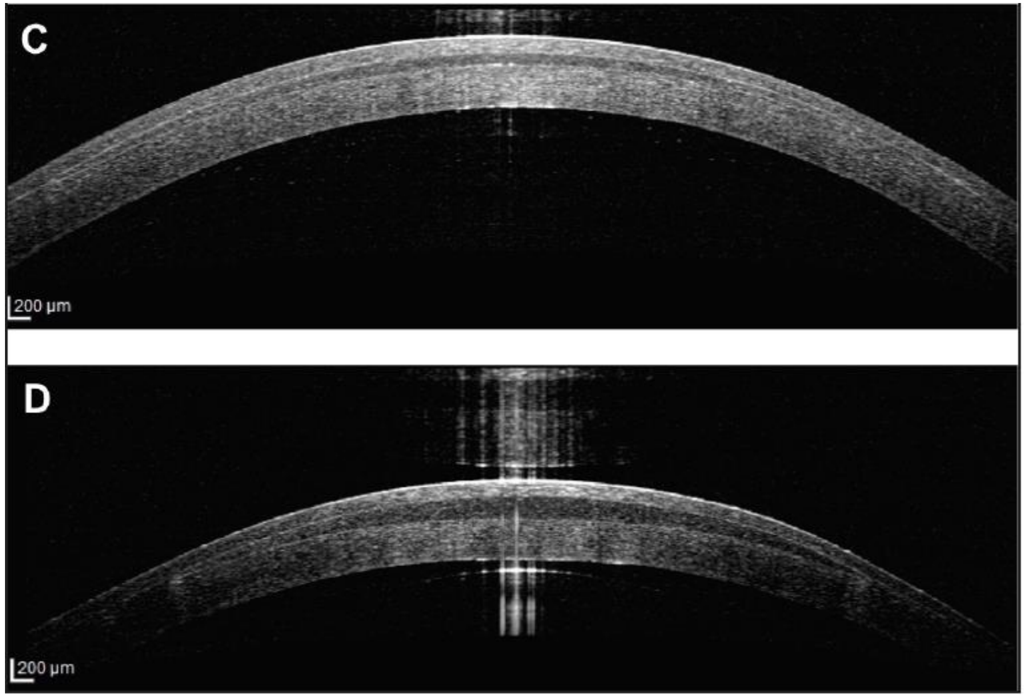
- **Correction of Hyperopia**

- **Supplementing corneal volume after keratitis**

- **Treatment of keratoconus**

Purpose – In vitro study related to hyperopia

- To evaluate changes in corneal tomography after stromal lenticule implantation ex vivo, with respect to
- **the dependency of the lenticule thickness and implantation depth on the corneal curvature**
- **the postoperative biomechanical strength at increased chamber pressure.**



Materials & Methods

- **56 human donor corneas** unsuitable for patient treatment: 28 for lenticule harvesting and 28 for lenticule implantation

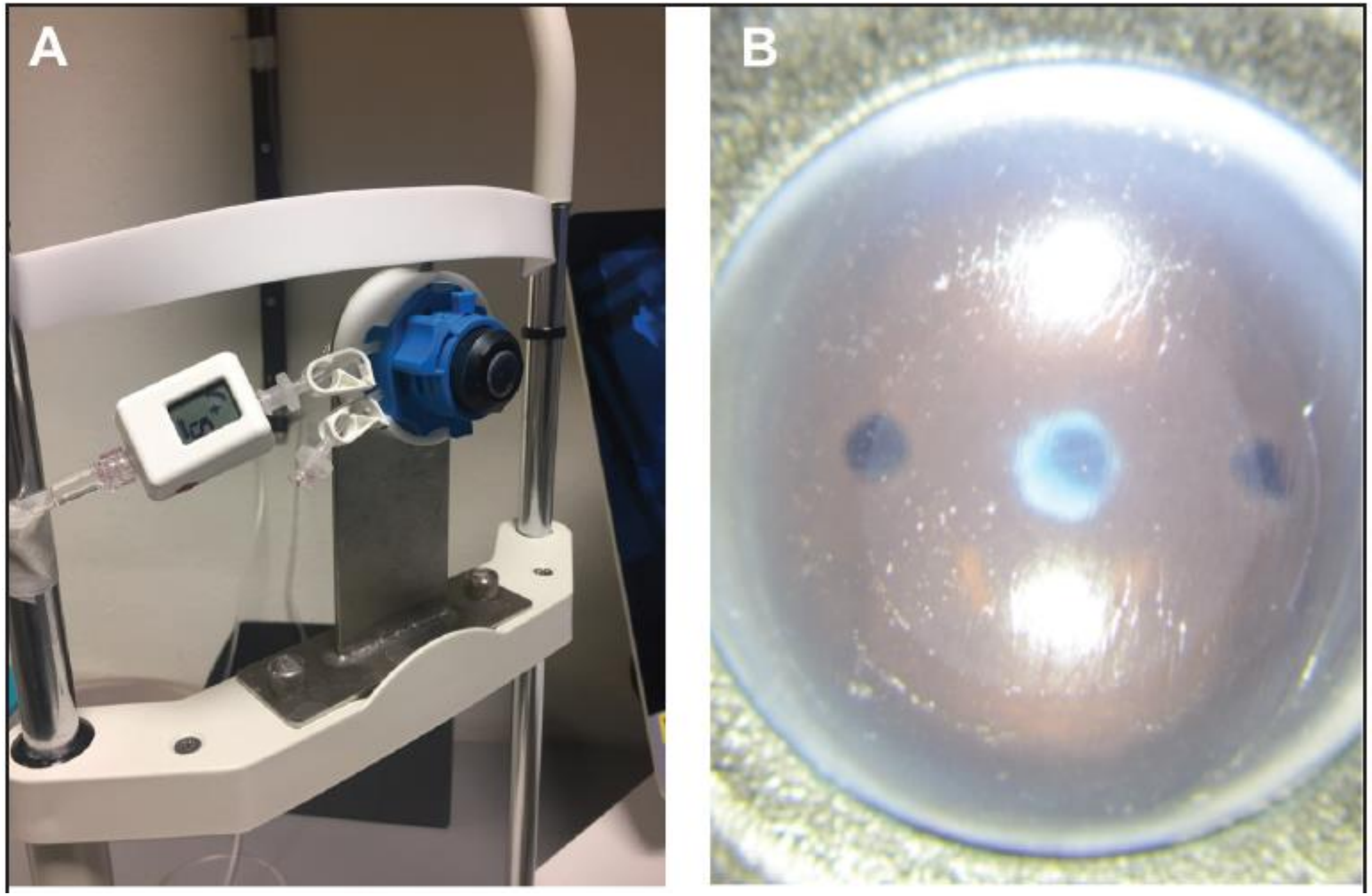
- Four groups of seven mounted donor corneas with a combination of one of **two implantation depths (110 and 160 µm)** and one of **two thicknesses of the implanted lenticules (95 and 150 µm).**

- Measurements at **15 and 40 mmHg** chamber pressure

- Controlled (normo-) hydration of the cornea using 8% Dextran-containing organ-culture medium

Materials & Methods

- **Pentacam HR**

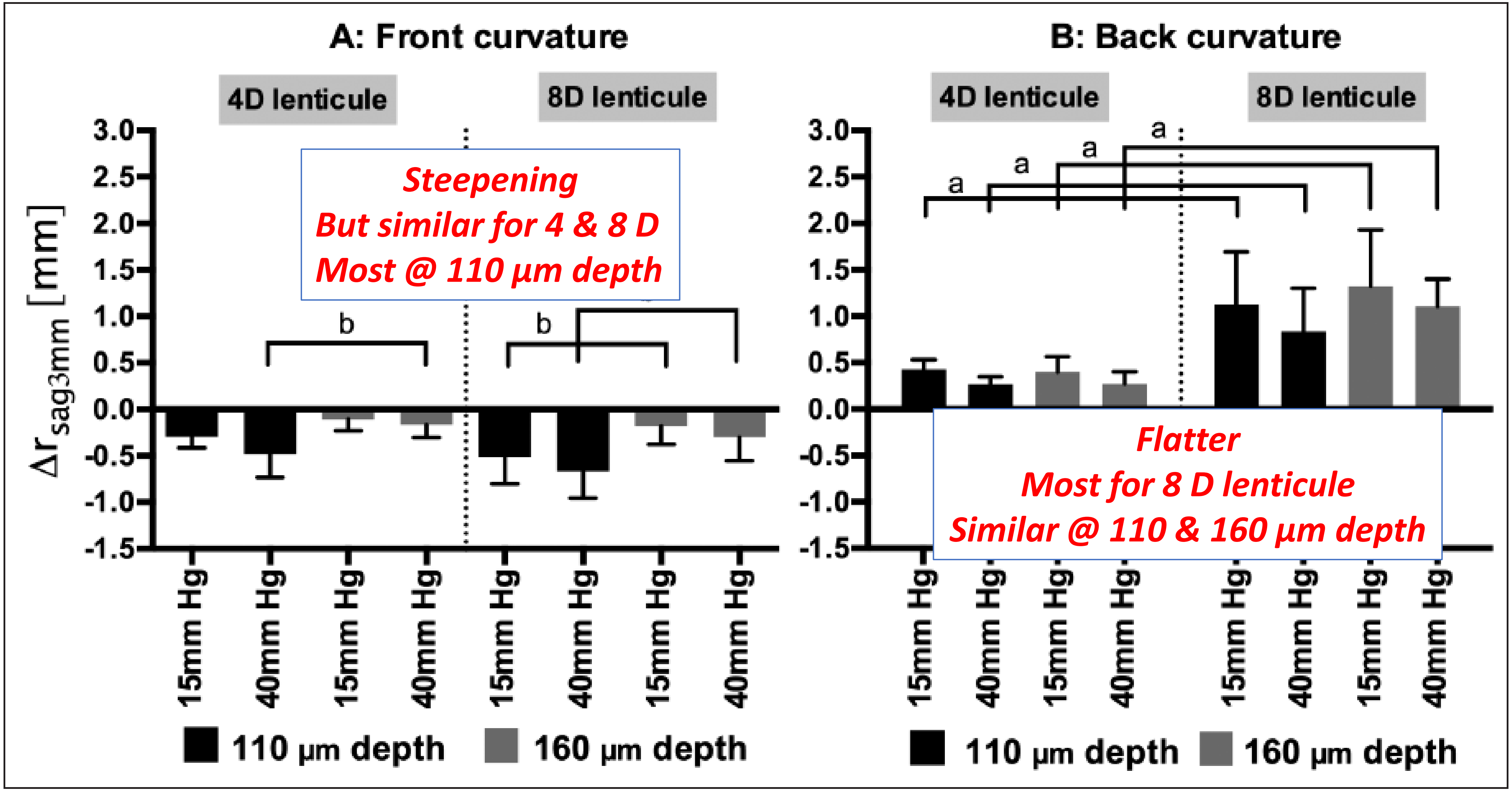


- Radius of curvature of front- and back-surface
- Total Corneal Refractive Power (TCPR)

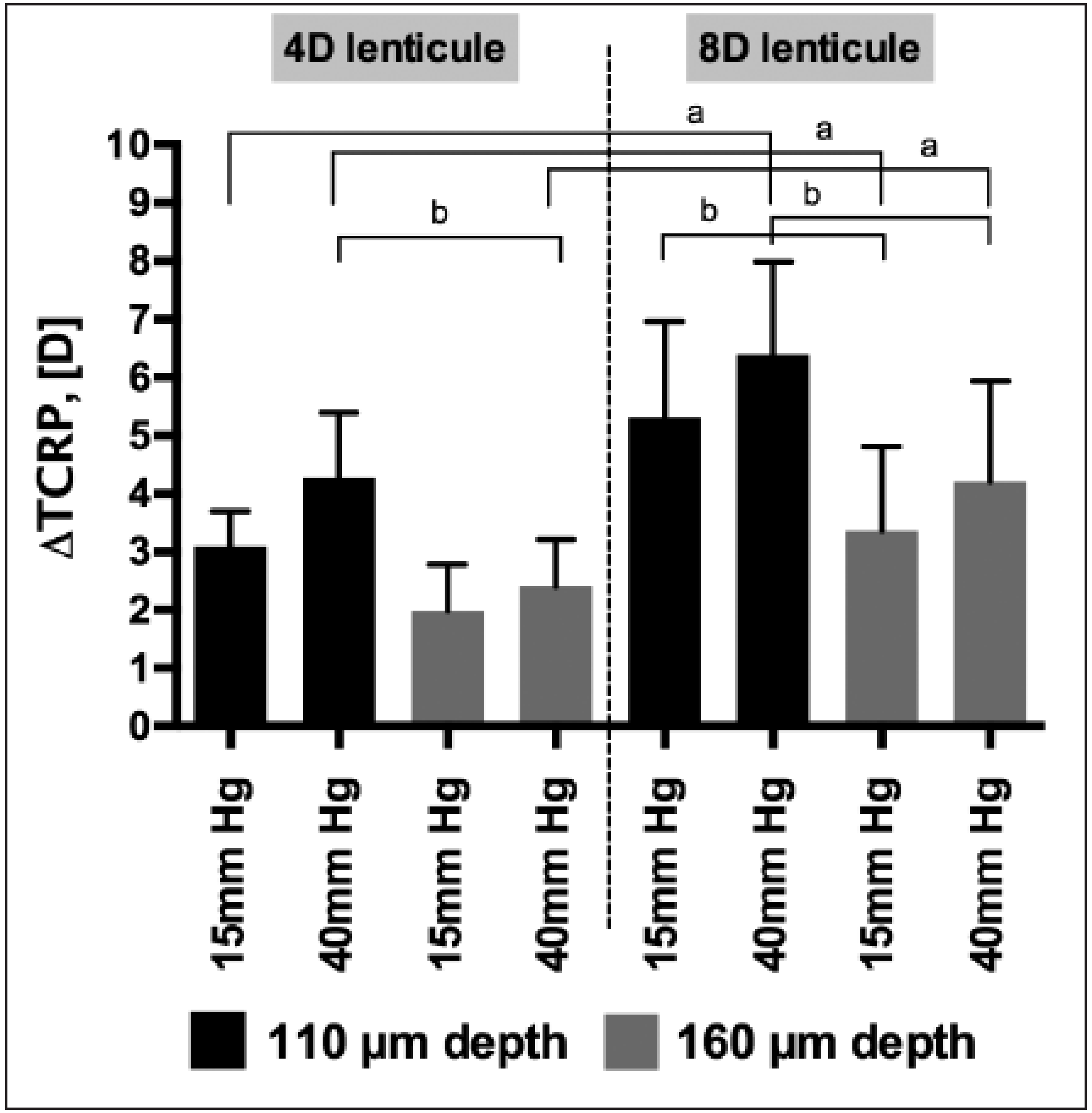
- Measurements before and after lenticule implantation

- Measurements at 15 and 40 mmHg

Results – Radius of Curvature



Results – Total Corneal Refractive Power



- Change in refractive power was less than the power of implanted the lenticules
- Change in refractive power was less when lenticules were implanted at 160 µm depth
- Change in refractive power was highest at high pressure levels

Conclusions

- The current study showed that the achieved correction was generally lower than the power of the implanted lenticule.
- Higher powered lenticules tended to induce more posterior flattening than anterior curvature steepening.
- Increased chamber pressure after implantation caused significant steepening of the anterior surface possibly due to weakening of the corneal tissue, and consequently higher TCRP values.
- However, further studies are needed to confirm these findings.

Remember

- Implantation of corneal lenticules is a **tissue** transplantation

- In the EU, you have to comply with DIRECTIVE 2004/23/EC OF THE EUROPEAN PARLIAMENT AND OF THE COUNCIL of 31 March 2004 on setting standards of quality and safety for the donation, procurement, testing, processing, preservation, storage and distribution of human tissues and cells

- **In practice only lenticules harvested from corneal donor tissue under the responsibility of a corneal bank can be used clinically**

ORIGINAL ARTICLE

Biological Lenticule Implantation for Correction of Hyperopia: An Ex Vivo Study in Human Corneas

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ABSTRACT

PURPOSE: To evaluate changes in corneal tomography after stromal lenticule implantation ex vivo, with respect to the dependency of the lenticule thickness and implantation depth on the corneal curvature and the postoperative biomechanical strength at increased chamber pressure.

METHODS: Twenty-eight human donor corneas underwent pocket implantation of refractive stromal lenticules. Four groups were created by the combination of two implantation depths (110 and 160 µm) and two lenticule thicknesses (95 µm = 4.00 diopters [D], 150 µm = 8.00 D). Sagittal keratometry and total corneal refractive power ($TCRP_{4mm,apex,zone}$) were obtained for the front and back curvature with Pentacam HR (Oculus Optikgeräte GmbH, Wetzlar, Germany) at chamber pressures of 15 and 40 mm Hg.

RESULTS: The anterior curvature steepening was comparable between the 4.00 D and 8.00 D groups (P > .141), but more pronounced with 110 µm implantation depth (P < .038). The posterior curvature flattened significantly more after implantation of 8.00 D than 4.00 D lenticules (P < .002), but was similar at 110 and 160 µm implantation depths (P > .071). Average ΔTCRP for the 4.00 D and 8.00 D groups was 3.10 ± 0.60 and 5.30 ± 1.66 diopters (D) at 110-µm depth, respectively (P = .003), but 1.99 ± 0.79 and 3.36 ± 1.45 D at 160-µm depth, respectively (P = .066). The relative correction achieved was 66% to 78% at 110-µm depth and 42% to 50% at 160-µm depth, but similar when using 4.00 D and 8.00 D lenticules. Increased chamber pressure caused significant anterior and posterior curvature steepening after implantation in all four groups (P < .001), but not before implantation (P > .632).

CONCLUSIONS: The power of the implanted lenticule must be higher than the intended correction, and customized to the chosen implantation depth. Biomechanical strength seems to decrease after lenticule implantation.

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Small incision lenticule extraction (SMILE) performed with femtosecond laser technology has optimized the treatment of refractive errors.[1-4] During the flap-free SMILE procedure, an intrastromal lenticule is created with femtosecond laser and mechanically removed through a minor incision. The extracted corneal lenticules are normally discarded after surgery, but could potentially be used for treatment of other refractive conditions such as hyperopia,[5,6] aphakia,[7] and presbyopia.[8]

Lenticule implantation was suggested as a tissue additive procedure in 1966 by Jose Barraquer,[9] later followed by several studies on synthetic hydrogel inlays for correcting hyperopia. Although the hydrogel inlays were generally tolerated in short-term studies of monkeys[10] and humans,[11] complications arose due to substantial problems with the nutrition diffusion. Studies reported necrosis of the central anterior layer, opacities, and lipid deposits around the inlays that in some cases had to be removed years after surgery.[11,12]

The refinement of femtosecond laser technology facilitates new possibilities for tissue additive procedures. The extracted lenticule in SMILE for myopia may now be implanted into a laser-cut intrastromal pocket in a hyperopic patient to induce steepening of the anterior corneal curvature.[13] Furthermore, the insertion of a refractive stromal lenticule may also serve as a potential method for stromal volume restoration

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Cornea

Refractive Correction and Biomechanical Strength Following SMILE With a 110- or 160-µm Cap Thickness, Evaluated Ex Vivo by Inflation Test

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PURPOSE. To examine the refractive correction and corneal biomechanical strength after small incision lenticule extraction (SMILE) by using a 110- or 160-µm cap thickness.

METHODS. Thirty-two human donor corneas were allocated into 4 groups, combining one of two cap thicknesses (110 and 160 µm) with one of two spherical corrections (−4 D and −8 D). Each cornea was mounted on an artificial anterior chamber. The chamber pressure was adjusted by an attached 8% dextran media column.

The anterior and posterior sagittal 3-mm-diameter curvature (r_{sag3mm}) and the total corneal refractive power ($TCRP_{4mm,apex,zone}$) were obtained before and after SMILE at a chamber pressure of 15 or 40 mm Hg. The average changes after surgery (Δ = postoperative − preoperative) and at increased chamber pressure (δ = 40 mm Hg − 15 mm Hg) were compared.

RESULTS. A 110-µm cap thickness caused more anterior flattening ($\Delta r_{15,-8D}$, 1.02 ± 0.08 mm versus 0.60 ± 0.17 mm), less posterior steepening ($\Delta r_{15,-8D}$, −0.19 ± 0.11 mm versus −0.45 ± 0.20 mm), and more myopic correction ($\Delta TCRP_{15,-8D}$, −6.30 ± 0.96 D versus −4.55 ± 1.66 D) than a 160-µm cap thickness for −8 D SMILE (P < 0.034), but not for −4 D SMILE ($\Delta TCRP_{15,-4D,110\mu m}$, −3.86 ± 1.31 D versus $\Delta TCRP_{15,-4D,160\mu m}$, −3.57 ± 1.27 D, P = 0.718). After SMILE, increased chamber pressure caused anterior steepening (P < 0.014), which was similar at cap thicknesses of 110 and 160 µm (δr_{-4D}, −0.13 ± 0.14 mm versus −0.09 ± 0.05 mm, P = 0.431).

CONCLUSIONS. For high myopic corrections, a 160-µm cap caused less anterior curvature flattening and more posterior steepening than a 110-µm cap, and consequently less myopic correction. The inflation test revealed a reduction in the biomechanical strength after SMILE; this was similar when using a 110- or 160-µm cap thickness.

Keywords: small incision lenticule extraction, SMILE, cap thickness, inflation test, corneal biomechanical properties

Since its introduction in 2011, small incision lenticule extraction (SMILE) for myopia or myopic astigmatism has been commonly performed by refractive surgeons worldwide.[1,2] With a femtosecond laser, an intrastromal lenticule is created and sequentially removed though a minor incision to flatten the anterior corneal surface.[3] The intrastromal lenticule can be created in the desired corneal depth and leaves the anterior stromal layer (the cap) intact. Mathematical[4] and computational modelling analyses[5,6] suggest that SMILE may be better at preserving the biomechanical integrity than other flap-based laser refractive procedures such as laser-assisted in situ keratomileusis (LASIK) and femtosecond lenticule extraction (FLEX). In vivo biomechanical studies evaluating the corneal deformation response with noncontact tonometry have been inconsistent, and SMILE has been equal or superior to LASIK.[7-15] Furthermore, iatrogenic ectasia has been reported after both LASIK[16] and SMILE,[17-20] which is characterized by corneal biomechanical weakening, severe protrusion, and decreased visual acuity.

Although a considerable amount of the literature has compared the biomechanical response after SMILE with flap-based laser refractive procedures,[7-15,21] fewer studies have assessed the dependency of cap thickness on the postoperative biomechanical strength.[4,22,23] The anterior one-third of the corneal stroma consists of an interwoven arrangement of collagen fibers, while the collagen fibers in the posterior two-thirds of the corneal stroma are arranged in distinct lamellae with a predominant vertical and horizontal arrangement.[24] The collagen arrangement seems to be responsible for the depth-dependent exponential decrease in the corneal tensile strength, with the 40% anterior stroma being the strongest region, and the 60% posterior stroma being at least 50% weaker.[25]

In SMILE, a cap thickness of 110 to 130 µm is commonly used for myopic correction. Consequently, the stromal lenticule is usually removed in the stronger part of the cornea. The lamellar cut during cap creation may cause only a minor reduction in the corneal biomechanical strength,[26] but the shape of the removed lenticule still requires that several collagen fibers are damaged during the procedure. Hence, removal of the lenticule in the deeper layers (thicker cap) may better preserve the corneal biomechanical strength than removal in the superficial layer. Furthermore, a thicker cap