Experimental Results of Preparing Laser-shaped Stromal Implants for Laser-assisted Intrastromal Keratophakia in Extremely Complicated Laser in situ Keratomileusis Cases

Mirko Jankov, MD; Michael C. Mrochen, PhD; Michael Bueeler; Theo Seiler, MD, PhD

ABSTRACT

PURPOSE: To evaluate the feasibility of laser-shaped stromal implants from a donor eye for correcting extreme high hyperopia with irregular astigmatism and an exceptionally thin corneal bed.

METHODS: Thirty-one fresh enucleated porcine eyes were used. The procedure was initiated with mechanical de-epithelialization followed by a lamellar cut with a microkeratome, resulting in a hinged flap (thickness 150 µm, diameter 9.5 mm). The cornea was photoablated with PRK treatment for +8.00 D sphere (hyperopic lenticule group) and -5.00 D sphere (myopic group) by a scanning spot excimer laser. A customized scanning software algorithm was used to create a circumferential cut with a 6.5-mm internal diameter. The lenticule was removed from the stromal bed and measured by a surface profiling system. A clinical case was performed on a patient with previous LASIK and highly irregular hyperopic astigmatism to verify the clinical utility of the experimental setup.

RESULTS: Under the microscope, lenticules seemed round, regular, and transparent. The average surface profile of porcine corneas demonstrated good parabolic shape with individual variations as large as 30 µm, probably due to the corneal size and curvature differences between the porcine eye and the human eye—for which the microkeratome is designed. The patient underwent a topography-guided treatment after laser-assisted intrastromal keratophakia (LAIK) and 1-month follow-up showed an increase of UCVA, BSCVA, and central corneal thickness.

CONCLUSIONS: The use of modern scanning-spot excimer lasers and microkeratomes enabled us to produce stromal lenticules of good quality, which might be acceptable to implant into a human eye. [*J Refract Surg* 2002;18:S639-S643]

We have witnessed the rapid development of surgical methods for the correction of myopia, hyperopia, and astigmatism. Although most patients who undergo refractive surgery are elective first time patients, there is also an emergent group of secondary iatrogenic hyperopic and astigmatic patients after complicated laser treatments with a decreased residual corneal thickness.

The first techniques of adding more corneal tissue for refractive purposes were keratophakia, epikeratophakia, and keratomileusis. They were introduced by Barraquer in the 1950s and were used during the 1980s, but due to the complexity of the procedure and equipment, the inaccuracy of refractive results, postoperative complications, and delayed visual rehabilitation[1], they are rarely performed today, even after recent studies of the laser assisted lenticule lathing.[2] Another alternative with promising but inconclusive results is provided by artificial lenses made of different materials (flint glass, polymethylmethacryate, polysulfone, and hydrogel) that are implanted in the stroma.[3-7]

None of the previous techniques were successful in the treatment of irregular astigmatism or high hyperopia, especially in cases of a very thin corneal bed, because of the optical zone size and the corneal ablation depth.[8,9] We propose intrastromal implantation of a laser-shaped corneal lenticule prepared

From Augenklinik, UniversitätsSpital Zürich, Switzerland (all authors) and Departamento de Oftalmologia, Santa Casa de Sao Paulo, Brazil (Jankov).

Presented at the 3rd International Congress of Wavefront Sensing and Aberration-free Refractive Correction, February 15-17, 2002, Interlaken, Switzerland.

Drs Mrochen and Seiler are scientific consultants for WaveLight Laser Technologie AG. Dr. Jankov has no proprietary interest.

Research includes results from the student semester study of U. Schelling and T. Menzi, graduate students from the Institute of Biomedical Technics and Medical Informatics D-BEPR, ETH Zürich, Switzerland.

Correspondence: Mirko Jankov, MD, R. Mal. JB Bormann 586, 80730-350 Curitiba – PR, Brazil. Tel: 55.41.322.2020; Fax: 55.41.222.2020; E-mail: mirkojankov@hotmail.com

from a human donor eye in a technique called laser-assisted intrastromal keratophakia (LAIK). The aim of this study was to evaluate the feasibility of preparing laser-shaped stromal implants from a donor eye for possibly correcting some extreme cases of high hyperopia with irregular astigmatism and an exceptionally thin corneal bed.

METHODS

Experimental Study

Thirty-one fresh enucleated porcine eyes were used to perform LAIK under experimental conditions. The entire globe was positioned onto the eye holder and filled with BSS through the optical nerve to restore normal intraocular pressure (IOP). The procedure was initiated with mechanical de-epithelialization using a hockey knife. Lamellar microkeratotomy was performed using a commercially available microkeratome (Berlin, Schwind Inc., Kleinostheim, Germany) with a hinged flap of a 150 µm thickness and a flap diameter of approximately 9.5 mm. The flap surface of the porcine eye was then photoablated with a treatment profile for +8.00 diopters (D) sphere (hyperopic lenticule group, n=18 eyes) and -5.00 D sphere (myopic group, n=13 eyes) by a scanning spot excimer laser (Allegretto WAVE, WaveLight Laser Technologie AG, Erlangen, Germany). A customized scanning software algorithm was used to create a circumferential cut with internal diameter of 6.5 mm. The lenticule was then removed from within the flap overlying the residual stromal bed and measured by a surface profiling system in two directions: in the direction of the microkeratome cut and perpendicularly to it. The surface profiling system (Homelwerke, T8000, Konturtaster, Germany) was designed for measuring hard surfaces with 1.5-µm precision, and consists of a moving arm holding the probe over a measuring table, connected with the PC computer equipped with an adequate user program.

Clinical Case

A 42-year-old white female patient was referred to our clinic for treatment of high irregular compound hyperopic astigmatism resulting from various earlier LASIK procedures, by different ophthalmologists. Initially she had best spectacle-corrected visual acuity (BSCVA) of 20/20 in both eyes and underwent simultaneous bilateral LASIK for OD: +4.00 D, and OS: +4.50 D, in November 1996. Her visual acuity partially recovered in her left eye but never did so in her right eye, and she had two enhancement procedures on the right eye in the following 2 months by the first refractive surgeon. However, there was no significant improvement of the uncorrected visual acuity (UCVA) (OD: 20/200, OS: 20/50). Having been examined by a second ophthalmologist in July 1997, corneal topography revealed a decentered ablation zone toward inferior-temporal of approximately 1.5 mm in both eyes, with the ablation zone diameter of 4.5 mm OD and 5 mm OS, as determined from corneal topography. In November 1997, she was scheduled for topography-guided LASIK on the right eye, which resulted in partial re-centralization (now 0.5 mm inferiorly) of the ablation zone (now 4 mm in diameter) with an UCVA of 20/400, BSCVA of 20/100, and -5.00 -2.00 x 170°. An additional enhancement LASIK was performed in July 1998 to correct pure sphere of -5.00 D on the right eye. After this procedure, the patient had significant monocular diplopia and halos, even under physiological pupil sizes of 3 to 4 mm. In January 1999, she had an additional topography-guided LASIK in order to “reverse back into a more regular hyperopic cornea,” as defined by her ophthalmologist, without satisfactory visual outcome (BSCVA 20/200, +5.00 D sphere).

After 4 years and seven enhancements, the patient was referred to our service in December 2000. UCVA was 20/125; autorefractor data (Automatic Refractor/Keratometer model 599, Humphrey Instruments - Carl Zeiss, Switzerland) was +6.75 -5.25 x 170°, highly irregular corneal topography (Keratograph type 70600 with customized software version, Oculus, Wetzlar, Germany), and gross flap irregularities and folds; central ultrasonic pachymetry (Pachymeter SP-2000, Tomey Corp., Nagoya, Japan) was 286 µm. An automated lamellar keratoplasty in the right eye was performed in our clinic at this time, resulting in a transparent graft and minimal striae, but with some small epithelial ingrowth islands diagnosed in January 2001, with UCVA and BSCVA of 20/160. In March 2001, her UCVA was 20/300, BSCVA was 20/200 (pinhole 20/40), with +8.00 -1.00 x 130°, and central pachymetry of 398 µm.

After having ethical commission board approval and the patient's consent, LAIK was performed using a hyperopic sphere +8.00-D lenticule on the right eye in April 2001.

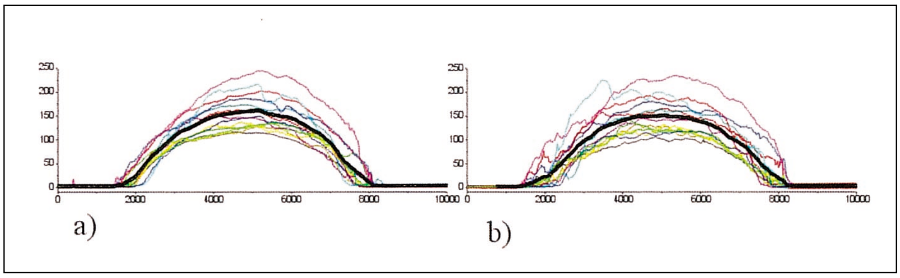

Figure 1. Surface profile of 18 hyperopic lenticules measured in (a) and perpendicular to (b) the cutting direction (thin lines) with the average value (thick line).

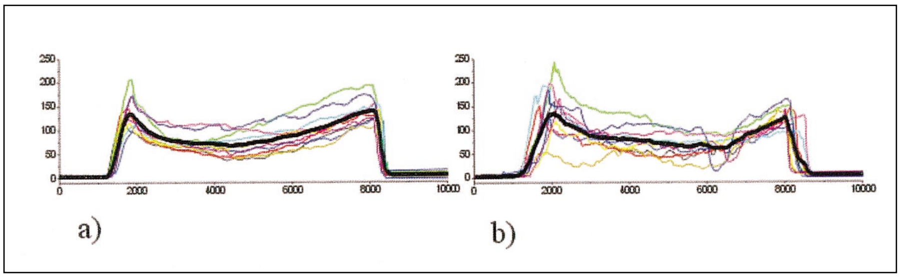

Figure 2. Surface profile of 13 myopic lenticules measured in (a) and perpendicular to (b) the cutting direction (thin lines) with the average value (thick line).

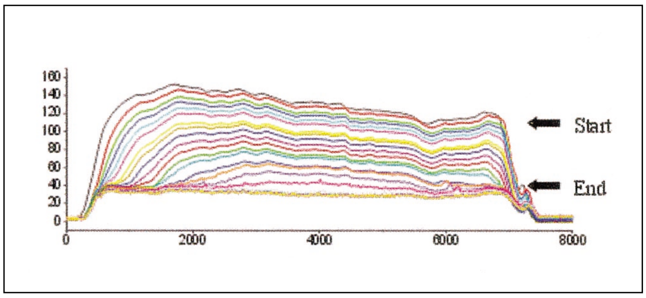

Figure 3. Dehydration of the lenticule over time.

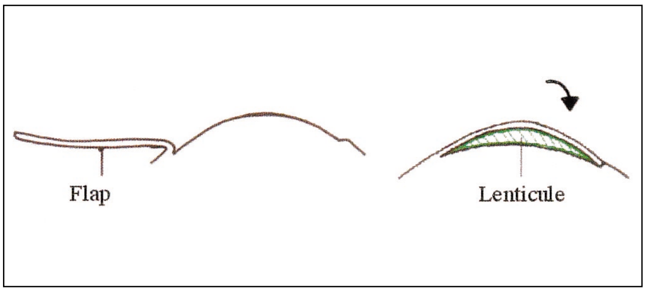

Figure 4. Schematic representation of the laser-assisted intrastromal keratophakia (LAIK) procedure; implantation in the human eye.

RESULTS

Experimental Study

Under the surgical microscope, the lenticules seemed perfectly round, with a regular surface and good transparency. The average surface profile of porcine corneas demonstrated a good parabolic shape with well-defined edges.

Eighteen lenticules from the hyperopia group measured in the flap-cutting direction had an average maximal central thickness of 161 ± 28 µm, range 110 to 240 µm (Fig 1a). The same lenticules measured perpendicular to the flap-cutting direction averaged 157 ± 32 µm, range 105 to 230 µm (Fig 1b).

In the myopia group, the 13 lenticules measured in the flap-cutting direction showed an average minimal central thickness of 71 ± 29 µm, range 49 to 104 µm (Fig 2a). Repeated measurements of the same lenticules perpendicular to the flap-cutting direction averaged 67 ± 30 µm, range 29 to 98 µm (Fig 2b).

Taking 24 consecutive measurements at intervals of 10 minutes (total experiment time 4 hours), tissue evaporation decreased thickness to less than one-third of the original value (Fig 3).

Clinical Case

The LAIK operation was uneventful (Fig 4), and 30 days after implantation of the lenticule, UCVA improved from 20/300 to 20/125 and BSCVA from 20/200 to 20/80 (with pinhole 20/60). Manifest refraction was +1.25 -2.00 x 130°, and corneal topography showed a significantly steeper and more regular corneal front surface. The patient underwent a topography-guided treatment 6 months after LAIK, and 1 month follow-up resulted in UCVA of 20/60 and BSCVA of 20/40 (pinhole 20/30) with manifest refraction of +1.00 -3.25 x 105°.

DISCUSSION

The average thickness of the hyperopic lenticules was slightly higher than the attempted flap thickness (150 µm) declared by the microkeratome manufacturer. Nevertheless, a good parabolic shape with well-defined edges showed that all of them were of similar size.

Myopic lenticules were inferior in quality and uniformity. This might be due to a very thin center, which made it difficult to manage the lenticules, as well as a steep peripheral "cliff," causing possible measurement errors.

Considering the cutting mechanism of the microkeratome, certain thickness differences throughout the cut might be expected. With advancement of the microkeratome blade, the corneal stroma is pushed and "fed" more and more to the advancing blade, resulting in a slight increase of flap thickness in the cutting direction. On the contrary, comparing the measurements for the cutting direction and perpendicular to the cutting direction for hyperopic lenticules, one can observe no asymmetry in any direction. Although the results for the myopic lenticules are not of uniform quality, they still show the same pattern of asymmetry independent of the cutting direction, suggesting that the reason for the irregularity is the measurement probe that pushed and wrinkled the corneal tissue while measuring, rather than the microkeratome cut itself.

However, all the lenticules in both the hyperopic and myopic groups showed irregularities in the surface profile and important individual variations expressed through a large standard deviation, as high as 30 µm. Those individual variations have not been reported in previous polymethylmethacrylate ablations, and are probably due to a long death-to-preparation time of the porcine corneas (>4 hours) and a consequent biomechanical heterogeneity that caused irregular microkeratome cuts. Another possible reason is the microkeratome cutting prinicple itself. As the microkeratome is designed for the human eye and human cornea, the differences in corneal size and curvature between the porcine and the human eye could be responsible for the large individual differences in the lencticule thickness.

We performed a system error analysis using two tests. In the first test, three subsequent measurements within 3 minutes both in the cutting direction and perpendicularly were carried out, and resulted in the thickness variance of 10 and 12 µm, respectively. The number of measurements was small due to the measurement time and the dehydration of the cornea, which itself produces differences in thickness.

In the second test, five subsequent measurements within 3 minutes in the cutting direction and perpendicular to the cutting direction were performed, and the variance of lenticule thickness was 7 and 11 µm, respectively. As expected, the variance was smaller due to the fact that the lenticule, once positioned, was not moved between the measurements, which decreased the manipulation-induced error.

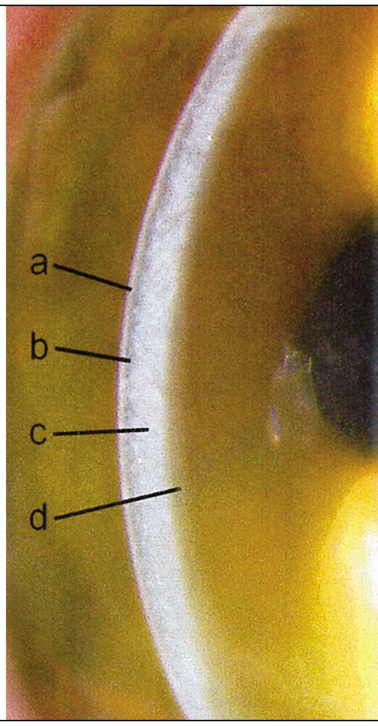

Figure 5. First day of follow-up: significant lenticule edema, where four layers can easily be identified: (a) superficial, white line – CL; (b) anterior, less edematous – flap; (c) middle, very edematous – lenticule; and (d) deep, non-edematous – corneal bed.

Nevertheless, the error differences were not significantly dissimilar, which points out that manipulation-induced errors are not significantly higher than the measuring errors themselves. Measuring errors are significantly higher than the measuring precision of 1.5 µm claimed by the manufacturer, which indicated problems with the measuring procedure itself. The suggested explanation could lie in the biomechanical properties of the corneal surface. The jelly-like surface of the cornea, unlike homogeneous and steady hard surfaces, was possibly wrinkling away from the probe, being slightly compressed forward while being measured. A certain, albeit small, amount of water probably caused the cornea to occasionally slip in the way of the measuring probe, resulting in a jerky measuring profile and emphasizing the existing individual irregularities.

The surgical technique in which the lenticule would be implanted into the cornea between the flap and the corneal bed is called laser-assisted intrastromal keratophakia (LAIK) (Fig 5). The principal aim when performing LAIK is to increase corneal thickness by a lenticule that already has the shape of the attempted spherical correction, in order to bring it back into the treatable range of thickness. Adding more corneal tissue over the corneal bed was not expected to change the biomechanical properties of the cornea, ie, it was neither meant to compensate nor to stabilize an iatrogenic keratoconus of the corneal bed (if already in course). It was rather thought to facilitate a sufficient addition of corneal stroma that would make the cornea less irregular and allow it to be subject to further ablation, if needed. We have already implanted lenticules in two patients and have reported the results of one of these patients in this manuscript. Our reported patient had improved visual acuity, as well as regularization of corneal topography, which suggests that any irregularities with human lenticules are likely smaller than described in the experimental study with the porcine lenticules. Alternatively, the importance of these irregularities decreases when positioning the lenticule under a flap, which serves to smooth them.

The use of the WaveLight Allegretto WAVE scanning-spot excimer laser and the Schwind Berlin microkeratome enabled us to produce stromal lenticules of good quality that might be implanted into the eye for correction of high hyperopia, irregular astigmatism, or to manage complicated LASIK eyes with a thin residual stromal bed. First clinical results with implantation of the lenticules in humans are encouraging.

REFERENCES

1. Barraquer JI. Queratoplastia refractiva. Estudios Inform Oftalmol Inst Barraquer 1949;10:2-21.
2. Homolka P, Biowski R, Kaminski S, Barisani T, Husinsky W, Bergman F, Grabner G. Laser shaping of corneal transplants in vitro: area ablation with small overlapping laser spots produced by pulsed scanning laser beam using an optimising ablation algorithm. Phys Med Biol 1999;44: 1169-1180.
3. McDonald MB, McCarey BE, Storie B, Beuerman RW, Salmeron B, van Rij G, Knight PM. Assesment of the long-term corneal response to hydrogel intrastromal lenses implanted in monkey eyes for up to five years. J Cataract Refract Surg 1993;19:213-222.
4. Keates RH, Martines E, Tennen D, Reich C. Small-diameter corneal inlay in presbyopic or pseudophakic patients. J Cataract Refract Surg 1995;21:519-521.
5. Horgan SE, Fraser SG, Choyce DP, Alexander WL. Twelve year follow-up of unfenestrated polysulfone intracorneal lenses in human sighted eyes. J Cataract Refract Surg 1996;22:1045-1051.
6. Ohrloff C, Duffin RM, Apple DJ, Olson RJ. Opacification, vascularization, and chronic inflammation produced by hydrogel corneal lamellar implants. Am J Ophthalmol 1984;98:422-425.
7. Werblin TP, Patel AS. Myopic hydrogel keratophakia: improvements in lens design. Cornea 1987;6:197-201.
8. Roberts CW, Koesten CJ. Optical zone diameters for photorefractive corneal surgery. Invest Ophthalmol Vis Sci 1993;34:2275-2281.
9. Azar DT, Primack JD. Theoretical analysis of ablation depths and profiles in laser in situ keratomileusis for compound hyperopic and mixed astigmatism. J Cataract Refract Surg 2000;26:1123-1136.