Pentacam Assessment of Posterior Lamellar Grafts to Explain Hyperopization after Descemet's Stripping Automated Endothelial Keratoplasty

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Purpose: To evaluate changes in posterior corneal curvature as a possible cause of the hyperopic refractive shift observed after Descemet's stripping automated endothelial keratoplasty (DSAEK).

Design: Prospective, noncomparative, interventional case series.

Participants: Thirty-four eyes of 29 patients with Fuchs' endothelial dystrophy or pseudophakic bullous keratopathy.

Methods: A standard DSAEK procedure was performed in 34 eyes using the pull-through technique for graft delivery. When cataract was present (n = 7), phacoemulsification with posterior chamber intraocular lens implantation was combined. Each eye underwent Pentacam (Oculus, Wetzlar, Germany) evaluation 1, 3, and 12 months after surgery. Corneal graft thickness was calculated on Scheimpflug scans at 9 locations (1 central, 4 peripheral, and 4 mid peripheral). The mean radius of posterior corneal curvature (Rm) was recorded. At each postoperative examination time, manifest refraction was determined and compared with pre-DSAEK values in simple procedures or with intended postoperative refraction, if cataract surgery had been performed.

Main Outcome Measures: Manifest refraction, Rm, and corneal graft thickness at 1, 3, and 12 months after surgery.

Results: The mean$\pm$standard deviation posterior corneal curvature was 6.5$\pm$0.56 mm before surgery and varied from 5.52$\pm$0.39 mm 1 month after surgery to 5.83$\pm$0.37 mm at 3 months after surgery and 5.92$\pm$0.35 mm at 12 months after surgery. The grafts were significantly thicker in the periphery and mid periphery than in the center at all examination times. Thickening diminished significantly over time at all locations. The average reduction of corneal thickness was higher at the edges (91.5 μm) than in the mid periphery (38.3 μm) or in the center (24.2 μm). The average postoperative spherical equivalent$\pm$standard deviation changed from -0.31 ± 2.35 diopters (D) before surgery to 1.03$\pm$2.21 D 1 month after surgery, 0.61$\pm$2.07 D 3 months after surgery, and $+0.31\pm2.03$ D 12 months after surgery.

Conclusions: The difference in thickness between center and periphery of the DSAEK graft induces a change in posterior corneal curvature, resulting in a hyperopic shift that decreases with time and is negligible for spectacle correction. However, when performing a triple procedure, intraocular lens selection should take into account the refractive change induced by DSAEK.

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Posterior lamellar keratoplasty has emerged as a leading surgical approach for the treatment of endothelial failure.[1,2] Descemet's-stripping automated endothelial keratoplasty (DSAEK) involves mechanical stripping of diseased host Descemet–endothelium complex and replacement with a donor graft of endothelium, the Descemet's membrane, and a thin layer of posterior stroma harvested with an automated microkeratome.[3] Performing DSAEK for corneal endothelial dysfunction offers many advantages over penetrating keratoplasty, including intraoperative closed-system conditions, minimal change of preoperative refraction, faster postoperative visual rehabilitation, and elimination of all suture-related late postoperative complications.

Although endothelial keratoplasty initially was thought to be a refractively neutral procedure, several authors recently reported a mild postoperative hyperopic shift after DSAEK.[4–6] Theoretically, this could be induced by a postoperative increase in posterior corneal curvature related to the meniscus shape of the DSAEK graft, which has been demonstrated to be thicker in the periphery than it is in the center.[4]

In an attempt to correlate the postoperative changes in posterior corneal curvature with the post-DSAEK refraction, a prospective evaluation of patients undergoing DSAEK was undertaken by means of the Pentacam Scheimpflug imaging system (Oculus, Wetzlar, Germany), a noncontact instru-

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ment that provides high-resolution images of the anterior segment of the eye, as well as anterior and posterior corneal topography and complete corneal pachymetry of the entire cornea.

Patients and Methods

All eyes undergoing DSAEK surgery by the same surgeon (MB) at the authors' hospital between January 2006 and October 2006 were enrolled in this prospective study. Each patient signed an informed consent approved by the institutional review board. Each eye had substantial visual impairment (best-corrected visual acuity, ≤20/40) secondary to endothelial failure. Eyes with significant stromal scarring were excluded, but eyes with macular degeneration, glaucoma, ischemic optic neuropathy, or other known comorbidities were not excluded.

All patients underwent standard DSAEK surgery, according to the technique previously described.[7] In particular, stripping of the Descemet's membrane was performed under air to optimize direct visualization, and a peripheral iridectomy was performed at the 6-o'clock position to eliminate the risk of pupillary block. The donor corneas were mounted on the artificial chamber of the automated lamellar therapeutic keratoplasty system (Moria, Antony, France), and a microkeratome with a 300-μm head was used to remove most of the anterior stroma. The donor lamellae obtained this way were punched to the required size of 9 mm, using a Barron punch (Katena Products Inc, Denville, NJ).

In those cases also requiring cataract extraction and intraocular lens implantation, phacoemulsification was performed before DSAEK. Intraocular lens implantation with an injector was performed under continuous flow of balanced salt solution through an anterior chamber maintainer, thus avoiding the use of any viscoelastic substance. In these eyes, the postoperative refractive target was −1.50 diopters (D), to compensate for the expected postoperative hyperopic shift.

Before surgery, as well as at 1, 3, and 12 months after surgery, all patients underwent a complete ophthalmologic examination, including best spectacle-corrected visual acuity, manifest refraction, complete slit-lamp examination, measurement of intraocular pressure, fundus examination, and, when necessary, B-scan ultrasonography. In addition, at each examination, Pentacam analysis of the cornea was performed in all eyes by the same investigator (VS). In this analysis, 25 single images, separated by 7.2 degrees, were captured by the rotating Scheimpflug camera in fewer than 2 seconds with the patient staring at the fixation target. The automatic release mode was used, which achieves correct focus and alignment with the corneal apex before starting the scanning. If necessary, Pentacam analysis was repeated until an acceptable scan could be obtained, as indicated by the quality scan index, or when at least 10.0 mm of the cornea had been scanned without extrapolation.

The mean radius of posterior corneal curvature (Rm) value, calculated by ray tracing, was extrapolated from the Pentacam main display, where all data derived from the anterior and posterior corneal surface were collected.

The graft thickness was calculated from the 2 Scheimpflug camera images obtained at the 12- and 3-o'clock meridians. Five measurements were obtained from each meridian, 1 centrally, 2 in the mid periphery (2 mm from the central one), and 2 in the periphery, 0.5 mm from the edge of the graft (Fig 1). The averages

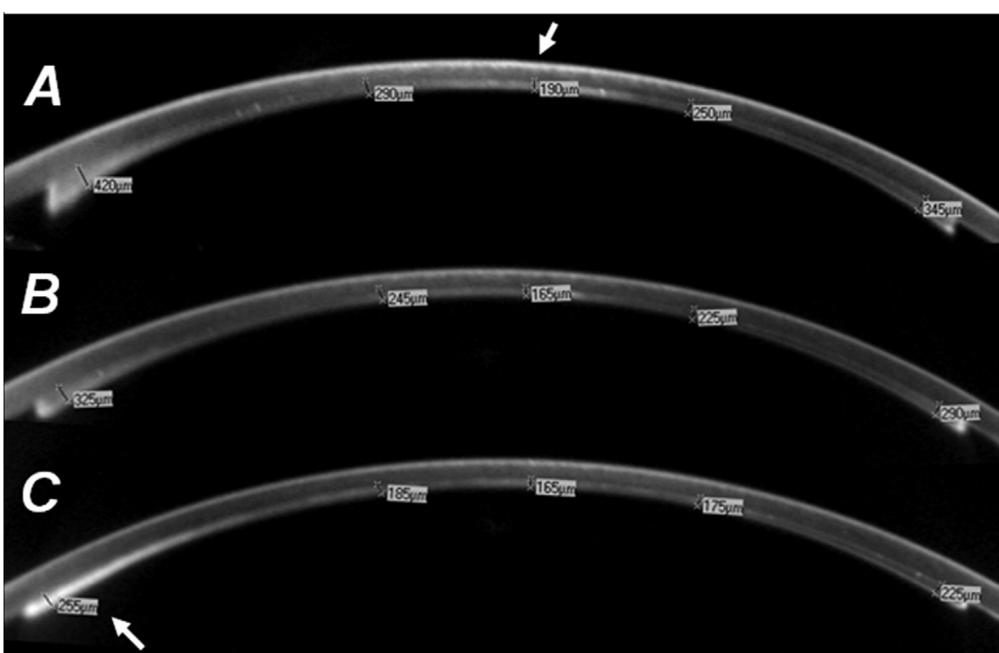

Figure 1. Scheimpflug camera images illustrating the measurement sites in a patient at different examination times after Descemet's stripping automated endothelial keratoplasty (DSAEK). **A**, One month after surgery, the scan shows a mild central hyperreflectivity (downward-pointing arrow) in the recipient cornea probably resulting from transient stromal edema. The graft peripheral edges are thicker than the central zone, causing an increase of posterior curvature. **B**, Three months after surgery, deswelling of the periphery of the donor button is evident, with the edge standing out of the posterior corneal surface to a less pronounced extent. **C**, Twelve months after surgery, the white appearance on the edge (upward-pointing arrow) confirms scarring of the exposed stroma with further reduction in thickness. Now the edge of the graft appears to be beveled and almost continues the contour of the posterior surface of the recipient cornea.

Table 1. Change of Outcome Measurements over Time

Outcome Measurements	Before Surgery (Mean±Standard Deviation)	1 Month (Mean±Standard Deviation)	3 Months (Mean±Standard Deviation)	12 Months (Mean±Standard Deviation)
Rm value	6.5±0.56	5.52±0.39	5.83±0.37	5.92±0.35
Refractive SE (D)	−0.31±2.35	1.03±2.21	0.61±2.07	0.31±2.03
Central graft thickness (μm)	N/A	196.0±29.3	181.8±30.4	171.3±29.5
Mid peripheral graft thickness (μm)	N/A	251.0±32.7	226.0±31.9	213.0±29.7
Peripheral graft thickness (μm)	N/A	362.2±35.3	303.4±29.3	270.6±28.4

D = diopters; N/A = not available; Rm = mean radius of posterior corneal curvature; SE = spherical equivalent.

of the 4 peripheral measurements and the 4 mid-peripheral measurements were determined. Then the average central, mid-peripheral, and peripheral values for all patients were determined.

Statistical Analysis

Postoperative changes in graft thickness, Rm, and spherical equivalent (SE) at 1, 3, and 12 months were evaluated with an analysis of variance. Analyses were conducted using Stata software version 10.0 (Stata, Inc, College Station, TX). A P value of less than 0.05 was considered to be statistically significant.

Results

Thirty-four eyes of 29 patients were included in this series. The average age at surgery in the study was 72.1±10.8 years (mean±standard deviation), ranging from 50 to 88 years. Eighteen patients were females (52.9%) and 16 were males (47.1%). Primary endothelial dysfunction secondary to Fuchs' dystrophy was diagnosed in 22 eyes (64.7%), and pseudophakic bullous keratopathy was diagnosed in 12 eyes (35.3%). In 7 eyes (20.6%), a cataract was present and was removed at the time of DSAEK surgery.

Best spectacle-corrected visual acuity improved from an average of 20/106 before surgery to 20/75 at 1 month, 20/52 at 3 months, and 20/48 at 12 months after surgery. Table 1 summarizes all outcome measurements recorded in the study at different examination times. One month after DSAEK, the mean graft thickness was 196.0±29.3 μm centrally, 251.0±32.7 μm in the mid periphery, and 362.2±35.3 μm at the edges; 3 months after surgery, the thickness decreased at each location, measuring 181.8±30.4 μm at the central site and 226.0±31.9 μm and 303.4±29.3 μm at the 2 most peripheral positions. Finally, 12 months after surgery, the mean graft thickness decreased further to 171.3±29.5 μm centrally, 213.0±29.7 μm in the mid periphery, and 270.6±28.4 μm in the periphery. Figure 2 illustrates these results.

The statistical analysis of thickness variations at different locations demonstrated a significant difference between central, mid-peripheral, and peripheral measurements at each postoperative examination time ($P<0.005$). In addition, the decrease in thickness over time was significant at each location ($P<0.0001$). The average thinning 12 months after surgery was greater at the edges (91.6 μm), than in the mid periphery (38.0 μm) or in the center (24.7 μm). This corresponded to an overall thinning of 25.3%, 15.3%, and 12.6%, respectively, from the values recorded 1 month after surgery.

As illustrated by Figure 3, the average Rm varied from 6.50±0.56 mm before surgery to 5.52±0.39 mm at 1 month, 5.83±0.37 mm at 3 months, and 5.92±0.35 mm at 12 months after surgery. The change was statistically significant all examination times ($P<0.0001$).

The average refractive SE was −0.31±2.35 D (range, −5.75 to 4.36 D) before surgery. After surgery, it was 1.03±2.21 D (range, −4.25 to 5.25 D) at 1 month, 0.61±2.07 D (range, −4.50 to 5.00 D) at 3 months, and 0.31±2.03 D (range, −4.75 to 4.50 D) at 12 months after surgery. The change in average spherical refractive error from the value recorded before surgery was 1.34 D at 1 month, 0.92 D at 3 months, and 0.62 D at 12 months. Similar to what was seen for Rm and graft thickness, changes in SE also were found to be significant at all postoperative examination times ($P<0.0001$).

Two patients were phakic and no new lens opacification developed. In 2 eyes with prior glaucoma surgery, intraocular pressure

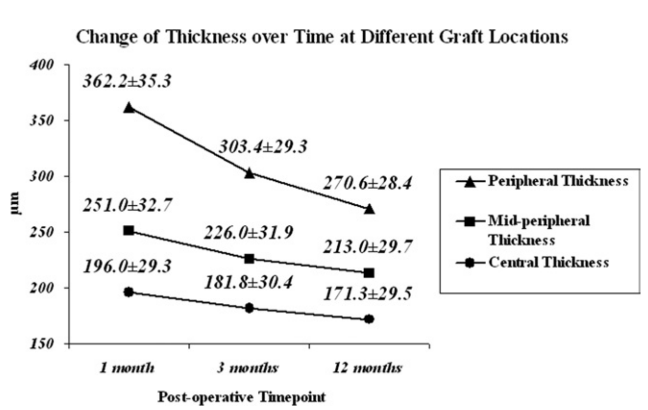

Figure 2. Graph showing variation over time of graft thickness measured at different locations.

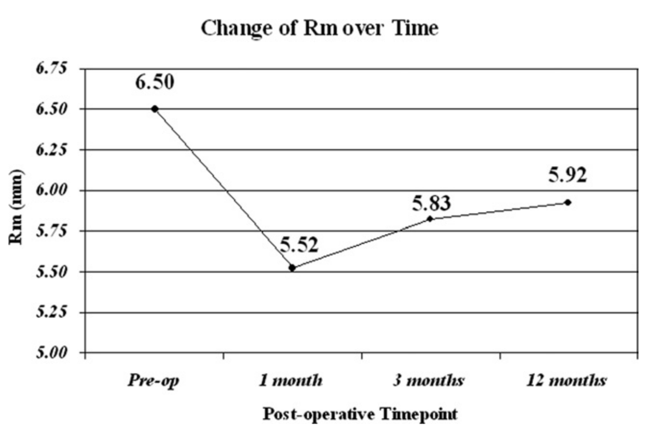

Figure 3. Graph showing variation over time of graft mean radius of posterior curvature (Rm).

remained controlled with ongoing medical treatment. Three patients experienced an intense ocular pain during the first few hours after surgery because of increased intraocular pressure, despite intraoperative peripheral iridectomy; in all cases, the pupillary block was relieved by partial air removal from the anterior chamber (AC). None of the patients experienced any episode or signs of graft rejection during the follow-up.

Discussion

The recently developed procedures of posterior lamellar keratoplasty allow selective replacement of diseased endothelium with minimal changes in the anterior corneal surface. The first studies reporting the advantages of these selective techniques highlighted the corneal stability with a minimal induction of astigmatism.[8,9] Although endothelial keratoplasty initially was thought to be a refractively neutral procedure, several authors have described a mild hyperopic shift in eyes undergoing Descemet's stripping endothelial keratoplasty (DSEK) or DSAEK.[4–6,8]

In this study, the average change in SE between values recorded before and 12 months after surgery was 0.62 D; this was approximately half the amount of refractive shift found in previous series.[5,10] Price and Price[11] found a hyperopic shift of 0.66 D in patients who received grafts dissected manually, but observed no change in refractive error when the microkeratome was used to prepare the donor tissue. No clear reason for this difference was given by the authors.

Previous authors have proposed that the postoperative reduction in corneal power may result from the concave meniscus shape of the donor button, which can be observed easily on slit-lamp examination (Fig 4).[4,12] The increased curvature of the posterior corneal surface enhances its negative refractive power, thus reducing the total refractive power of the cornea.

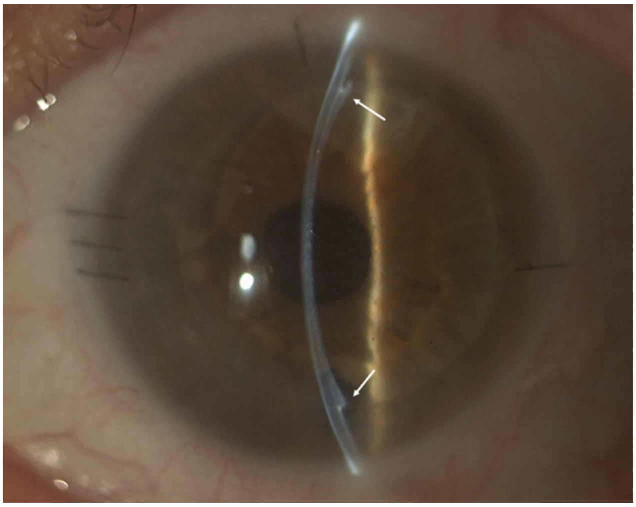

Figure 4. Slit-lamp photograph of a patient obtained 1 month after Descemet's stripping automated endothelial keratoplasty showing a clear recipient cornea with a meniscus-shaped graft attached to its posterior surface. The arrows indicate the sharp, vertical edges of the graft typical of the early postoperative stages.

Holz et al[4] used anterior segment optical coherence tomography to evaluate the corneal profile in 9 patients after DSEK and reported that the edges of the graft decreased in thickness significantly faster than its central part. However, no comprehensive, quantitative measurements of Rm or its changes over time were obtained with this method. One or few thickness measurements poorly reflect the true shape of the graft, which may be far from regular, especially if the microkeratome cut or the trephination, or both, are not properly centered and aligned on the donor tissue. Only multiple measurements, along more meridians (i.e., 0° and 90°, as in this study), can assess accurately the posterior profile of the graft, as done by the Pentacam technology, which also determines the Rm.

Repeatability and reproducibility of Pentacam measurements already have been proven in published studies,[13,14] but the system has not been used to date specifically to evaluate changes in thickness of posterior lamellar grafts. Although it is possible that the accuracy of these measurements may be altered by features inherent to the Pentacam system, the bias, being always present, would be neutralized in serial measurements with the same machine of the same structures. In addition, considering the posterior corneal curvature as a whole, that is, a value resulting from several measurements, reduces the weight of errors obtained in single measurements.

The Pentacam system uses a rotating Scheimpflug camera to visualize directly the posterior cornea, obtaining good quality scans even in corneas with advanced endothelial disease that cannot be usually evaluated by keratometry and topography. To date, it is 1 of the only 2 systems available on the market that are capable of evaluating Rm quantitatively.

Several authors share the opinion that corneal thickness does not affect refraction per se.[12,15,16] Indeed, it is a common observation that patients whose corneas become homogeneously thicker for various reasons (i.e., impending corneal decompensation), do not experience changes in their refraction. On the contrary, if for any reason corneal thickness is affected to a different extent in its different parts, a substantial change in corneal anterior or posterior curvature, or both, results. In this study, the changes measured in Rm related closely to the variations of refraction. Between 1 and 12 months after surgery, the postoperative hyperopic shift decreased progressively along with the overall reduction of corneal thickness in general, but correlated in particular with the difference in thickness between central and peripheral cornea (Table 1). This proves other authors' theory that variations of Rm substantially affect final post-DSAEK refraction.[4,6,12]

The change in Rm over time was secondary to a relatively greater reduction in thickness or edema of the peripheral donor button than the central (25.3% vs. 12.6%). Most probably, early after surgery, aqueous enters easily into the DSAEK graft through the exposed stroma at its edge. As healing takes place, scar tissue formation blocks this inflow and progressive deswelling of the peripheral part of the graft is seen. The Scheimpflug images document these changes at the graft edge, which with time acquires a more beveled shape (Fig 1B) and shows a mild gain in reflectivity (Fig 1C) as a possible effect of scar formation.

Pentacam technology also may be used in future to evaluate whether different characteristics of grafts obtained with the microkeratome (i.e., size, depth of dissection, etc.) may affect final refraction. In addition, other methods used for the preparation of DSAEK grafts, in particular femtosecond laser-assisted dissection, may prove instrumental in obtaining plano donor lenticulas, thus eliminating postoperative changes in refraction.

In conclusion, this study showed that the Pentacam Scheimpflug camera system can be used effectively to evaluate the shape of DSAEK grafts, as well as their effect on postoperative final refraction. The changes of Rm values measured have shown a good correlation with the spherical hyperopic error recorded, with a clear tendency to a decrease over time along with the progressive peripheral graft thinning. Although the extent of the hyperopic shift caused by DSAEK is limited, it should be taken into account when cataract surgery is to be performed at the time of DSAEK, thus improving the predictability of the desired refractive outcome.

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Footnotes and Financial Disclosures

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