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Lower Corneal Haze and Aberrations in DMEK versus DSAEK in Fellow Eyes for Fuchs' Endothelial Corneal Dystrophy

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Abstract

Purpose: To investigate the long term corneal changes in patients with Fuchs' endothelial corneal dystrophy (FECD) contributing to superior postoperative visual outcomes after Descemet membrane endothelial keratoplasty (DMEK) compared to Descemet stripping automated endothelial keratoplasty (DSAEK).

Methods: Using retrospective analysis, we evaluated nine patients with FECD who underwent DSAEK in one eye and DMEK in the fellow eye. Patients were genotyped for the triplet repeat expansion in the *TCF4* gene and imaged using optical coherence tomography, Scheimpflug imaging, and in vivo confocal microscopy through focusing (CMTF).

Results: Eight of nine subjects were genotyped and all were found to harbor the triplet repeat expansion. Average time between endothelial keratoplasty and imaging was 76 $\pm$ 22 and 37 $\pm$ 9 months after DSAEK and DMEK respectively. Mean best spectacle corrected visual acuity (logMAR) was 0.04 $\pm$ 0.05 and 0.11 $\pm$ 0.03 in the DMEK eyes versus DSAEK eyes ($P=0.02$). Posterior corneal higher order aberrations (HOAs) were less in DMEK eyes compared to fellow DSAEK eyes (0.25 $\pm$ 0.06 and 0.66 $\pm$ 0.25 respectively, $P<0.01$). Using CMTF, we found the persistent anterior stromal haze is correlated between right and left eyes ($R=0.73$, $P<0.05$) but total stromal backscattering was higher for DSAEK eyes ($P<0.05$).

Conclusions: DSAEK inherently results in higher total stromal backscattering (haze) compared to DMEK due to the addition of stromal tissue. Lower HOAs of posterior cornea and lower total stromal backscattering (haze) may both contribute to superior visual outcomes after DMEK compared to DSAEK.

Keywords

Endothelial keratoplasty; Fuchs' endothelial corneal dystrophy; in vivo confocal microscopy; optical coherence tomography; Scheimpflug imaging

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Introduction

Over the last 15 years, endothelial keratoplasty (EK) has largely supplanted full thickness penetrating keratoplasty (PK) for surgical treatment of corneal edema stemming from endothelial dysfunction including Fuchs' endothelial corneal dystrophy (FECD).¹ EK procedures maintain structural integrity of the globe and avoid suture related astigmatism and complications.

The two main forms of EK, Descemet stripping automated endothelial keratoplasty (DSAEK) and Descemet membrane endothelial keratoplasty (DMEK) differ mainly in that the former transplants endothelium and Descemet's membrane along with a small portion of stroma and the latter selectively transplants only the endothelium and Descemet's membrane.^{1, 2}

Retrospective data comparing DSAEK and DMEK outcomes suggest DMEK offers faster recovery, superior visual outcomes, and a lower rejection rate but with a higher surgical learning curve and in some cases higher rebubbling rate.^{3–5} The additional donor stroma unique to DSAEK may contribute to increased posterior corneal curvature, hyperopic shift, and greater higher order aberrations (HOAs).^{1, 6–9} A recent randomized controlled trial comparing "ultra-thin" DSAEK (UT-DSAEK) to DMEK for FECD or pseudophakic bullous keratopathy found better best spectacle corrected visual acuity (BSCVA) in the DMEK eyes up to 12 months out from surgery.¹⁰ The same group published data from their trial that lower HOAs in the posterior cornea correlated with better 6 and 12 month visual acuity outcomes in DMEK eyes.¹¹

In this fellow eye study of a genetically homogenous cohort of FECD subjects, we examined the long term optical, anatomical, and ultra-structural / cellular changes of the cornea after DSAEK and DMEK. We examined differences in wavefront aberrations between these EK procedures. Optical coherence tomography (OCT) was used to measure the recipient stromal tissue thickness in all eyes as well as graft stromal tissue thickness in the DSAEK eyes. Additionally, we assessed backscattering (haze) and reflectivity throughout the corneal layers including the anterior stroma and the donor-recipient interface using in vivo confocal biomicroscopy through focusing (CMTF).¹²

Materials and Methods

Subjects

This retrospective study was conducted with informed consent and approved by the institutional review board of The University of Texas Southwestern Medical Center (UTSW) in adherence to the principles of the Declaration of Helsinki. Potential subjects were initially identified by reviewing the UTSW Transplant Services Center records to find all patients who had received DMEK in one eye between January 2014 and January 2017, and DSAEK in the fellow eye at our institution during that timeframe or prior. Inclusion criteria were subjects with Fuchs' endothelial corneal dystrophy who had undergone DSAEK or DMEK for disease severity of >5-mm confluent central guttae with stromal edema based on slit-

lamp examination before onset of bullous keratopathy. Those patients excluded from our study were those with any prior ocular surgery other than cataract surgery before their EK and those with any subsequent corneal surgery after DMEK or DSAEK other than successful DMEK rebubbling (1 eye). Additionally, eyes were excluded if they had additional corneal pathology or scar, history of uveitis or other condition that would predispose to graft failure, or visually significant ocular condition that could impact the outcome of the surgeries or post-operative vision, including any anterior segment, lens, optic nerve or macular pathology. 18 eyes of 9 patients (five men, four women) who underwent DSAEK in one eye followed by DMEK in the fellow eye were included in the study.

Surgical Techniques

The DSAEK and DMEK procedures used in these eyes were done with very little variation to the versions described previously.^{13, 14} A clear corneal incision was used. Standard phacoemulsification was used in all cases when cataract surgery was combined with EK. The only eye that did not have EK combined with cataract surgery had cataract surgery prior to DMEK. The DSAEK donor graft diameters were between 8–8.5 mm with a surgeon requested graft thickness of 125 microns; the DMEK graft size ranged from 7.5–7.75 mm. Of note, none of the donors had a reported history of diabetes mellitus. Stripping of Descemet's membrane was performed in all recipient eyes using a reverse Sinskey hook to score and detach the Descemet's membrane. Care was taken not to disturb the stromal interface during the stripping of Descemet's membrane from the paracentral and central cornea. For the DSAEK eyes, the stripping diameter was not over-sized and peripheral stromal scraping was performed using the Terry Scraper (Moria SA, Antony, France). For DMEK eyes, the stripping was over-sized and peripheral stromal scraping was not performed. The same surgeon (VVM) performed 14 of the 18 EKs, with two other surgeons performing the remaining three surgeries utilizing the same techniques. In nine patients, the same surgeon performed both surgeries on each eye. None of the eyes underwent superficial keratectomy at the time of the EK.

One patient underwent successful rebubbling in the first post-operative week after DMEK. Standard post-operative regimens of prednisolone derivative and fluoroquinolone drops were used and tapered slowly over the first 6 months to one year after the transplant.

Genotyping

Genomic DNA was extracted from leukocytes of peripheral blood samples with Nucleon Blood Extraction Kit (Amersham, Biosciences, Buckinghamshire, UK). The CTG18.1 trinucleotide repeat polymorphism was genotyped using short tandem repeat (STR) and triplet repeat primed polymerase chain reaction (TP-PCR) assays as previously described.^{15–17}

Clinical Evaluation

LogMAR best spectacle-corrected visual acuities (BSCVA) were converted from measurements at post-operative visits that included manifest refraction, slit-lamp biomicroscopy, and intraocular pressure measurement. The BSCVA included in the correlation analysis was the vision obtained closest to the time of Scheimpflug imaging.

Contrast sensitivity testing was performed using the CSV-1000E standardized contrast sensitivity test (Vector Vision, Greenville, Ohio, USA). Monocular testing was performed at the manufacturer recommended distance of 8 ft (2.5 meters) in a dark room. The log contrast sensitivity values provided by the manufacturer for each spatial frequency (3, 6, 12, and 18 cycles/degree) included on the CSV-1000E were used for statistical analysis.

All patients were imaged between April 2017 and May 2019 using the Scheimpflug Pentacam system (Oculus GmbH, Wetzlar, Germany), OCT Avanti system (Optovue, Fremont, California, USA), and *in-vivo* confocal microscopy (IVCM) using the Heidelberg Retinal Tomograph II with Rostock Corneal Module (HRT-RCM) (Heidelberg, Germany). The “touchless” measurements of the Pentacam and OCT were performed before the IVCM. All measurements were made at least 23 months after the second eye’s DMEK surgery and after all sutures had been removed.

Scheimpflug Tomography

The Pentacam rotating Scheimpflug imaging system (Oculus GmbH, Wetzlar, Germany) was used to image all eyes. The system evaluated the corneal wavefront aberrations from the anterior, posterior, and total corneal surfaces within the central 6.0-mm zone. Standardized Scheimpflug imaging of the patients was done as previously reported by our group.¹⁸ The rotating Scheimpflug imaging allows for efficient and accurate measurements of corneal wave-front analysis. The aberrations are expressed as a root mean square (RMS) deviation from a best-fit sphere reference surface. The Pentacam software converts the corneal elevation profile into corneal wave-front data by using the Zernike polynomials with an expansion (possible up to the sixth order).¹⁸ We examined the RMS of the wave-front, as well as the total HOAs and lower order aberrations (LOA) separately.

Optical Coherence Tomography

Using the horizontal and vertical axis OCT images, the central (within 0.5 mm of center) and peripheral (2 mm from center) recipient stroma thickness was measured. The caliper tool in the Avanti analysis software was used to make thickness measurements (Supplemental Figure 1). For each eye, the peripheral measurement was calculated as the mean of four individual measurements (one measurement 2 mm in each direction from center for both the horizontal and vertical OCT slices). The central measurement was calculated as the mean of 6 individual measurements (3 central measurements for both the horizontal and vertical OCT slices).

For DSAEK eyes, the recipient stromal thickness was measured directly as the distance between the epithelium-host stroma interface and the donor-recipient interface. The stromal thickness of DSAEK grafts was calculated as the measured distance from the epithelium-host stroma interface to endothelium minus the measured distance from the epithelium-host stroma interface to donor-recipient interface minus an additional 14 μ m adjustment to account for the thickness of Descemet’s membrane and the endothelium.^{19, 20} For DMEK eyes, the recipient stromal thickness was calculated as the measured distance between epithelium-host stroma interface and the endothelium minus a 14 μ m adjustment to account for the thickness of Descemet’s membrane and the endothelium.^{19, 20}

In Vivo Confocal Microscopy

Confocal imaging was performed using a modified Heidelberg Retinal Tomograph with Rostock Corneal Module (HRT-RCM; Heidelberg Engineering, GmbH, Dossenheim, Germany) in vivo confocal microscope with CMTF software as previously described.^{21, 22} Both eyes were imaged on the same day, with the right eye imaged first. Patients were locally anesthetized with 1 drop of proparacaine. The objective was positioned on the cornea to create a flat field-of-view image in the central cornea. CMTF scans were collected by starting the scan in the anterior chamber and finishing above the epithelium with a constant speed of 60 μm per second. Images were acquired with the acquisition rate set to 30 frames per second on the HRT. To allow quantitative assessment of haze, scans were collected using a constant gain setting by unchecking the “auto brightness” box in the HRT software interface. Each scan was conducted using a gain of 20.²³ At least 3 scans with minimal patient movement were collected within the central area of the cornea. Each CMTF scan contained a 3-D stack of 384×384 -pixel images ($400 \times 400 \mu\text{m}$), with a step size of approximately 2 μm between images.

After image acquisition, CMTF scans were saved as “.vol” files, which could be opened into our in-house software to analyze the 3-D changes in cell morphology and cell/extracellular matrix (ECM) reflectivity.²² The program generates an intensity vs. depth curve, corresponding to the average pixel intensity of each image and the z-depth of that image within the scan, respectively. Prior to analysis, CMTF scans with large amounts of patient movement were discarded. It is well established that small movements during a scan can cause blurring of structures within an image, but do not impact the average backscatter measured in each image.^{12, 21, 22} The relative amount of total corneal backscatter, or haze, associated with the stromal keratocytes and ECM was measured by taking the area under the curve between the location of the basal lamina peak (or top of the stroma) and the endothelial peak. Anterior stromal haze was measured by taking the area under the curve for only the first 50 microns of the stroma. A baseline of 15 was chosen for haze calculations, since this value was below the baseline intensity for the normal stroma and just above the intensity of the anterior chamber. This background value for the anterior chamber remained consistent throughout the duration of the study. Haze was expressed as Confocal Backscatter Units (CBU).

For CMTF analysis, all images were reviewed and measured by a single observer. It was not possible to mask the observer, since it is immediately obvious from the CMTF scans which eyes had a DSAEK interface. However, the analysis procedure followed a strict protocol which did not change between patients. Specifically, the stromal backscatter measurements are based on the basal lamina and endothelial peaks observed in the intensity-depth curve, and a baseline value that was kept the same for all analyses. In addition, the anterior stromal backscatter was always measured for first 50 microns of the stroma. By standardizing the analyses in this way, any potential user bias should be eliminated.

Statistical Evaluation

SigmaPlot (version 12.5; Systat Software, Inc., San Jose, CA, USA) was used for statistical analysis. Paired t-tests were used to compare the mean values of DMEK and DSAEK

variables in fellow eyes. For non-parametric data, the Mann-Whitney rank sum test was used. To account for potential type I errors resulting from multiple comparisons, a Holm-Bonferroni method was applied to P value sets.¹¹ In some cases, Pearson Product Moment correlation was used to assess relationships between variables.

Results

Eight of our nine subjects (those with available DNA) were genotyped, and all were found to harbor an expanded CTG18.1 triplet repeat allele in the *TCF4* gene (Table 1). All patients in the study had had the DSAEK procedure in their first eye and DMEK subsequently in their fellow eye. The average time between DSAEK and imaging was 76 $\pm$ 22 months, and the average time between DMEK and imaging was 37 $\pm$ 9 months (Table 2).

Visual acuity and contrast sensitivity

Mean BSCVA (logMAR) was 0.04 $\pm$ 0.05 and 0.11 $\pm$ 0.03 in the DMEK eyes versus DSAEK eyes ($P=0.02$, Table 2). Contrast sensitivity was similar between DSAEK and DMEK eyes (Table 2).

Wavefront aberrometry

Wavefront aberrometry measurements of the anterior cornea were not statistically different between DMEK and DSAEK. The HOA of the posterior cornea were significantly higher statistically in the DSAEK eyes compared to their fellow DMEK eyes ($P < 0.01$; Table 2). For the total cornea, we found no differences in RMS, LOA, or HOA between the two procedures.

Evaluation of recipient and graft stromal thickness

To further investigate the anatomical changes after EK, we used OCT to measure thickness of the recipient stroma in both eyes as well as the stromal thickness of the graft lenticule in the DSAEK eyes (Supplemental Figure 1). Recipient stromal thickness in fellow eyes was the same after DMEK or DSAEK, both centrally and peripherally (Supplemental Figure 2). The stromal thickness of DSAEK grafts ranged from 72.7 to 215 microns; 133 $\pm$ 46.2 (mean $\pm$ SD) centrally and from 87.0 to 259 microns; 158 $\pm$ 54.2 (mean $\pm$ SD) peripherally. The total stromal thickness was 28% greater in DSAEK eyes as compared to DMEK eyes centrally (579 $\pm$ 87 versus 452 $\pm$ 40, $P < 0.001$) and 30% greater in DSAEK eyes peripherally (640 $\pm$ 101 versus 491 $\pm$ 37, $P < 0.001$) (Supplemental Figure 3). Although we found no correlation to contrast sensitivity, anterior HOA, or posterior HOA, we found that thicker DSAEK grafts tend to have higher total corneal HOA ($R = 0.752$, $P=0.03$).

Confocal biomicroscopy

Figure 1 shows representative images of CMTF scans collected using the HRT-RCM after DSAEK and DMEK in the same patient. The location of the donor-recipient interface was easily visualized in 3-D CMTF reconstructions after DSAEK (Fig. 1a), but not after DMEK (Fig. 1b). In general, cell activation and diffuse haze was observed in the anterior stroma in both DSAEK and DMEK corneas (Fig. 1c&d). In the mid-stroma, keratocyte nuclei

appeared similar to that observed in the normal cornea (Fig. 1e&f). Reflective particles were observed at the donor-recipient interface following both DSAEK and DMEK (Fig. 1 g&h), but these were more numerous and prominent after DSAEK. The corneal endothelium generally appeared normal, although cell density was somewhat variable. Other confocal observations include increased anterior stromal reflectivity in most cases (with cell activation in some cases), needle-like structures in stroma in some cases, and increased keratocyte reflectivity at the DSAEK interface in some cases (Figure 2). Fragmented cells were observed in the DSAEK graft in one patient (Figure 2h). The peripheral stromal interface was scraped in the DSAEK eyes but not the DMEK eyes which could contribute to some observed confocal microscopic findings.

The results of quantitative CMTF analysis are shown in Table 3. The total stromal backscattering was higher after DSAEK as compared to DMEK ($34,669 \pm 7,928$ CBU vs. $28,888 \pm 7,147$ CBU, $P = <0.05$). This 20.0% increase in backscatter corresponds to a 28% increase in stromal thickness which is inherent to inclusion of stromal tissue in a DSAEK graft. Using CMTF scans, we noted increased reflectivity in the anterior 50 microns of the stroma in all DMEK and DSAEK eyes imaged. There was a trend for this anterior corneal haze to be higher in DSAEK, but this did not reach statistical significance ($5,979 \pm 642$ CBU vs $5,589 \pm 1,283$ CBU, $P = 0.27$). Interestingly, the amount of anterior haze was correlated between fellow eyes ($R = 0.73$, $P = <0.05$).

Discussion

The motivation of this study was to understand the long-term post-operative changes to the cornea contributing to the superior visual outcomes after DMEK relative to DSAEK. To our knowledge, this is the first study to combine Scheimpflug, OCT, and confocal imaging to compare these related EK procedures in fellow eyes.

FECD is the leading indication for keratoplasty in the United States as well as the developed world.^{24, 25} Eight of the nine FECD subjects in this study were genotyped and all were found to harbor the the CTG18.1 triplet repeat expansion in the *TCF4* gene which accounts for 70% of cases in whites.²⁶ These results help establish this FECD cohort as genetically homogenous and therefore particularly well-suited for a rigorous comparative fellow-eye study to examine the post-operative corneal changes after DMEK and DSAEK.²⁶ We previously reported that the modified Krachmer grade of disease severity was greater in FECD cases with the *TCF4* expansion compared to those without the expansion.²⁶ FECD subjects with the expansion had a higher central corneal thickness and were more likely to undergo keratoplasty than their FECD counterparts without the expansion.

Consistent with previous reports comparing DSAEK with DMEK in fellow eyes, we found the BSCVA and contrast sensitivity to be better in the DMEK eyes and note that this difference was detected ~6 and ~3 years after DSAEK and DMEK respectively in our cohort.^{6, 8, 27}

In 2009, our group reported that the posterior corneal HOAs of the central 6 mm assessed by Scheimpflug imaging were significantly higher after DSAEK compared to PKP.¹⁸ In 2012,

Rudolph et al showed that HOAs are significantly higher in the posterior cornea in most parameters except coma when comparing DSAEK to DMEK.⁷ The thickness and shape of the DSAEK graft are thought to contribute to posterior corneal HOAs.²⁸

In this fellow-eye study, we that HOAs are significantly higher in the posterior surface of the DSAEK eyes compared to the DMEK eyes. Although the individual HOAs of the posterior cornea including spherical aberration and coma (horizontal and vertical) were not statistically different, the combined effect of all HOAs resulted in an increased posterior cornea HOA measurement in DSAEK eyes. We found that total cornea HOA is no different between DMEK and DSAEK in fellow eyes. The only previous fellow eye study comparing DSAEK to DMEK in terms of post-operative HOAs found no difference in total corneal HOAs using the Galilei system which is unable to differentiate between the anterior and posterior cornea.⁸ In contrast, our fellow eye study utilized the Pentacam system to evaluate the differences in HOAs in the anterior and posterior surfaces. A recent randomized clinical trial by Duggan et al found that the posterior corneal surface had significantly less coma and total HOAs in DMEK compared with UT-DSAEK at 6 and 12 months post-operatively which correlated to BSCVA.¹¹

We utilized OCT to precisely measure the recipient stromal thickness in all eyes as well as the graft stromal thickness of the DSAEK grafts. We found no difference in the central or peripheral recipient stromal thickness between the fellow eyes suggesting that both types of EK grafts deturgesce the recipient stromal tissue comparably. Of note, we found a positive correlation between stromal thickness of DSAEK graft and total cornea HOA. Although our study may not have been adequately powered to correlate stromal thickness of DSAEK grafts to BSCVA, it should be noted that a randomized clinical trial by Dickman et al found BSCVA to be significantly better after UT-DSAEK compared to DSAEK at 6 and 12 months.²⁹

Confocal biomicroscopy revealed qualitative findings of persistent subepithelial haze, recipient stromal needle-like structures, and reflective donor-recipient interface particles after DSAEK and DMEK as previously reported in subjects with FECD.^{30, 31} In this study, the use of the CMTF methodology enabled quantitative comparative assessment of haze in the fellow eyes. Previously, our group had used CMTF to detect keratocyte activation and anterior stromal reflectivity that was significantly greater than the mean donor-recipient interface reflectivity after DSAEK for FECD.³¹ In this study, we noted increased reflectivity in the anterior 50 microns of the stroma in all DMEK and DSAEK eyes imaged and the amount of anterior haze was correlated between fellow eyes. Amin SR et al reported that anterior cellular and structural changes occur early in the FECD disease course and suggested that the chronicity of these changes might account for their incomplete resolution after EK.³² Although there was a trend for the anterior haze to be higher in DSAEK, this observation did not reach statistical significance. Regardless the type of EK procedure, some residual anterior stromal haze appears to persist in FECD patients many years after successful transplant surgery.

A notable observation in this fellow eye study is that backscatter (haze) is higher in the stroma after DSAEK compared to DMEK. Backscatter is measured by integrating over the

entire stroma. The additional stromal tissue of the DSAEK graft results in a thicker stroma contributing to increased backscatter or haze relative to DMEK. In this study, backscatter and stromal thickness were 20% and 28% higher, respectively, in DSAEK corneas. Since corneal backscatter generally decreases with depth, it is not surprising that the percent increase in total stromal backscatter is somewhat less than the amount of tissue added to the posterior stroma. A recent study in which stromal light scatter was measured using Pentacam densitometry noted more light scattering in the anterior stroma versus posterior stroma in both DSAEK and DMEK patients, consistent with our results. Comparison of average light scatter (normalized for thickness) with the Pentacam did not detect a difference between DMEK and DSAEK patients. This is consistent with our finding that total stromal light scatter after DSAEK is greater than after DMEK, since stromal thickness is larger.³³ An additional contributing factor to the observed increased backscatter after DSAEK may be increased keratocyte reflectivity of the donor-recipient interface, which we noted in some cases.

We acknowledge limitations of our retrospective study including the small sample size limiting our detection of differences between the forms of EK. The significant variation in the timing of the post-operative evaluation (76 months for DSAEK, 37 months for DMEK) may have contributed to higher HOAs and haze in the DSAEK eyes with older grafts. The sequential timing of DSAEK and then DMEK could introduce confounding factors given that the worse eye was operated on first and underwent DSAEK. However, we waited approximately 2–3 years until the fellow eyes had reached a comparable FECD disease severity (>5-mm confluent central guttae with stromal edema before onset of bullous keratopathy) before performing DMEK. Despite these limitations, this fellow eye study of a genetically homogenous cohort of FECD subjects gives some insights into corneal remodeling after these related EK procedures.

In conclusion, our fellow eye study comparing DSAEK to DMEK in subjects with FECD found superior visual acuity in the DMEK eyes many years after EK surgery. Our results confirm that posterior total HOAs are higher in DSAEK versus DMEK. To our knowledge, we report for the first time that total stromal backscatter or haze is higher in DSAEK eyes versus DMEK eyes. While the anterior stromal haze is comparable in fellow FECD eyes after both forms of EK, the additional stromal tissue of DSAEK graft and increased keratocyte reflectivity at donor-recipient interface may account for the increased stromal backscatter after DSAEK. Lower posterior corneal HOAs and lower stromal backscattering (haze) may both contribute to the better visual outcomes seen after DMEK.

Supplementary Material

Refer to Web version on PubMed Central for supplementary material.

Conflict of Interest and Source of Funding:

The authors have no financial interest in any of the issues contained in this article and have no proprietary or conflict of interest in the development or marketing of or materials used in this study. This study was supported by grants R01EY022161 (VVM), R01 EY013322 (WMP) and P30 EY030413 (VVM & WMP) from the National Institutes of Health, Bethesda, MD and an unrestricted grant from Research to Prevent Blindness, New York.

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Figure 1.

Images from Confocal Microscopy Through Focusing (CMTF) scans collected using the Heidelberg Retinal Tomograph with Rostock Corneal Module (HRT-RCM) after Descemet stripping automated endothelial keratoplasty (a,c,e,g,i) and Descemet membrane endothelial keratoplasty (b,d,f,h,j) in the same patient. a&b) 3-dimensional reconstructions of the confocal z-stack. c&d) sub-epithelial images showing cell activation and diffuse haze. e&f) images from the mid-stroma showing normal keratocyte nuclei. g&h) reflective particles observed at the donor-recipient interface. i&j) corneal endothelium appears normal.

Figure 2.

Confocal images from Descemet stripping automated endothelial keratoplasty (a-h) and Descemet membrane endothelial keratoplasty (i-l) eyes. a) sub-epithelial cell activation and haze. b) reflective particles in the host stroma. c) reflective particles at the donor-recipient interface. d) normal appearing stromal cells in the graft stroma. e) possible myofibroblast transformation in the sub-epithelial region. f) needle-like structures in the host stroma. g) apparent reflective cell nuclei in the donor-recipient interface. h) fragmented cells in the graft stroma. i) highly reflective stromal tissue in the sub-epithelial region. j) needle-like structures in the host stroma. k) reflective particles in the host stroma. l) needle-like structures observed at the donor-recipient interface in one eye.

Table 1.Patient Demographics and *TCF4* Genotyping Results

Patient	Gender	Race	<i>TCF4</i> CTG18.1 Alleles	Age at Postoperative Imaging
1	Male	White	18, 91	71
2	Male	White	12, >100	83
3	Male	White	64, >100	67
4	Female	White	18, >100	72
5	Female	White	24, >100	68
6	Male	White	12, >100	73
7	Female	White	12, >100	67
8	Male	White	15, 81	76
9	Female	White	NA	83
Mean				73
Standard Deviation				5.9

NA=not available

Alleles with >40 CTG triplet repeats in bold

Table 2.

Inter-Eye Comparisons of DMEK Eye to Fellow DSAEK Eye

	DMEK (n=9)	DSAEK (n=9)	P-value
Time between surgery and imaging (months)	36.8 ± 9.0	76.3 ± 22.0	<0.001
BCVA (logMAR)	0.04 ± 0.05	0.11 ± 0.03	0.02
Contrast sensitivity (log units)			
A (3.0 cycles per degree)	1.417 ± 0.228	1.362 ± 0.250	0.47
B (6.0 cycles per degree)	1.556 ± 0.450	1.554 ± 0.241	0.99
C (12.0 cycles per degree)	1.184 ± 0.409	0.783 ± 0.388	0.03
D (18.0 cycles per degree)	0.517 ± 0.435	0.449 ± 0.355	0.59
Wavefront aberrometry (micrometers) (n=8)			
Anterior Cornea			
RMS	2.21 ± 0.85	2.14 ± 0.87	0.80
LOA	2.10 ± 0.88	2.06 ± 0.87	0.88
HOA	0.63 ± 0.15	0.45 ± 0.19	0.06
SA	0.33 ± 0.11	0.35 ± 0.14	0.65
V Coma	0.14 ± 0.22	0.02 ± 0.09	0.22
H Coma	-0.04 ± 0.28	-0.19 ± 0.31	0.81
Posterior Cornea			
RMS	0.92 ± 0.27	1.78 ± 0.65	0.01
LOA	0.88 ± 0.27	1.64 ± 0.64	0.02
HOA	0.25 ± 0.06	0.66 ± 0.25	<0.01
SA	-0.14 ± 0.11	-0.17 ± 0.14	0.58
V Coma	-0.02 ± 0.07	0.03 ± 0.16	0.33
H Coma	0.02 ± 0.04	0.09 ± 0.24	0.47
Total Cornea			
RMS	2.39 ± 0.82	2.42 ± 0.94	0.89
LOA	2.28 ± 0.82	2.27 ± 0.98	0.97
HOA	0.69 ± 0.15	0.78 ± 0.17	0.28

DMEK=Descemet membrane endothelial keratoplasty

DSAEK=Descemet stripping automated endothelial keratoplasty

BSCVA=best spectacle corrected visual acuity

Wavefront aberrometry values expressed as root mean square with standard deviation

RMS=root mean square

LOA=lower order aberrations

HOA=higher order aberrations

SA=spherical aberration

V Coma=vertical coma

H Coma=horizontal coma

P-values by paired t-test; significant values (P < 0.05 after Holm-Bonferroni adjustment) in bold

Table 3.

Comparisons of DMEK Eye to Fellow DSAEK Eye Using a Modified HRT-RCM In Vivo Confocal Microscope with CMTF

Outcome Measure	DMEK (n=9)	DSAEK (n=9)	P-Value
Total stromal backscatter (CBU)	28,888 $\pm$ 7,147	34,669 $\pm$ 7,928	<0.05
Anterior corneal haze (CBU)	5,589 $\pm$ 1,283	5,979 $\pm$ 642	0.27
Correlation of anterior haze between fellow eyes	R = 0.73		<0.05

DMEK=Descemet membrane endothelial keratoplasty

DSAEK=Descemet stripping automated endothelial keratoplasty

HRT-RCM=Heidelberg Retinal Tomograph with Rostock Corneal Module

CMTF=Confocal Microscopy Through Focusing

CBU=Confocal Backscatter Units