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## Clinical outcomes of modern lamellar keratoplasty techniques

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# Chapter 4

## Optical quality of the cornea after Descemet membrane endothelial keratoplasty

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## ABSTRACT

**Purpose.** To evaluate corneal higher order aberrations (HOAs) and backscattered light before and after Descemet membrane endothelial keratoplasty (DMEK) and their correlation with visual outcome.

**Design.** Retrospective study.

**Methods.** In a total of 118 consecutive eyes of 118 patients who underwent uneventful DMEK for Fuchs endothelial dystrophy at a tertiary referral center, best spectacle-corrected visual acuity (BSCVA), corneal HOAs and backscattered light were evaluated preoperatively and at 6 months postoperatively. Outcome data were compared to an age-matched control group with uncomplicated eyes (n=27).

**Results.** Compared to the control group, Fuchs endothelial dystrophy eyes, before as well as 6 months after DMEK showed higher values of anterior and posterior HOAs and backscattered light ( $P<.033$ ). Postoperative anterior HOAs and backscattered light (0-2 mm) were associated with lower 6 months BSCVA (positively related with LogMAR BSCVA) ( $P\leq.020$ ). Anterior corneal HOAs did not change from preoperative to 6 months after DMEK ( $P=.649$ ), while total posterior HOAs (RMS 3<sup>rd</sup> to 6<sup>th</sup> Zernike order), and haze decreased ( $P<.001$ ).

**Conclusions.** Anterior and posterior corneal HOAs, as well as backscattered light from the cornea were elevated in eyes suffering from Fuchs endothelial dystrophy and remained higher throughout 6 months after DMEK. If present, anterior surface irregularities and anterior corneal haze may be the most important limiting factors in visual rehabilitation after DMEK.

**Keywords:** Cornea, Descemet membrane endothelial keratoplasty (DMEK), corneal transplantation, endothelium, optical quality, Fuchs endothelial dystrophy, higher order aberrations, backscattered light, densitometry

## INTRODUCTION

In the last decade, we have introduced various techniques for endothelial keratoplasty (EK), popularized as 'deep lamellar endothelial keratoplasty' (DLEK), 'Descemet stripping (automated) endothelial keratoplasty' (DSEK/DSAEK) and Descemet membrane endothelial keratoplasty (DMEK) for the management of corneal endothelial disease.<sup>1-3</sup> By replacing only the inner layers of the cornea, the anterior corneal surface is not compromised, minimizing the risk of surgery-induced anterior corneal surface irregularities and providing faster and more complete visual rehabilitation.<sup>4-8</sup>

However, it has been shown that, also after EK, the final visual outcome may be limited by corneal irregularities or light scatter deriving from the cornea.<sup>2,9,10</sup> In DSEK/DSAEK, subnormal visual acuities of 20/30 (0.6) or less are frequently encountered, and have been mentioned to result from irregularities at the stroma-to-stroma interface, haze, or the presence of donor posterior stroma itself.<sup>10-15</sup> Furthermore, anterior corneal surface irregularities in the postoperative EK cornea have been recognized as a potential cause for incomplete visual recovery.<sup>9,16,17</sup>

With DMEK, only an isolated Descemet membrane (DM) and its endothelium is transplanted, apparently resulting in near normal anatomical corneal restoration and visual outcomes up to 20/17 (1.2) or even 20/13 (1.5).<sup>2,18</sup> If so, a transplanted DMEK cornea may approach the optical quality of a virgin cornea. The purpose of our study was to find evidence for near normal recovery of optical quality after DMEK by evaluating HOAs and back scattered light before and after DMEK in a large group of eyes operated on for Fuchs endothelial dystrophy. These parameters were compared to those in virgin corneas to determine to what extent donor-to-host interface irregularities or other postoperative corneal abnormalities may affect the final visual outcome after DMEK.

## METHODS

### Subjects

From a total of 192 consecutive eyes of 165 patients without clinically significant graft detachment or delayed corneal clearance after DMEK surgery for Fuchs endothelial dystrophy (stage 2 - 4),<sup>19</sup> 118 eyes were included in our retrospective study. In case of a bilateral DMEK (n=27), only the initial DMEK eye was included. Eyes with visual impairment due to maculopathy (n=14), optic neuropathy (n=2), or amblyopia (n=1) were excluded. Also, preexisting corneal scarring (n=2) and posterior capsular opacities (n=2) at the 6 months follow-up were exclusion criteria. Furthermore, eyes with incomplete postoperative follow-up data (n=16) or Pentacam (Oculus, Wetzlar, Germany) measurements not meeting acceptable criteria according to the Pentacam software indications

(n=10) were excluded. Of the 118 eyes of 118 patients (53 male, 65 female) 30 were phakic and 88 pseudophakic. Mean age was 66 ( $\pm 12$ ) years (range, 33 to 89 years). An age-matched control group of 27 eyes (23 phakic, 4 pseudophakic) of 27 participants (average age 64 ( $\pm 14$ ) years ( $P=0.434$ ); 12 male and 15 female) with no history of ocular disease or surgery, except for phacoemulsification in 4 eyes, was recruited for comparison (Table 1).

All participants signed an informed consent for research participation, conducted in compliance with the Institutional Review Board (Dutch 'METC' board) and Informed Consent requirements; this retrospective study of prospectively collected data was conducted according to the Declaration of Helsinki, and registered at [www.clinicaltrials.gov](http://www.clinicaltrials.gov) (Study registration NCT00521898).

**Table 1.** Demographics of Descemet membrane endothelial keratoplasty eyes and control eyes

	DMEK eyes	Control eyes	<i>P</i> -value (DMEK-controls)
n=	118	27	
Male / Female	53 / 65	12 / 15	
Mean age (Years)	66 ( $\pm 12$ )	64 ( $\pm 14$ )	0.434
Age range (Years)	33 - 89	38 - 86	
Phakic / Pseudophakic	30 / 88	23 / 4	

DMEK: Descemet membrane endothelial keratoplasty

### Surgical procedure

All DMEK surgeries were conducted as previously described.<sup>20</sup> In short, from corneoscleral buttons stored by organ culture at 31° C for one week, DM was stripped off, so that a 9.5-mm diameter flap of posterior DM with its endothelial monolayer was obtained.<sup>21</sup> Owing to the elastic properties of the membrane, a 'Descemet-roll' formed spontaneously with the endothelium at the outer side. Each Descemet-roll was then stored 'free-floating' in organ culture medium until the time of transplantation.<sup>21</sup>

In all eyes, a YAG-laser peripheral iridotomy was made at 12 o'clock, 1 to 2 weeks before surgery (because patients were requested to lie in a supine position for several hours, Bell's phenomenon may render an iridotomy at the 6-o'clock position ineffective). After the eyes were anesthetized with retrobulbar injection (4 ml 1% ropivacain hydrochloride with 150IU Hyason, Riemser Pharma GmbH, Greifswald, Germany), ocular massage, oculopressure with a Honan balloon for 10 minutes, and patient positioning in the anti-Trendelenburg position were done. Three side ports were made, the anterior chamber was filled with air, and a circular portion of DM was scored and stripped from the posterior stroma with a reversed Sinsky hook (D.O.R.C. International, Zuidland, The Netherlands), thereby performing a 9.0-mm diameter 'descemetorhexis'.<sup>20,22</sup> A 3.0-mm tunnel incision was made at the limbus for insertion of the graft.<sup>20</sup>

The donor Descemet-roll was stained with 0.06% trypan blue solution (VisionBlue™, D.O.R.C. International), and sucked into a custom-made injector (D.O.R.C. International).<sup>20</sup> The donor Descemet roll was inserted into the anterior chamber and the graft was oriented endothelial side down (donor DM facing recipient posterior stroma). The graft was centered, unfolded, and lifted onto the recipient posterior stroma by careful, indirect manipulation of the tissue with air and fluid. The anterior chamber was completely filled with air for at least 60 minutes followed by an air-liquid exchange to pressurize the eye.<sup>20</sup>

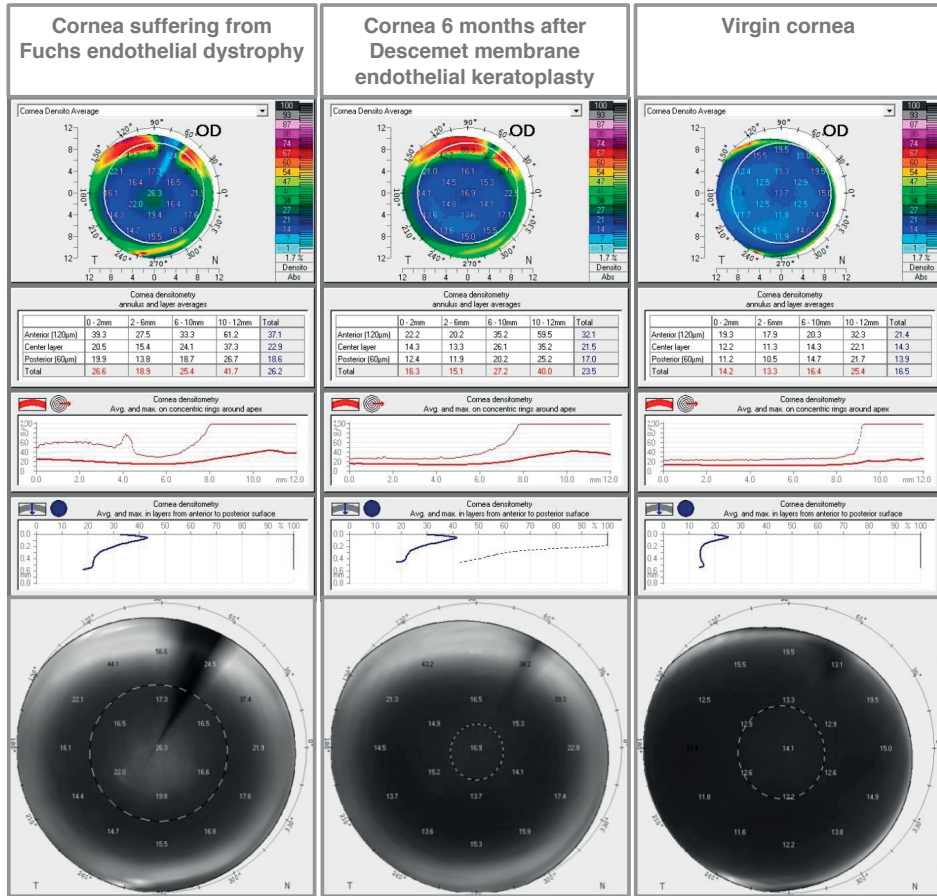
## Examinations

All eyes of participants underwent complete ophthalmologic evaluation and Pentacam rotating Scheimpflug imaging examination. DMEK eyes were examined before and at 1, 3 and 6 months after surgery. Best spectacle-corrected visual acuity (BSCVA) and Pentacam measurements of the preoperative and 6 months postoperative examinations were used for evaluation. During Pentacam examination, the automatic release mode was used to eliminate operator-induced errors. Only good quality images of the front and back corneal surfaces were used for analysis.

BSCVA was measured using a forced choice test with a 100% contrast Snellen projection letter chart at 6 meters in mesopic lighting conditions, and was based on the Snellen letter size for which at least 4 out of 5 optotypes were recognized. After converting BSCVA values to LogMAR, calculations were performed.

Corneal HOAs were calculated using the Pentacam software (software version 1.17) for Zernike analysis based on height data only, with an ellipsoid fixed eccentricity as a reference, which was from before the release of the Pentacam software providing HOAs based on wavefront data.<sup>23</sup> The software allowed evaluation of HOAs of both anterior and posterior corneal surfaces. The different refractive indices for air, corneal tissue and aqueous did not have any effect on the data of the Zernike coefficients.<sup>23</sup> The HOAs in the central 6-mm area up to the sixth Zernike order were analyzed. For each pair of Zernike terms, one value for its contribution was calculated by Zernike vector analysis.<sup>23</sup> Combinations of individual Zernike terms and total HOAs for each Zernike order were defined as the root mean square (RMS).

Backscattered light was examined in different layers and zones throughout the cornea with the Pentacam 'corneal densitometry' display (Figure 1). To standardize ambient light conditions, all measurements were performed in a windowless clinical assessment room with a uniform ambient light level of 4 lux as measured by a luxmeter (Voltcraft BL-10 L Luxmeter, Conrad Electronic SE, Hirschau, Germany). Additionally, it was analyzed whether the "background" grey scale outside the cornea of the Pentacam examinations was stable over time for randomly selected cases. Corneal density was quantified on a scale from 0 (no obscuring) to 100 (completely opaque). The software allowed for comparison of the corneal densitometry (backscattered light) in 3 different fixed corneal



**Figure 1.** Examples of backscatter images of a cornea suffering from Fuchs endothelial dystrophy before and 6 months after Descemet membrane endothelial keratoplasty and of a healthy cornea. Note that backscatter (densitometry) values decreased from (Left) preoperative to (Middle) 6 months postoperative, but remained higher than for (Right) the normal cornea.

layers (anterior layer (anterior 120 µm), central layer, posterior layer (posterior 60 µm) as well as in fixed corneal concentric rings around the apex (central 0-2 mm, 2-6 mm, 6-10 mm, 10-12 mm)).<sup>23</sup> For the analysis, we evaluated the total corneal densitometry (backscattered light), as well as the 3 different fixed layers in the 0-2 and 2-6 mm zone.

**Statistical analysis**

Statistical analyses were performed using SPSS Statistics 20 and R 2.15.1.<sup>24</sup>

Paired t-tests were used to compare preoperative and postoperative measures of HOAs and backscatter for the DMEK group. Because of the high volume of tests performed, alpha inflation and power loss were minimized by controlling the false discovery rate



using the method by Benjamini and Hochberg.<sup>25</sup> A *P*-value of  $<.05$  after correction was considered statistically significant.

For comparison between the DMEK and control group, a multivariate analysis of covariance (MANCOVA analysis) was performed with age as a covariate to correct for this parameter. Pearson correlations were obtained to assess relationships between BSCVA, HOAs and backscattered light. To determine the unique relation of each parameter with postoperative BSCVA and to analyze all parameters simultaneously, a ridge regression analysis (which was necessary due to the high correlations between the optical quality parameters, which leads to unstable regression weights) was carried out for DMEK eyes versus controls with 6 months postoperative LogMAR BSCVA as a dependent variable, and HOAs and backscattered light, along with preoperative LogMAR BSCVA and patient demographics as predictor variables. The relative importance of each predictor is presented as scaled estimate: representing a small, medium or large effect (values of 0.10, 0.31 or 0.58 respectively). The outcomes of this analysis were corrected for the other included parameters.

## RESULTS

In the DMEK group, average LogMAR BSCVA improved from 0.42 ( $\pm 0.24$ ) preoperatively to 0.08 ( $\pm 0.13$ ) at 6 months postoperatively ( $P < .001$ ), representing an improvement in Snellen equivalent of 20/50 (0.4) before to 20/25 (0.8) after DMEK (Table 2). Average LogMAR BSCVA in the control group was -0.02 ( $\pm 0.08$ ) (20/20 (1.0) Snellen equivalent), which differed from BSCVA in pre- as well as postoperative DMEK eyes ( $P < .001$ ) (Table 2).

From preoperative to 6 months postoperatively, anterior HOAs did not change in DMEK eyes ( $P > .1$ ) (Figure 2 and Table 2). All posterior HOAs decreased ( $P < .025$ ), except for trefoil and RMS 5th and 6th order ( $P > .3$ ) (Figure 2 and Table 2). All densitometry (backscattered light) values improved from preoperative to 6 month postoperatively ( $P < .001$ ) (Figure 1 and Table 2).

Compared to the control eyes, DMEK eyes showed higher values of anterior and posterior HOAs (RMS 3rd to 6th Zernike order) and backscattered light ( $P < .033$ ) before and 6 months after surgery (Figures 1 and 2 and Table 2).

With Pearson analysis, most optical quality parameters showed a positive correlation with postoperative LogMAR BSCVA (i.e. negatively affecting Snellen BSCVA), and backscattered light parameters correlated with HOAs (Table 3). Regression analysis showed that the most important predictors for postoperative BSCVA were preoperative BSCVA and patient age ( $P < .001$ ) (Table 4). In addition, anterior backscattered light (0-2 mm zone) and anterior HOAs showed a significant positive relation with postoperative LogMAR BSCVA, i.e. negatively affecting Snellen BSCVA ( $P = .015$  and  $P = .020$ , respectively) (Table 4). All other variables were not related with postoperative BSCVA ( $P > .05$ ).

**Table 2.** Best spectacle-corrected visual acuity, corneal higher order aberrations and densitometry (backscattered light) in the Descemet membrane endothelial keratoplasty group (preoperative and at 6 months follow up) and in the control group

	DMEK eyes (n=118)		Control eyes (n=27)		6m FU DMEK – control eyes	
	Pre op (mean (±SD))	6m FU (mean (±SD))	(mean (±SD))	P-value*	DMEK eyes Pre op – 6m FU	P-value**
BSCVA (LogMAR)	0.42 (±0.24)	0.08 (±0.13)	-0.02 (±0.08)	<b>0.000</b>		<b>0.000</b>
Central corneal thickness (µm)	660 (±79)	519 (±38)	554 (±33)	<b>0.000</b>		<b>0.000</b>
HOAs in central 6 mm (µm)						
Anterior (RMS 3rd to 6th order)	0.50 (±0.20)	0.51 (±0.18)	0.42 (±0.10)	0.649		<b>0.032</b>
Posterior (RMS 3rd to 6th order)	1.63 (±0.92)	1.17 (±0.57)	0.73 (±0.13)	<b>0.000</b>		<b>0.001</b>
Densitometry						
Anterior 0 - 2 mm	39.0 (±13.2)	27.0 (±7.0)	21.1 (±3.5)	<b>0.000</b>		<b>0.001</b>
Anterior 2 - 6 mm	31.6 (±8.7)	25.2 (±6.2)	20.7 (±4.7)	<b>0.000</b>		<b>0.001</b>
Central 0 - 2 mm	20.1 (±4.7)	15.9 (±2.5)	14.0 (±2.2)	<b>0.000</b>		<b>0.001</b>
Central 2 - 6 mm	17.7 (±3.9)	15.7 (±3.1)	14.0 (±3.3)	<b>0.000</b>		<b>0.022</b>
Posterior 0 - 2 mm	21.2 (±4.6)	14.8 (±2.3)	13.0 (±2.1)	<b>0.000</b>		<b>0.001</b>
Posterior 2 - 6 mm	17.9 (±4.0)	15.4 (±3.1)	12.9 (±2.7)	<b>0.000</b>		<b>0.001</b>

BSCVA = Best spectacle-corrected visual acuity

mm = millimeter

µm = micrometer

DMEK = Descemet membrane endothelial keratoplasty

FU = Follow-up

SD = Standard deviation

RMS = Root mean square

P-values corrected for alpha-inflation with Benjamini and Hochberg

"Bold" = statistically significant

\* = Paired T-test

\*\* = MANCOVA (multivariate analysis of covariance) analyses (corrected for age)

**Table 3.** Pearson correlations between higher order aberrations (in the 6 mm central zone), densitometry (backscattered light) and LogMAR best visual acuity in control eyes and eyes 6 months after Descemet membrane endothelial keratoplasty

Pearson correlations at 6 months follow up											
	BSCVA (LogMAR)	Anterior HOAs (RMS 3rd to 6th order)	Posterior HOAs (RMS 3rd to 6th order)	Anterior densitometry (0-2 mm)	Anterior densitometry (2-6 mm)	Posterior densitometry (0-2 mm)	Posterior densitometry (2-6 mm)				
BSCVA (LogMAR)	1	0.427**	0.364**	0.371**	0.343**	0.244**	0.254**				
	Significance (2-tailed)	0.000	0.000	0.000	0.000	0.003	0.002				
	n=	145	145	145	145	145	145				
Anterior HOAs (RMS 3rd to 6th order)	0.427**	1	0.438**	0.366**	0.278**	0.112	0.160				
	Significance (2-tailed)	0.000	0.000	0.000	0.001	0.179	0.054				
	n=	145	145	145	145	145	145				
Posterior HOAs (RMS 3rd to 6th order)	0.364**	0.438**	1	0.299**	0.346**	0.185*	0.364**				
	Significance (2-tailed)	0.000	0.000	0.000	0.000	0.026	0.000				
	n=	145	145	145	145	145	145				
Anterior densitometry (0-2 mm)	0.371**	0.366**	0.299**	1	0.891**	0.573**	0.451**				
	Significance (2-tailed)	0.000	0.000	0.000	0.000	0.000	0.000				
	n=	145	145	145	145	145	145				
Anterior densitometry (2-6 mm)	0.343**	0.278**	0.346**	0.891**	1	0.595**	0.612**				
	Significance (2-tailed)	0.000	0.001	0.000	0.000	0.000	0.000				
	n=	145	145	145	145	145	145				
Posterior densitometry (0-2 mm)	0.244**	0.112	0.185*	0.573**	0.595**	1	0.818**				
	Significance (2-tailed)	0.003	0.179	0.026	0.000	0.000	0.000				
	n=	145	145	145	145	145	145				
Posterior densitometry (2-6 mm)	0.254**	0.160	0.364**	0.451**	0.612**	0.818**	1				
	Significance (2-tailed)	0.002	0.054	0.000	0.000	0.000	0.000				
	n=	145	145	145	145	145	145				

BSCVA = Best spectacle-corrected visual acuity      HOAs = Higher order aberrations      RMS = Root mean square  
 \* = Correlation is significant at the 0.05 level (2-tailed)      \*\* = Correlation is significant at the 0.01 level (2-tailed)

**Table 4.** Ridge regression analysis, with 6 months postoperative LogMAR best spectacle-corrected visual acuity as a dependent variable, and higher order aberrations, densitometry (backscattered light), lens status and demographics as predictor variables

Variable	Scaled estimate	P-value
Pre op logMAR BSCVA	0.316	<b>0.000</b>
RMS (3rd-6th order) HOAs anterior at 6m FU	0.201	<b>0.020</b>
RMS (3rd-6th order) HOAs posterior at 6m FU	0.164	0.055
Densitometry anterior 0-2 mm at 6m FU	0.181	<b>0.015</b>
Densitometry anterior 2-6 mm at 6m FU	0.051	0.464
Densitometry posterior 0-2 mm at 6m FU	0.094	0.232
Densitometry posterior 2-6 mm at 6m FU	0.018	0.834
DMEK vs. control	0.071	0.410
Age	0.318	<b>0.000</b>
Gender	0.01	0.379
Lens status	-0.078	0.247

BSCVA = Best spectacle-corrected visual acuity

RMS = Root mean square

HOAs = Higher order aberrations

FU = Follow-up

m = months

DMEK = Descemet membrane endothelial keratoplasty

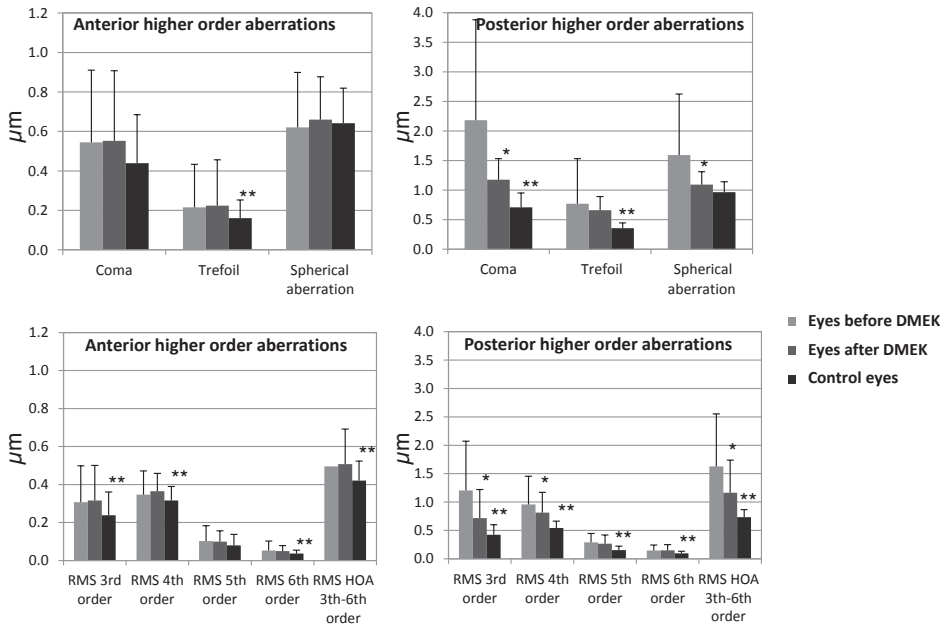
Scaled estimate = Relative importance of each predictor: 0.10=small, 0.31=medium, 0.58=large

“Bold” = statistical significant

## DISCUSSION

Before commencing our study, we hypothesized that a transplanted DMEK cornea could reach an optical quality approximating that of a virgin cornea, given the fact that visual acuities of  $\geq 20/17$  (1.2) are seen in about 10-15% of eyes in our series.<sup>18</sup> Therefore, we evaluated HOAs and backscattered light before and after DMEK in a large group of eyes operated on for Fuchs endothelial dystrophy, and compared the outcome with an age matched control group.

Nevertheless, the DMEK eyes in our study showed abnormal levels of anterior HOAs and backscattered light not only before surgery (while still suffering from Fuchs endothelial dystrophy) but also after surgery. This agrees with the findings of other investigators, who reported on haze and abnormal anterior HOAs after DSEK/DSAEK.<sup>8,16,26-30</sup> The presence of irregularities and haze in the anterior cornea before surgery is not surprising given the fact that Fuchs endothelial dystrophy may induce changes in the anterior corneal anatomy, such as anterior stromal keratocyte loss and degeneration, collagen disorganization and subepithelial fibrosis.<sup>17,19,26-29</sup> Especially in case of prolonged pre-operative corneal edema, these abnormalities may persist after EK, and will then prob-



**Figure 2.** Bar graphs showing the averages and standard deviations of different anterior and posterior corneal higher-order aberrations (HOAs) of Fuchs endothelial dystrophy eyes before and 6 months after Descemet membrane endothelial keratoplasty (DMEK) and of control eyes. HOAs were defined as (Top Left, Top Right) Zernike vector terms and as (Bottom Left, Bottom Right) root mean square when combinations of individual Zernike terms for the third, fourth and fifth Zernike order were used. Statistically significant differences between preoperative and postoperative are indicated by 1 asterisk (\*) and between postoperative and the control group by 2 asterisks (\*\*). (Top Left, Bottom Left) The anterior corneal HOAs remained unchanged from before to after DMEK and sustained higher than the control group. Instead, (Top Right, Bottom Right) the posterior HOAs decreased from preoperative to postoperative, although were still elevated compared to controls.

ably contribute to surface irregularity and backscattered light that may affect visual outcomes.<sup>17,27</sup> If so, the presence or absence of postoperative anterior HOAs and haze may depend on the timing of surgical intervention, rather than the type of EK technique employed.

In addition, the higher amounts of posterior HOAs and haze in eyes with Fuchs endothelial dystrophy were to be expected since these eyes normally peak in backscattered light at the posterior corneal surface owing to the diseased Descemet membrane and its endothelium.<sup>26</sup> Furthermore, disease progression commonly results in stromal edema, and deformation of the posterior corneal surface would cause higher levels of posterior HOAs. Although DMEK provided significant improvement in posterior HOAs and backscattered light, these levels remained somewhat elevated and did not reach those of controls. However, compared to DSEK/DSEK, DMEK eyes may show lower amounts of aberrations and backscattered light values of the posterior corneal surface,<sup>31</sup> because

the DMEK graft may better fit the posterior curvature of the host cornea and there is no stroma-to-stroma interface.<sup>13,18</sup>

Although posterior HOAs and backscattered light in DMEK eyes were elevated compared to control eyes, final visual outcome did not seem to be restricted by these factors. Instead, regression analysis showed that with patient's age and preoperative visual acuity, visual rehabilitation after DMEK was mainly affected by residual anterior HOAs and haze. Our findings agree with other studies that demonstrated that especially HOAs of the anterior cornea, but not of the posterior corneal surface, influenced final visual outcome in DSEK/DSAEK.<sup>6,16,28,32</sup> Although anterior corneal residual haze has been suggested as a potential cause for decreased visual outcome, its effect may differ from that of HOAs.<sup>9,26,30</sup> While HOAs may influence BSCVA more directly, haze (backscattered light) itself should not compromise the visual acuity.<sup>9,26</sup> Nevertheless, haze is associated with corneal changes that induce forward scattered light, which may induce glare and therefore decrease visual performance in unfavorable ambient light conditions.<sup>9,26,30</sup> However, high contrast visual acuity measurements will suffer less from light scatter than from HOAs.<sup>9</sup>

Our finding that BSCVA was affected by HOAs as well as backscattered light from the anterior cornea, may be explained by the fact that HOAs and haze coexist. The origin of backscattered light within the anterior cornea may be attributed to changes in the anterior stroma, such as subepithelial fibrosis resulting from longstanding corneal edema.<sup>17,26-29</sup> These anterior corneal opacities may be associated with anterior corneal irregularities, which would then cause an incomplete visual rehabilitation or other visual complaints such as ghost images.<sup>17</sup> To improve the vision in these cases, contact lenses have proven to be effective.<sup>17</sup>

However, if the final visual outcome depends on the optical quality of the anterior corneal surface rather than the posterior corneal surface in both DMEK and DSEK/DSAEK, how should better visual results after DMEK then be explained? Even though the intact, regular anterior corneal surface may contribute most to good visual rehabilitation after EK (because of the larger refractive index at the anterior than posterior corneal surface), it has been suggested that BSCVA after EK can be improved by promoting a more regular posterior corneal (graft) surface.<sup>9,12,13,15</sup> If so, a better match in curvature between the transplant and posterior host stroma as well as the uniformity of graft thickness,<sup>13,15</sup> resulting in a more regular posterior corneal surface, might explain the higher visual outcomes in DMEK.<sup>31</sup> Moreover, it has been shown that after DSAEK, posterior corneal aberrations may increase rather than decrease whole-eye aberrations, while in normal eyes, total corneal HOAs are partly compensated by the posterior corneal HOAs.<sup>33</sup> This is thought to be induced by a disruption of parallelism between anterior and posterior corneal surface,<sup>33</sup> which may consequently decrease the visual potential. It seems plau-

sible that with a thin DMEK graft directly positioned against the host posterior stroma, such an imbalance between anterior and posterior corneal surface does not occur.

Our study further indicated that, apart from postoperative HOAs and backscattered light from the anterior corneal surface, final visual outcome was influenced by preoperative visual acuity and patient age. Because eyes with concomitant ocular disease were excluded from our study, this correlation may imply that older and more disturbed recipient corneas limited or at least slowed down the visual recovery. As such, it may be prudent to consider performing EK in a relatively early phase of endothelial disease, such as Fuchs endothelial dystrophy, i.e. before secondary corneal changes develop.<sup>17,28</sup>

Data on HOAs in our study were based on height differences only. In contrast to wavefront analysis, the different refractive indices for air, corneal tissue and aqueous were not taken into account in this analysis.<sup>23</sup> Consequently, although the contribution of the posterior HOAs to the total corneal wavefront error will be much smaller than that of the anterior corneal HOAs, the posterior corneal surface showed relatively more HOAs than the anterior corneal surface. As a result, the outcome data are not directly comparable with some studies on corneal wavefront error after EK.<sup>16,31</sup> However, our overall results agree with studies on HOAs reporting more elevated aberrations after EK than in virgin corneas, and with the fact that mainly anterior corneal HOAs, more than posterior HOAs, influence the final visual acuity outcome.<sup>6,16,28,32</sup>

In conclusion, anterior and posterior corneal HOAs, as well as corneal backscattered light are elevated in eyes suffering from Fuchs endothelial dystrophy, and remained elevated throughout 6 months after DMEK. Apart from preoperative BSCVA and patient age, irregularities and haze of the anterior corneal surface, rather than the posterior surface, may be important factors for visual rehabilitation after DMEK.

## REFERENCES

1. Melles GRJ. Posterior lamellar keratoplasty. DLEK to DSEK to DMEK. *Cornea* 2006;25:879-881
2. Dapena I, Ham L, Melles GRJ. Endothelial keratoplasty: DSEK/DSAEK or DMEK - the thinner the better? *Curr Opin Ophthalmol* 2009;20:299-307
3. Ham L, Dapena I, van Luijk, et al. Descemet membrane endothelial keratoplasty (DMEK) for Fuchs endothelial dystrophy: review of the first 50 consecutive cases. *Eye* 2009;23:1990-1998
4. Melles GRJ, Lander F, van Dooren BTH, et al.. Preliminary clinical results of posterior lamellar keratoplasty through a sclerocorneal incision. *Ophthalmology* 2000;107:1850-1857
5. Bahar I, Kaiserman I, McAllum P, et al. Comparison of posterior lamellar keratoplasty techniques to penetrating keratoplasty. *Ophthalmology* 2008;115:1525-1533
6. Muftuoglu O, Prasher P, Bowman RW, et al. Corneal higher-order aberrations after Descemet's stripping automated endothelial keratoplasty. *Ophthalmology* 2010;117:878-884
7. Chamberlain W, Omid N, Lin A, et al. Comparison of corneal surface higher-order aberrations after endothelial keratoplasty, femtosecond laser-assisted keratoplasty, and conventional penetrating keratoplasty. *Cornea* 2012;31:6-13
8. Koh S, Maeda N, Nakagawa T et al. Characteristic higher-order aberrations of the anterior and posterior corneal surfaces in 3 corneal transplantation techniques. *Am J Ophthalmol* 2012;153:284-290
9. McLaren JW, Patel SV. Modeling the effect of forward scatter and aberrations on visual acuity after endothelial keratoplasty. *Invest Ophthalmol Vis Sci* 2012;53:5545-5551
10. Pantanelli SM, Sabesan R, Ching SS, et al. Visual performance with wave aberration correction after penetrating, deep anterior lamellar or endothelial keratoplasty. *Invest Ophthalmol Vis Sci* 2012;53:4797-4804
11. Ham L, Dapena I, van der Wees J, Melles GR. Secondary DMEK for poor visual outcome after DSEK: donor posterior stroma may limit visual acuity in endothelial keratoplasty. *Cornea* 2010;29:1278-1283
12. Moutsouris K, Ham L, Dapena I, et al. Radial graft contraction may relate to subnormal visual acuity in Descemet stripping (automated) endothelial keratoplasty. *Br J Ophthalmol* 2010;94:951-953
13. Dirisamer M, Parker J, Naveiras M et al. Identifying causes for poor visual outcome after DSEK/DSAEK following secondary DMEK in the same eye. *Acta Ophthalmol* 2013;91(2):131-139
14. Chen M, Gong L, Xu J, et al. Ultrastructural and in vivo confocal microscopic evaluation of interface after Descemet's stripping endothelial keratoplasty in rabbits. *Acta Ophthalmol* 2012;90:43-47
15. Seery LS, Nau CB, McLaren JW, et al. Graft thickness, graft folds, and aberrations after Descemet stripping endothelial keratoplasty for Fuchs dystrophy. *Am J Ophthalmol* 2011;152:910-916
16. Patel SV, Baratz KH, Maguire LJ, et al. Anterior corneal aberrations after Descemet's stripping endothelial keratoplasty for Fuchs' endothelial dystrophy. *Ophthalmology* 2012;119:1522-1529
17. Van Dijk K, Parker J, Liarakos V, et al. Incidence of irregular astigmatism eligible for contact lens fitting after Descemet membrane endothelial keratoplasty (DMEK). *J Cataract Refract Surg* 2013;39:1036-1046
18. Van Dijk K, Ham L, Tse WHW et al. Near complete visual recovery and refractive stability in modern corneal transplantation: Descemet membrane endothelial keratoplasty (DMEK). *Contact Lens Anterior Eye* 2013;36:13-21
19. Elhali H, Azizi B, Jurkunas UV. Fuchs endothelial corneal dystrophy. *Ocul Surf* 2010;8:173-184



20. Dapena I, Moutsouris K, Droutsas K, et al. Standardized 'no touch' technique for Descemet membrane endothelial keratoplasty (DMEK). *Arch Ophthalmol* 2011;129:88-94
21. Lie JT, Birbal R, Ham L, et al. Donor tissue preparation for Descemet membrane endothelial keratoplasty. *J Cataract Refract Surg* 2008;34:1578-1583
22. Melles GRJ, Wijdh RH, Nieuwendaal CP. A technique to excise the Descemet membrane from a recipient cornea (descemetorhexis). *Cornea* 2004;23:286-288
23. Oculus Optikgeräte GmbH (2005): Oculus Pentacam Instruction Manual. Measurement and evaluation system for the anterior segment of the eye. Oculus Optikgeräte GmbH, Münchholzhäuser Str. 29, 35582 Wetzlar, Germany
24. R Core Team. R: A language and environment for statistical computing. R Foundation for Statistical Computing. 2013 Vienna, Austria. Available at <http://www.R-project.org/>. Accessed November 27, 2013
25. Benjamini Y, Hochberg, Y. Controlling the false discovery rate: A practical and powerful approach to multiple testing. *J R Statist Soc B* 1995;57:289-300
26. Patel SV, Baratz KH, Hodge DO, et al. The effect of corneal light scatter on vision after descemet stripping with endothelial keratoplasty. *Arch Ophthalmol* 2009;127:153-160
27. Morishige N, Yamada N, Teranishi S, et al. Detection of subepithelial fibrosis associated with corneal stromal edema by second harmonic generation imaging microscopy. *Invest Ophthalmol Vis Sci* 2009;50:3145-3150
28. Morishige N, Chikama T, Yamada N et al. Effect of preoperative duration of stromal edema in bullous keratopathy on early visual acuity after endothelial keratoplasty. *J Cataract Refract Surg* 2012;38:303-308
29. Alomar TS, Al-Aqaba M, Gray T, et al. Histological and confocal microscopy changes in chronic corneal edema: implications for endothelial transplantation. *Invest Ophthalmol Vis Sci* 2011;52:8193-8207
30. Baratz KH, McLaren JW, Maguire LJ, Patel SV. Corneal haze determined by confocal microscopy 2 years after Descemet stripping with endothelial keratoplasty for Fuchs corneal dystrophy. *Arch Ophthalmol* 2012;130:867-874
31. Rudolph M, Laaser K, Bachmann BO, et al. Corneal higher-order aberrations after Descemet's membrane endothelial keratoplasty. *Ophthalmology* 2012;119:528-535
32. Yamaguchi T, Negishi K, Yamaguchi K, et al. Effect of anterior and posterior corneal surface irregularity on vision after Descemet stripping endothelial keratoplasty. *J Cataract Refract Surg* 2009; 35:688-694
33. Yamaguchi T, Ohnuma K, Tomida D, et al. The contribution of the posterior surface to the corneal aberrations in eyes after keratoplasty. *Invest Ophthalmol Vis Sci* 2011;52:6222-6229

