Straylight in anterior segment disorders of the eye

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Chapter 6

CORRELATION OF STRAYLIGHT AND VISUAL ACUITY IN LONG-TERM FOLLOW-UP OF MANUAL DESCemet STRIPPING ENDOThelial KERATOPLASTY

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ABSTRACT

Purpose
Long-term quality of vision after Descemet stripping endothelial keratoplasty (DSEK) was evaluated and correlated with corneal characteristics and subjective complaints.

Methods
Thirty-four eyes were examined; patients had a single visit 6 to 64 months after DSEK for Fuchs’ dystrophy. Best-corrected distance acuity (BCDA) and straylight were analyzed. To better evaluate long-term postoperative BCDA changes, longitudinal data were used from earlier visits. Corneal thickness was measured with the Visante anterior segment Optical Coherence Tomography (OCT). Interface, stromal and endothelial haze were semi-quantitatively graded using the slitlamp. Vision-related quality of life was evaluated with the 39-item National Eye Institute Visual Function Questionnaire (NEI VFQ-39) and a straylight questionnaire. Correlation analysis comparing corneal characteristics with visual quality was performed.

Results
Mean postoperative time was 1027 ± 453 days. Mean BCDA at this time was 0.33 ± 0.19 logMAR. BCDA remained stable with long-term postoperative follow-up. Straylight averaged 1.47 ± 0.19, on average 0.12 log units higher than normal values for age-related pseudophakic eyes (P < 0.001). BCDA correlated with corneal haze (r = 0.50), whereas straylight showed a non-significant association (P = 0.12). Neither BCDA nor straylight correlated with corneal thickness. Mean VFQ-39 score was 77/100, and mean score of the straylight questionnaire was 46/100.

Conclusion
Quality of vision after DSEK does not return to normal levels of age-matched pseudophakic eyes, with decreased BCDA and increased straylight. Questionnaire scores indicate mild (VFQ-39) to moderate (straylight) subjective visual impairment. Corneal thickness and haze do not offer an adequate explanation for the decreased visual quality.
INTRODUCTION

Since its introduction in 2002, Descemet stripping endothelial keratoplasty (DSEK) has become the most commonly performed procedure of posterior lamellar keratoplasty (PLK), used for treatment of corneal endothelial dysfunction, in particular Fuchs' endothelial dystrophy.1,2 The donor disks for DSEK can be dissected manually,3-6 mechanically using a microkeratome,6-9 or with a femtosecond laser.7 Main advantages of PLK and its modifications are rapid visual rehabilitation,1,9 minimal induced astigmatism,3 and absence of suture-related complications1.

Because DSEK is a relatively new surgical technique, most studies concerning the results of this treatment show results up to 6-18 months postoperatively and focus exclusively on (equivalents of high contrast) visual acuity. However, visual acuity assessment underestimates visual problems caused by straylight and is therefore not sufficient for evaluating quality of vision.11-15 Straylight is caused by light scattered by imperfect optical media of the eye, falling on the retina, and diminishing the contrast of the retinal image. Straylight is proportional to forward light-scatter and translates into glare and contrast problems, as opposed to visual acuity that mainly tests for refractive type errors. Straylight is an objective physiologic measure of the large-angle domain of the retinal point-spread function, while visual acuity is influenced by the small angle domain of the retinal point-spread function.12 Problems with straylight occur quite independently from visual acuity problems in the general population.12,13,16 On the other hand, depending on the studied population, a statistical association may occur.17,18 With respect to DSEK, corneal haze and structural changes in corneal microstructure have been suggested as explanation for limited optical performance.14,15,18

In this study, long-term DSEK postoperative quality of vision by means of visual acuity and straylight measurements is evaluated. We report and correlate herein the 6-month to 5-year postoperative outcomes of straylight values and best-corrected distance visual acuity (BCDA) with several corneal characteristics (corneal thickness and amount of corneal haze) and subjective complaints as documented by questionnaires. To better understand long-term postoperative visual results, longitudinal data were used from earlier patient visits.

MATERIALS AND METHODS

Subjects

Forty-four eyes of 34 patients underwent DSEK for Fuchs' endothelial dystrophy between July 2003 and May 2008. Four eyes were excluded from this study because of other eminent ocular pathology. One eye had buphthalmos, two eyes suffered from severe macular degeneration, and one eye developed proliferative diabetic retinopathy after DSEK. Another two eyes were excluded because of early postoperative corneal decompensation for which they received a
penetrating keratoplasty (PK). Four eyes of three patients were excluded because the patients had died or were lost to follow-up. All 34 included eyes of 26 patients were diagnosed with Fuchs’ endothelial dystrophy and did not have any other disturbing ocular pathology, besides pseudophakia. Between September 2008 and January 2009, all patients were asked to visit the outpatient clinic once for a follow-up visit to undergo the examinations described below. The study complied with the tenets of the Declaration of Helsinki. Subjects gave oral and written informed consent. Institutional Review Board approval was obtained.

DSEK procedure
The DSEK technique as used in all eyes is similar to that previously described in detail by Melles et al.\textsuperscript{5} Posterior donor corneal disks were all manually dissected by the cornea donor bank (Amnitrans Cornea Bank, Rotterdam, the Netherlands).\textsuperscript{4} The cornea donor bank routinely prepares the donor posterior disks by manual dissection of the cornea of an intact globe. After the disks had been prepared, they remained in situ in the intact globes, after which 16-mm corneal-scleral buttons were excised and routinely processed by the cornea bank.\textsuperscript{4} This procedure allowed a check for possible contamination and to assess the viability of the donor endothelial cell layer. All recipient eyes were pseudophakic before DSEK surgery.

Outcome measures
High-contrast best corrected distance visual acuity (BCDA) was measured by using the Early Treatment of Diabetic Retinopathy Study (ETDRS) protocol\textsuperscript{19,20} and is given as the logarithm of the minimum angle of resolution (logMAR).

Straylight was measured with the C-Quant straylight meter (Oculus GmbH, Wetzlar, Germany), which can objectify in a functional sense the amount of intraocular forward light-scatter.\textsuperscript{21} The C-Quant straylight meter is a computerized instrument based on the compensation comparison method, which is described in detail elsewhere.\textsuperscript{21-23} Values found are expressed as the logarithm of the straylight parameter $s$, $\log(s)$. Measurements were considered reliable when the expected standard deviation (ESD), given by the instrument, reached values below 0.1.\textsuperscript{21} Because in this way only reliable data were included, the repeated-measures standard deviation of the straylight values was approximately 0.07 log units in the present study. Straylight values found in the population of this study can be best compared with those of normal pseudophakic eyes. In a recent study, straylight values in pseudophakic eyes were evaluated.\textsuperscript{24} In this study, 56 pseudophakic eyes of 47 patients were included, which were measured under the same conditions in the same period and with the same instrument as the population of the present study. Mean age of the pseudophakic patients was 66.2 (range, 31-87 years), with a mean straylight value of $\log(s) = 1.25$ (range, 0.68 – 2.13).\textsuperscript{24} In pseudophakic eyes, the effect of age...
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on the amount of straylight is supposed to be less important because the disturbing cataract is removed. However, straylight values in our population of pseudophakic patients did not return to values of healthy, young eyes. Some influence of age or surgery on pseudophakic eyes was thus assumed. In this pseudophakic, but otherwise healthy population, the age-related regression line for straylight values of pseudophakic eyes was found to be $y = 0.003x + 1.1261$, in which $y$ is the straylight value in log($s$) and $x$ is the age of the pseudophakic patient in years. The age-related straylight normal curve is not applicable because of the important role for the natural lens and its age-related changes in this curve.

For measuring and imaging the anterior segment, the time domain-based Visante anterior segment optical coherence tomography (AS-OCT; Carl Zeiss Meditec, Dublin, CA, USA) was used. Although no reproducibility studies concerning corneal thickness measurements have been published for this instrument, other studies have shown that OCT measurements correspond well with pachymetry and ultrasound measurements. The Visante AS-OCT obtains cross-sectional images of the cornea with a 1310 nm superluminescent LED, based on consecutive A-scans. Four consecutive high-resolution (512 A-scans, taken in 0.25 seconds each) corneal scans were acquired, in the horizontal, vertical and two diagonal planes, centered on the vertex. Thickness measurements of both donor disk and recipient stroma were performed at the centre of the cornea and at 1.5 and 3.0 mm from both sides of the centre in each scan line.

A semi-quantitative slitlamp grading of interface and stromal and endothelial haze was recorded (Table 6.1). The total grade of corneal haze was the sum of interface, stromal, and endothelial grades.

We administered the 39-item National Eye Institute Visual Function Questionnaire (NEI VFQ-39) to evaluate vision-related quality of life. This questionnaire is developed to measure multiple aspects of vision-related functioning and to allow comparison of vision-related quality of life in various ocular disorders. The NEI-VFQ-39 composite score is the mean of all vision-specific VFQ-39 scales, excluding general health. The NEI-VFQ-39 is scored from 0 to 100, with a higher score indicating better vision-related functioning. To capture straylight complaints, a 5-item straylight questionnaire was designed, based on clinical experience, and conducted (Table 6.2). All questions had to be answered on a scale from 0-5 except question nr. 4, which had a “not applicable” answering option, in which 0 = none, 1 = hardly any difficulty, 2= mild difficulty, 3 = moderate difficulty, 4 = severe difficulty and 5 = very severe difficulty. The resultant score of this questionnaire was determined as the average over all 5 (4) scores, with: answer 0 = 100 points, 1 = 80 points, 2 = 60 points, 3 = 40 points, 4 = 20 points and 5 = 0 points, resulting in a total score between 0 and 100, where 0 was the worst possible and 100 the best possible score. A higher
score thus indicated less straylight complaints. Earlier acquired values of postoperative BCDA (32 eyes) were retrieved from patients’ charts. Comparisons were made between these earlier values and our present results.

**Table 6.1** Scale of the semi-quantitative slitlamp grading

<table>
<thead>
<tr>
<th>Grade</th>
<th>Interface</th>
<th>Stroma</th>
<th>Endothelial</th>
</tr>
</thead>
<tbody>
<tr>
<td>grade 0</td>
<td>clear</td>
<td>clear</td>
<td>no guttae</td>
</tr>
<tr>
<td>grade 1</td>
<td>mild localized opacification, not in centre</td>
<td>localized mild haze</td>
<td>limited localized guttae</td>
</tr>
<tr>
<td>grade 2</td>
<td>localized moderate opacification not in centre</td>
<td>more diffuse mild haze, small spot with moderate haze, not in centre</td>
<td>more extensive guttae, but not covering the whole endothelium</td>
</tr>
<tr>
<td>grade 3</td>
<td>multiple spots with moderate opacification peripherally</td>
<td>moderate localized haze in multiple or larger peripheral spots</td>
<td>diffuse guttae, but a clear stroma</td>
</tr>
<tr>
<td>grade 4</td>
<td>mild central opacification, peripheral moderate opacification</td>
<td>localized dense haze or diffuse moderate haze, stromal folds or some localized Descemet folds</td>
<td>diffuse guttae, signs of stromal oedema, e.g. stromal folds or some localized Descemet folds</td>
</tr>
<tr>
<td>grade 5</td>
<td>diffuse dense opacification</td>
<td>diffuse dense haze, stromal oedema, Descemet folds</td>
<td>diffuse guttae, including oedema and Descemet folds</td>
</tr>
</tbody>
</table>

**Table 6.2** 5-Item straylight questionnaire.

**Straylight questionnaire**

- How much difficulty do you experience seeing what is ahead of you when you drive into a tunnel during the daytime?
- How much difficulty do you experience seeing what is ahead of you when an oncoming car has bright headlights on at night?
- How much difficulty do you experience seeing what is ahead of you when a low sun is shining in your eyes during the daytime?
- To what extent did you stop driving a car because of the above mentioned problems?
- How much difficulty do you experience recognizing faces against the light?

All questions had to be answered on a scale from 0-5 except question nr. 4 which had a “not applicable” answering option, in which 0 = none, 1 = hardly any difficulty, 2 = mild difficulty, 3 = moderate difficulty, 4 = severe difficulty and 5 = very severe difficulty. The resultant score of this questionnaire was determined as the average over all 5 (4) scores, with: answer 0 = 100 points, 1 = 80 points, 2 = 60 points, 3 = 40 points, 4 = 20 points and 5 = 0 points, resulting in a total score between 0 and 100, where 0 was the worst possible and 100 the best possible score.
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Statistical analysis
All statistical analyses were performed using Excel (Microsoft Corp., Redmond, WA, USA)) or SPSS 16.0.2 (SPSS Inc., Chicago, IL, USA). Correlations were made with the Pearson coefficient or when data were not normally distributed with the Spearman’s rho coefficient. A P value less than 0.05 was considered statistically significant (two-tailed). A Student’s t test was performed to analyse age dependence of straylight results.

RESULTS

Population
Fifteen patients were women (58%), and 11 patients were men. All patients were Caucasian. Mean age of the population was 72.1 years (SD 11 years, range 48 – 91 years). The follow-up visit for data collection occurred after a median of 1027 days (SD 453 days, range 189-1921 days). Thirty-four eyes of 26 participants were measured; eight patients had both eyes measured. Statistical analysis of the patients who had both eyes operated, did not show any correlation between the results of both eyes.

Visual acuity
Mean visual acuity was 0.33 logMAR (SD 0.19; range 0-0.72; Snellen equivalent: 20/42). From patients’ charts, mean BCDA at an average postoperative time of 248 days could be retrieved for 32 eyes. Mean earlier acquired BCDA was 0.27 logMAR (SD 0.18; range 0-0.8; Snellen equivalent: 20/37). When recent BCDA results are plotted against earlier acquired postoperative BCDA values, visual acuity values did not change much over time (Figure 6.1) (n = 32, r = 0.84, P < 0.001). Visual acuity correlated with recipient age (n = 33, r = -0.35, P = 0.045) and with total grade of corneal haze (n = 33, r = 0.50, P = 0.003).

Straylight values
Mean straylight was log(s) = 1.47 (SD 0.19; range 1.07 – 1.78). Figure 6.2 shows straylight values after DSEK compared with the regression line for the age-related straylight values of pseudophakic eyes, explained in the methods section. Comparing straylight values in DSEK patients (log(s) = 1.47) with this curve (log(s) = 1.35) resulted in a statistically significant (P < 0.001) average difference of 0.12 log units, which may be assumed to be caused by the cornea. In linear sense, this difference is Δs = 7. Straylight values showed a statistical relationship with BCDA, although the relationship is not very strong (n = 33, r = 0.46, P = 0.008). (Figure 6.3) Straylight values showed a weak relationship with the total grade of corneal haze (n = 34, r = 0.27, P = 0.12).
Figure 6.1 Present best corrected distance visual acuity (BCDA) values in logMar (logarithm of the minimal angle of resolution) against earlier acquired BCDA values in logMar. BCDA results hardly changed with long-term follow-up after DSEK.

Figure 6.2 Straylight (log(s)) versus age (years). The central line represents average straylight of healthy pseudophakic eyes, with the outer lines representing ± 0.2 log intervals. Postoperative straylight remains increased (average difference: 0.12 log units; P < 0.001) compared with normal pseudophakic eyes.
Corneal haze and thickness measurements

Mean grade of interface haze was 0.85 (SD 1.08; range 0 – 4), stromal haze 0.18 (SD, 0.46; range 0-2) and endothelial haze 0.50 (SD 0.56; range 0 – 2). Mean corneal thickness of the central cornea was 609 µm (SD 56; range 494 – 722). BCDA, straylight, grading of corneal haze or results of the questionnaires did not show a statistical relationship with any thickness measurements of the cornea, which may be because of the small sample size.

Questionnaires

The average VFQ-39 score was 77/100 (SD 16; range 34 – 99), against a 46/100 (SD 29; range 0-92) average score, which was found with the straylight questionnaire. The two questionnaires results correlated well (n = 23, r = 0.72, P <0.001). The VFQ-39 showed a weak relation with visual acuity (n = 23, r = -0.32, P = 0.08) but did not show a relation with any of the other parameters. Neither did the straylight questionnaire. This may be attributable to small sample size.

DISCUSSION

In this study, long-term quality of vision after manual DSEK is evaluated. Straylight values and visual acuity, corneal thickness, subjective complaints, and corneal haze were reported and correlated. Thirty-four eyes with an average postoperative time of almost 3 years, ranging from
six months to over 5 years, were included. Results of visual acuity measurements were compared with data acquired at an earlier date. Straylight values were compared with normal straylight values of (otherwise healthy) pseudophakic eyes. Our population size is small, and thus, a number of statements of lack of association will have wide confidence intervals if they were to be computed. Caution is needed about these statements.

The purpose of this article was to report on the long-term visual functioning of the first patients who have undergone manual DSEK. More recently, Descemet stripping automated endothelial keratoplasty (DSAEK) with micro-keratome-dissected donor tissue has become popular. However, many ophthalmologists who now perform DSAEK started with manual DSEK and consequently will still have patients under their care who have undergone this procedure. The long-term follow-up of these manual DSEK patients remains valuable. Visual functioning of patients who have undergone manual DSEK has been compared with that of DSAEK patients. No difference in visual outcomes between these groups was found at 3-, 6- and 12-month follow-up. It was suggested that this lack of difference in long-term follow-up could be because of stromal remodelling, which occurred eventually and which may reduce the influence of early interface irregularities on visual quality. Consequently, large differences in visual outcomes between our manual DSEK patients and DSAEK patients are unlikely with our follow-up of several years. In a recent report evaluating the results of endothelial keratoplasty, no explicit difference is made between DSEK and DSAEK, as method of donor tissue preparation is not considered important for the evaluation of safety and outcomes.

Quality of Vision
Straylight values of our population were compared with healthy pseudophakic eyes without DSEK surgery. Straylight values increase with age in the perfectly healthy eye because of increased (but normal) disturbances to the optical media, predominantly in the crystalline lens. In pseudophakic eyes, the effect of age on the amount of straylight can be expected to be less important, as the disturbing crystalline lens is removed. Because of the removal of the lens-effect, it is not possible to compare straylight values of pseudophakic eyes with straylight values of eyes which still contain the crystalline lens. Straylight values of pseudophakic eyes will have to be compared with those of other healthy (non-Fuchs) pseudophakic eyes. In previous studies, it was found that straylight values of healthy pseudophakic eyes do not return to values of a young normal eye and that they increase slightly with age. Some influence of age or surgery on pseudophakic eyes must thus be assumed. For unknown reasons, straylight values in healthy pseudophakic eyes remain quite variable. As the rather unpredictable influence of the DSEK cornea on postoperative quality of vision is added in our population, the variability of straylight values in this population will be even larger than that in otherwise normal pseudophakic eyes. Considering
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this large variability in our population, the lack of correlation between quality of vision and corneal characteristics is unsurprising. The standard deviation of the straylight measurements of 0.07 log units is comparable to other studies and shows the test results to be reliable and repeatable. Another issue to be considered is potential differences of the IOL and surgical procedure. However, IOL and surgical procedure in the present study are identical to those of the reference pseudophakic population. A significant average difference in straylight of 0.12 log units or $\Delta s = 7$ was found between healthy pseudophakic eyes and eyes after DSEK surgery in our population, which may be assumed to be caused by the cornea. A previous study showed that penetrating keratoplasty led to a postoperative reduction of straylight of 0.60 log units to $\log(s) = 1.05$ in an eye with a postherpetic corneal scar. Although we do not have pre- and postoperative straylight measurements, this reduction after penetrating keratoplasty is probably more than that observed in our patients. However, Patel and Patel et al suggested that decreased quality of vision after DSEK was caused by the influence of the graft-host interface, which probably increases forward light-scatter. Also, changes in the entire host cornea might contribute to increased straylight.

Chronic recipient subepithelial fibrosis and ultrastructural stromal changes occurring after longstanding endothelial dysfunction have been named to increase forward light-scatter and limit VA. These changes do not return to normal after DSEK, as corneal backscatter from the anterior and middle thirds of the cornea was shown to remain elevated postoperatively. Good preoperative vision because of minimal corneal changes is a predictor of better postoperative visual recovery. Older patients might have more advanced corneal stromal changes, more impairment of quality of vision, and a possibly limited recovery postoperatively. Thus, recipient age might also be a predictor of postoperative result, with younger patients having the best visual prognosis. This correlation between postoperative visual acuity and recipient age also exists in our population as detailed in the results section, although the correlation was not strong and could have been influenced by chance.

It is estimated that around one-third of the total amount of straylight in the normal healthy human eye is derived from the cornea, which corresponds to $s = 3$. If the same holds true for the pseudophakic reference eyes with average $\log(s) = 1.35$, this would correspond to $s = 7.5$ attributable to the cornea (if $\log(s) = 1.35$, $s = 10^{1.35} = 22.5$; if 1/3 of this value is derived from the cornea, then this is $s = 7.5$). So, an extra straylight increase of $\Delta s = 7$ after DSEK surgery is a sizeable amount compared with normal levels for the cornea. The average addition of 0.12 log unit to normal pseudophakic straylight values is comparable to loss of one line of a VA chart, which is similar to previously reported visual loss of on average 1 line because of the interface after deep lamellar endothelial keratoplasty surgery. This suggests that the straylight increase because of the cornea has limited practical impact for the patients of our group.
Corneal grading and Questionnaires

Corneal grades correlated with BCDA and weakly with straylight. So, slitlamp examination of the cornea can contribute to the understanding of that part of subjective complaints of visual functioning, which is caused by decreased visual acuity. However, straylight complaints cannot be very well predicted or understood from slitlamp examination. This can be because of the fact that the exact source and amount of straylight (which is forward scatter) within the cornea cannot be determined by slitlamp examination. Although subjective grading systems are complex to administer in a reproducible way, with the use of this grading system, it was aimed to get close to established and meaningful clinical practice. For most ophthalmologists, the slitlamp is the only instrument available to examine the anterior segment of the eye. To increase the reproducibility of the grading system, grading was performed in nearly all eyes by one ophthalmologist (IvdM). Although the use of corneal grading postoperatively might be doubtful, the corneal grading was added to be able to detect deterioration of the endothelial function of the graft with long-term follow-up after DSEK. However, in our population, mean value of all corneal grades was very low, indicating that little problems were detected. The level of endothelial dysfunction in our population with long-term follow-up after DSEK thus hardly disturbed quality of vision.

The subjective complaints, measured with both the VFQ-39 and the straylight questionnaires, did not correlate well to other parameters. The NEI-VFQ-39 composite score of 77 from our group of pseudophakic patients after DSEK is slightly higher than the mean baseline score (73) in patients with cataract who are planned to undergo cataract extraction. After cataract surgery, these patients showed a mean improvement of 21 to an average postoperative composite score of 93. The low value of 77, which is found among our patients, is probably attributed to suboptimal postoperative visual acuity and straylight levels in the present study. The score of the straylight questionnaire (46) was also surprisingly low. A problem in our population is that other pathology such as Fuchs endothelial dystrophy or cataract in the non-operated eye could have an influence as well, as most included patients had undergone DSEK surgery on one eye only. Patients’ satisfaction will not fully correspond to improving functional parameters after surgery of one eye, if the other eye is still functioning in a suboptimal way.

Conclusions

Posterior lamellar keratoplasty is a relatively new surgical technique with quite some variations. Little long-term follow-up results have been presented so far. With growing experience in posterior lamellar keratoplasty, it has been shown that functionally DSEK surgery is successful after five years follow-up. Visual acuity remained stable postoperatively until now. The present study shows that also straylight is surprisingly good with long-term follow-up. However, quality of vision after DSEK does not return to normal levels of age-matched pseudophakic eyes.
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Questionnaire scores indicate mild to moderate postoperative subjective visual impairment, mostly because of straylight. Better postoperative visual functioning with younger recipient age and less corneal changes because of longstanding endothelial dysfunction seem to point in the direction of offering DSEK surgery in an early stage to patients with Fuchs endothelial dystrophy.
Chapter 6

REFERENCES

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