Endothelial Cell Decay after Descemet’s Stripping Automated Endothelial Keratoplasty and Top Hat Penetrating Keratoplasty

Bart T. H. Van Dooren, Isabelle E. Y. Saelens, Isabel Bleyen, Paul G. H. Mulder, Marjolijn C. Bartels, and Gabriel Van Rij

PURPOSE. To analyze endothelial cell density (ECD) decay after Descemet’s stripping automated endothelial keratoplasty (DSAEK) and top hat keratoplasty (THPK) in patients with Fuchs’ endothelial dystrophy (FED) and/or pseudophakic bullous keratopathy (PPBK).

METHODS. Patients underwent either THPK (n = 33) or DSAEK (n = 39) at the Erasmus Medical Center, Rotterdam. For each nonrandomized cohort, a biexponential regression model for ECD decay was fitted. Factors associated with higher ECD decay were evaluated.

RESULTS. Median follow-up was 31.2 months (range, 11–91) in the THPK cohort, and 23.4 months (range, 6–61) in the DSAEK group. The early ECD decay was much higher after DSAEK (half time, 2.2 months) than after THPK (half time, 12.8 months). The late ECD decay after DSAEK was less steep (half time, 75.5 months) than after THPK (half time, 62 months). The 1-, 3- and 5-year endothelial cell losses derived from the models after DSAEK were 56%, 66%, and 73%, respectively, and after THPK were 24%, 50%, and 64%, respectively. For the DSAEK cohort, PPBK as an indication for surgery was associated with significantly higher late-phase decay rates. For the top-hat cohort, a significantly lower late-phase decay rate was found in PPBK. FED and same-session cataract surgery were confounding variables in the DSAEK cohort. Regarding DSAEK, postoperative re-bubbling was not found to have significant effects on early or late ECD decay rates. However, the small sample size and other limitations related to the method of evaluation may have influenced these findings.

CONCLUSIONS. After DSAEK, early ECD decay was stronger than after THPK, as opposed to late decay. Late decay was faster for PPBK than for FED after DSAEK. (Invest Ophthalmol Vis Sci. 2011;52:9226–9231) DOI:10.1167/iovs.11-8107

Penetrating keratoplasty (PK) has been the standard of care for treating endothelial failure for many years. The posterior mushroom or top hat penetrating keratoplasty (THPK) is a type of PK with a stepped wound configuration, in which the posterior diameter of the donor transplant (and the recipient wound bed) is larger than the anterior donor and recipient diameter. This technique has successfully been used for the treatment of Fuchs’ endothelial dystrophy and pseudophakic bullous keratopathy. Because of the large posterior diameter of the transplanted cornea, a higher percentage of diseased endothelium is replaced compared with standard PK. Also, the self-sealing posterior lip provides a better wound stability.

Currently, Descemet’s Stripping Automated Endothelial Keratoplasty (DSAEK) has replaced PK as the gold standard surgical treatment for corneal endothelial disorders. Its main advantages include the lack of sutures, less induced (irregular) astigmatism, and hence a faster visual recovery. Furthermore, it is a safer technique with less risk for expulsive hemorrhage and no suture-related complications. However, a main concern with this technique, especially regarding long-term results and long-term graft survival, remains the rate of postoperative endothelial cell loss.

Recently Price et al. showed that, overall, graft success was comparable for DSAEK and PK procedures. However, the endothelial cell loss was higher after DSAEK at 6 and 12 months after surgery, consistent with endothelial trauma caused by more donor tissue manipulation. In this study, relative endothelial cell loss was found to be 34% ± 22% for DSAEK versus 11% ± 20% for PK at 6 months after surgery, and 38% ± 22% versus 20% ± 23% at 12 months.

The first purpose of our present study was to evaluate endothelial cell loss and analyze endothelial cell decay patterns in two groups of patients who had undergone either THPK or DSAEK in our institution (Department of Ophthalmology, Erasmus Medical Center, Rotterdam, The Netherlands). We set out to fit bi-exponential endothelial regression models for endothelial cell decay, comparable with the biphasic models previously described by Armitage et al. and Börhringer et al. The second goal was to identify factors associated with faster or slower endothelial cell decay in both the early and late postoperative phases after both types of corneal transplantation. Therefore, additional analyses were performed to evaluate the effect of several pre-, intra- and postoperative factors on the decay rate coefficients of the early and late phases of both models.

METHODS

THPK has been performed in the Department of Ophthalmology of the Erasmus Medical Center Rotterdam since March 2003 and DSAEK since October 2004. After October 2004, indications for THPK were endothelium-related corneal disorders with concomitant stromal opacity, endothelial disorders in patients without any crystalline lens opacity, and pseudophakic bullous keratopathy (PPBK) in cases of absent or ruptured posterior capsule (because of the risk of air dislocation to the posterior segment when performing DSAEK). Patients with persistent stromal and epithelial edema resulting in the formation of microcysts, with or without bullae, are both deemed to have PPBK. Only patients...
with persistent stromal edema underwent surgery. Preoperative pachymetry measurements were not routinely performed.

The medical records of all patients who had undergone DSAEK or THPK, for Fuchs’ endothelial dystrophy (FED) or PPBK or both, at the Erasmus Medical Center, Rotterdam, The Netherlands, were reviewed in a protocol that complied with the Declaration of Helsinki. The few cases with other indications (e.g., regraft) and/or more extensive concomitant pathology besides FED or PPBK were excluded from the study, as were cases with a completed follow-up of <6 months. Our study includes the initial experiences with each respective surgical technique of both surgeons who first used them (GVR and MCB).

The main outcome measures in this study were endothelial cell density (ECD), obtained at different (flexible) follow-up time points. The ECD had been prospectively and longitudinally measured after transplantation, using a noncontact specular microscope (SP-3000P; Topcon Europe Medical B.V., IJssel, The Netherlands) and semiautomated endothelial cell analysis with endothelial cell–analysis software (Imagenet; Topcon Europe Medical B.V.).

Two cohorts, DSAEK and THPK, were identified, and data were separately analyzed for each cohort. Besides ECD, surgeon, date of surgery, whether simultaneous cataract extraction was performed (either with a routine phacoemulsification [MCB] or a Blumenthal manual extracapsular technique [GVR]), and postoperative complications were recorded.

Cases with clinically manifest endothelial rejection episodes during the postoperative follow-up window were excluded before analysis.

**DSAEK Surgical Technique**

DSAEK was performed under either general or retrobulbar block anesthesia, by two surgeons (GVR and MCB). The surgical technique is in many ways comparable to that used by Price et al. A superiorly located corneoscleral tunnel incision of 5.5 to 6.0 mm was used in all cases. The incision was sutured water tight at the end of the procedure and covered with conjunctiva. In all cases, the posterior lamella was cut during surgery from the donor corneoscleral disc with a microkeratome system with a 350-µm head on an artificial anterior chamber (Evolution 2; Moria, Paris, France). All donor corneas were preserved in organ culture medium at 31°C and were obtained from Bio Implant Service (Leiden, The Netherlands). A donor lamella of 8.5 mm was transplanted. In all cases, an anterior chamber maintainer was used during Descemetotomy and during donor lamella insertion, to prevent anterior chamber collapse. A drop of viscoelastic substance (Healon) was applied on to the donor endothelium before introduction of the donor lamella into the anterior chamber. No additional viscoelastic material was used. Donor insertion was performed with a pull-through technique using a Prolene 10-0 nylon suture and straight needles (Sabreloc Straight Transchamber; Ethicon, Auneau, France).

The first two donor insertions had been performed with forceps, and in one later case, the Busin glide and forceps were used. Both cases with forceps insertion and the case with Busin glide insertion were excluded from this study before analysis, to provide a more homogeneous data set.

**Additional DSAEK Data**

For the DSAEK group, other parameters included in the analysis were indication for surgery (FED, PPBK, or both); concomitant cataract surgery with the DSAEK procedure (yes or no); duration of high-pressure complete air fill (10 vs. 15 minutes) for donor attachment; suturing of the posterior lamella with one suture at 12 o’clock onto the anterior stroma (yes or no); late postoperative elevated intraocular pressure (IOP) (yes or no); whether or not a postoperative “re-bubbling” had been performed for (partial) donor detachment (yes or no); and a newly devised score to evaluate intra- and early postoperative manipulation of donor material. Using the DSAEK score, we evaluated intraoperative and postoperative donor lamella manipulation in DSAEK surgery. This score is an ordinal summation score, which had specifically been devised by us (GVR and MCB) for this purpose. In this scoring method, points were added when more than normal manipulation of donor tissue occurred during preparation and insertion of the donor lamella. More points were added when postoperative re-bubbling procedures had to be performed for donor lamella detachment (Table 1).

**THPK Surgical Technique**

All THPK cases were performed under general or retrobulbar block anesthesia by two surgeons (GVR and MB). The top hat surgical technique has been described in detail. Either 16 interrupted or 8 interrupted and 1 running 10-0 nylon sutures were used. No intraoperative complications occurred in the cases examined.

**Additional Top Hat Data**

Donor endothelial diameter was looked into; however, all included cases had an endothelial diameter of 9.0 mm, except five in which the endothelial diameter was slightly smaller (8.5 mm n = 2; 8.75 n = 3). Statistical evaluation of these two tiny subgroups was deemed infeasible.

The analyzed parameters included suturing technique (16 interrupted vs. 8 interrupted plus 1 running suture), concomitant cataract surgery (same types as in DSAEK) during THPK (yes or no), and later postoperative suture-related procedures (either suture addition or complete suture removal; yes or no for any suture procedure).

**Statistical Model**

Longitudinal ECD measurements (number of cells per square millimeter) were taken at various times in patients after cornea transplantation. To analyze ECD decay over time, a two-compartment exponential decay model was used. The parameters of that model were estimated using nonlinear mixed modeling (PROC NLMIXED of SAS, version 9.2, SAS, Cary, NC). NL MIXED uses an improved maximum-likelihood estimation method and can therefore deal with missing values; there is no need for imputing data.

The variable to be explained by that model is defined as the remaining ECD fraction at time t in patient ECDt/ECD0, with t measured in months. This fraction, by definition, equals 1 at time 0.

The two-compartment exponential decay model is specified as follows:

\[
ECD_t/ECD_0 = c_t \times \exp(at) + (1 - c_t) \times \exp(bt) + \mu_t
\]

For numerical purposes the term \( c_t \) is reparameterized as a logistic function:

\[
c_t = \exp(\delta_t)/(1 + \exp(\delta_t))
\]

so that 0 < \( c_t < 1 \). The parameters \( a < 0 \) and \( b < 0 \) are the monthly decay rates (coefficients) that are assumed constant in time and between subjects. For each patient \( t \) the term \( \delta_t \) is drawn from a normal distribution, with mean \( \delta \) and variance \( V_\delta \), representing the between-patient variability of the total decay functions. At each time \( t \) and

<table>
<thead>
<tr>
<th>TABLE 1. DSAEK Score</th>
</tr>
</thead>
<tbody>
<tr>
<td>Microkeratome cutting problems</td>
</tr>
<tr>
<td>Insertion of donor lamella for a second time</td>
</tr>
<tr>
<td>Insertion of donor lamella more than two times</td>
</tr>
<tr>
<td>Manipulation needed for unfolding the donor lamella</td>
</tr>
<tr>
<td>Graft upside down, reversal of graft performed</td>
</tr>
<tr>
<td>Remaining air bubble (partial fill) in AC after the procedure</td>
</tr>
<tr>
<td>Insufficient intraoperative adherence after initial air fill</td>
</tr>
<tr>
<td>further air fill</td>
</tr>
<tr>
<td>First postoperative re-bubbling</td>
</tr>
<tr>
<td>Second postoperative re-bubbling</td>
</tr>
</tbody>
</table>

AC, anterior chamber.
within each patient $i$ the residual term $u_i$ is drawn from a normal distribution with mean 0 and variance $V_u$, representing the within-patient variability of ECD fractions around the patient’s own total decay function.

The parameters to be estimated are $a$, $b$, $\delta$, $V_a$ and $V_u$. A 95% reference interval for the $c_i$ terms across subjects is given by $\exp(\delta \pm 1.96\sqrt{V_\delta})(1 + \exp(\delta \pm 1.96\sqrt{V_\delta})].$

The effect of possibly influencing factors, so-called explanatory variables $x_i$ of patient $i$ on his total decay function is explored by specifying the monthly decay rates $a$ and $b$ as linear functions of $x_i$:

$$a(x_i) = a_0 + a_1 x_i$$

and

$$b(x_i) = b_0 + b_1 x_i.$$  

Due to the sparse data (small number of patients and small number of measurements per patient relative to the number of parameters to be estimated), those effects were estimated for each explanatory variable $x_i$ and for either parameter $a$ or $b$ separately.

### RESULTS

#### Patient Data

In the THPK cohort eventually 33 cases were included (Table 2). In 6 of the 33 cases, concomitant cataract surgery was performed in the same session, either immediately before or during THPK surgery. In 11 cases, only interrupted sutures were used, in the remaining 22, eight interrupted and one running suture were used. In 5 of 33 cases, late postoperative suture-related procedures (either suture addition or complete suture removal) were performed.

In our DSAEK cohort, 39 cases were eventually included (Table 2). In 20 cases, concomitant cataract surgery was performed in the same session, immediately before DSAEK. In 7 of 39 cases, complete air fill was performed for 15 minutes, in the remaining 32 cases, complete air fill was performed for 10 minutes. Suturing of the posterior lamella occurred in 9 of 39 cases. In 11 cases, re-bubbling procedure was necessary, and in two more cases a second re-bubbling was performed. For the statistical analysis, we evaluated a group of 15 cases in which one or more re-bubbings were performed. Of 39 cases, 21 had a DSAEK score of 1, 7 had a score of 2, 8 had a score of 3, 2 had a score of 4, and 1 had a score of 5. After surgery, elevated IOP was observed in 6 of 39 cases.

In our THPK cohort, secondary failure of two grafts occurred (not related to endothelial rejection): in one patient, 4 years after transplantation and in the other, 2 years after transplantation. These cases were included in the model with an assumed last ECD of 0 cells/mm². In the DSAEK group, no secondary failures occurred. No primary graft failures were observed.

Median follow-up for the THPK cohort measured 31.2 months (range, 11–91) and 23.4 months (range, 6–61) for the DSAEK cohort.

#### Regression Models of ECD Decay and Descriptive Statistics

The estimated parameters of the global two-compartment exponential decay model are presented in Table 3 for DSAEK and THPK:

$$\frac{ECD_i}{ECD_{0i}} = c_i \times \exp(-at) + (1 - c_i) \times \exp(-bt) + u_i$$

with

$$c_i = \frac{\exp(\delta_i)}{1 + \exp(\delta_i)}.$$  

The estimated means and 95% confidence intervals of the $c_i$ terms across subjects for DSAEK and THPK are 0.472 (0.159–0.808) and 0.636 (0.447–0.791), respectively.

In DSAEK, $a = -0.00918$ is the estimated monthly decay rate coefficient of the late phase, and $b = -0.3102$ is the estimated decay rate of the early phase. ECD decay half times for DSAEK were calculated as $\ln(2)/0.00918 = 75.5$ months for the late phase and as $\ln(2)/0.3102 = 2.2$ months for the early phase.

In THPK, $a = -0.01030$ is the estimated decay rate of the late phase, and $b = -0.04222$ is the estimated decay rate of the early phase. ECD decay half times for THPK were calculated as $\ln(2)/0.01118 = 62.0$ months for the late phase and as $\ln(2)/0.05401 = 12.8$ months for the early phase.

Using the models with estimated parameters $a$, $b$, and $\delta$, ECD decay was depicted in Figure 1, starting at an average ECD level set at 2736 cells/mm². Both graphs were extrapolated to a follow-up of 10 years after surgery. Our longest actual follow-up durations were 91 months in the THPK group and 61 months in the DSAEK group.

From these extrapolated models, it was calculated that, on average, our THPK cohort would reach the 500 cells/mm² mark at 118 months after surgery and the DSAEK cohort at 103 months after surgery.

Using the estimated models, the 1-, 3-, and 5-year endothelial cell loss can also be predicted. The 1-, 3-, and 5-year endothelial cell loss after DSAEK measured 56%, 66%, and 73%, respectively. The 1-, 3-, and 5-year endothelial cell loss after THPK measured 24%, 50%, and 64%, respectively.
endothelial cell loss; after DSAEK the late-phase decay of endothelial cells was less steep than after THPK (Fig 1). Late-phase endothelial cell loss in DSAEK is much higher and faster (decay half time) compared to THPK (13.5 months vs. 75.5 months). This finding is in line with previously reported results on ECDs after DSAEK.

The effect of possibly influencing factors (explanatory variables) $x_i$ of patient $i$ on his total decay function was explored by specifying the monthly decay rates $a$ (late phase) and $b$ (early phase) as linear functions of $x_i$:

$$a(x_i) = a_0 + a_1 x_i$$

and

$$b(x_i) = b_0 + b_1 x_i.$$ 

These effects were estimated for each explanatory variable $x_i$ and for parameters $a$ and $b$ separately. For example, when $x_i = 0$ or 1, respectively, denoted whether FED was the indicator for surgery or not, then $a_0$ was the late ECD decay rate without an FED indication and the sum $a_0 + a_1$ is the late decay rate with an FED indication, the difference in late decay rates being represented by $a_1$.

**Top Hat Keratoplasty.** The effect of the indication for FED for keratoplasty was not significant on early- or late-phase ECD decay rates. However, when PPBK was the indication, the decay rate of the late phase was significantly weaker (i.e., less negative) than that of non-PPBK THPK ($0.00570$ vs. $-0.01464; P = 0.001$), whereas PPBK as an indication for surgery had no significant effect on the early-phase decay rate. When PPBK combined with FED was the indication, again the late-phase decay rate was significantly weaker ($0.00562$ vs. $-0.01409; P = 0.0002$); this outcome was not found for the early-phase decay rate.

Neither suturing technique nor late postoperative suture-related procedures had a significant effect on either early or late ECD decay rates.

Simultaneous cataract surgery during THPK had no significant effect on late-phase ECD decay; however the early-phase ECD decay rate was found to be significantly weaker in cases with simultaneous cataract extractions ($0.02586$ vs. $-0.05265; P = 0.0044$).

**Descemet's Stripping Automated Endothelial Keratoplasty.** When FED was the indication for DSAEK, the late-phase ECD decay rate was significantly weaker (i.e., less negative) than in non-FED DSAEK ($0.00852$ vs. $-0.01962; P = 0.0001$). The effect of FED as the indication for DSAEK on the early-phase decay rate could not be estimated, probably because none of the 10 non-FED subjects had more than three visits. Late-phase decay rate was significantly stronger (i.e., more negative) in PPBK DSAEK compared with non-PPBK DSAEK ($0.01524$ vs. $-0.00784; P = 0.0026$); no significant effect of PPBK as indication for surgery was found on early-phase decay. Simultaneous FED and PPBK, as indicated, had no significant effects on either early- or late-phase ECD decay rates.

A difference in the duration of complete air fill for donor lamella adherence of 5 minutes (10 vs. 15 minutes complete fill) did not cause a significant difference in early or late ECD decay rates, nor did whether the donor lamella was sutured to the anterior recipient stroma.

Same-session cataract surgery (cataract surgery immediately before DSAEK) caused a significantly weaker late-phase ECD decay rate ($-0.00785$ vs. $-0.01512; P = 0.0039$), but no significant difference in early-phase rate. (Late) postoperative IOP elevation had no significant effects on either late- or early-phase ECD decay rates.

Whether one or more re-bubbling procedure had to be performed to obtain definitive donor lamella adherence was not found to have a significant effect on either early- or late-phase ECD decay rates. Each additional point in our DSAEK score (i.e., small increases in the perceived amount of donor tissue manipulation before, during, and/or after donor lamella insertion) increased the ECD decay rate coefficients of both the early and late phases slightly, but these effects were not significant.

**Discussion**

In our study we were able to fit a single regression equation for endothelial cell decay to the complete data set of each technique. Our regression model took both repeated intrapatient measurements, and inter- and intrapatient variance into account. We did not have to use imputed data, such as was done by Bohringer et al. Although the patients in our study had not been randomly assigned to one of the two transplantation techniques, our cohorts were each other's historical control groups. Comparing the different decay coefficients still allowed for in-depth comparison of endothelial cell decay between both groups.

Our results show that the early-phase postoperative endothelial cell loss in DSAEK is much higher and faster (decay half time was 2.2 months) compared with THPK (half time, 12.8 months). This finding is in line with previously reported results and is consistent with the conclusion that more endothelial trauma occurs in endothelial keratoplasty, due to more donor tissue manipulation. The opposite is true of the late-phase endothelial cell loss; after DSAEK the late-phase decay of endothelial cells was less steep than after THPK (Fig 1). Late-phase ECD decay half time in DSAEK was 75.5 months versus 62.0 months for late-phase THPK half time. This also is consistent with earlier findings.

Compared to other reported results on ECDs after DSAEK, the early-phase endothelial cell losses in our study appeared to be higher. This may be explained by our learning curve; our data included the very first DSAEK cases performed in our center. In contrast, in our study, no significant effect of more donor tissue manipulation on ECD decay (the "DSAEK score") was demonstrated. However, it should be noted that we were only able to test the effect of a 1-point increment on the DSAEK score. Such a small increment in score in fact did result in a slightly higher decay rate coefficient (either early or late phase), but this was not a significant effect. Stronger effects of higher manipulation scores may be expected and were sug-
gested by our raw data, but this could not be tested with our statistical analysis methods. We also could not demonstrate that re-bubbling procedures were detrimental to the endothelial cell decay rates. Similarly, other investigators have also not been able to demonstrate higher endothelial cell losses after re-bubbling procedures. The re-bubbling rate in our study was remarkably high (up to 30%). Since these re-bubblings occurred predominantly in the first 15 cases, a learning curve in surgical technique and/or intraoperative donor tissue preparation is highly likely. There were no differences regarding donor tissue handling or preservation techniques in the non-attached cases.

In the THPK cohort, as expected, no relation was found between early or late endothelial cell loss rates and suturing techniques (continuous versus interrupted). Late postoperative suture-related procedures (additional suture placements or removal of all sutures) were also not found to cause detrimental ECD decay rates, possibly because no endothelial rejections or other major events such as dehiscence were induced.

Performing simultaneous cataract extraction caused a significantly lower early endothelial cell loss rate in THPK. This is not an easy finding to explain. Deepening of the anterior chambers may occur after recent cataract surgery, which in turn may lead to a decrease in the rate of early-phase endothelial cell loss. Circumstantial evidence supporting this explanation can be found in increased endothelial cell loss when shallow anterior chambers occur after trabeculectomy, or increased endothelial cell loss after hypermetropic anterior chamber iris-attached phakic IOLs, when glaucoma drainage tubing is in close proximity to the endothelium. However, anterior chamber depths were not measured and hence this explanation is merely conjecture.

In the DSAEK cohort, the diagnosis of PPBK was associated with a significantly higher late-phase endothelial cell loss rate and the late-phase ECD decay rate was significantly lower when FED was the indication for surgery. In 20 of the 22 patients with FED, DSAEK was combined with same-session cataract extraction. The variable “intraoperative cataract surgery” therefore is highly confounded with the indication FED. Interpretation of separate effects of both variables on ECD loss after DSAEK therefore is not possible.

These findings support the hypothesis that the often reported higher than physiological late-phase ECD loss after corneal transplantation may be caused by the phenomenon of endothelial cell redistribution onto the recipient cornea. Redistribution of endothelial cells onto the recipient cornea is supposedly stronger in cases of PPBK where the recipient endothelium has been largely or completely depleted, than in (phakic) cases with FED with better peripheral recipient endothelium. In the recent study by Börhringer et al. PKP for keratoconus (with healthy recipient endothelium) was shown to have lower late-phase ECD losses than those for PPBK. These findings are also consistent with earlier findings that (PK) graft survival in PPBK is lower than survival after surgery for keratoconus and FED.

As Börhringer et al. pointed out, redistribution of donor endothelial cells to the recipient cornea is not only responsible for high late-phase endothelial cell decay rate (i.e., for higher than physiological loss), but hence also for the development of late endothelial failure of grafts. The concept of late endothelial failure of a corneal graft was first recognized by Polack and defined by Nishimura and Bourne. Nishimura and Bourne and Armitage et al. described late endothelial failure as a function of the higher than physiological ECD decay in the late-phase after transplantation and also of the level of ECD at which this higher than physiological decay starts. When initial ECDs are already low, increased decay will cause late endothelial failure sooner. The results in our DSAEK cohort present us with some concerns in this respect.

The rate of endothelial cell loss tapered off more after DSAEK than after THPK. The reason for the difference between late endothelial cell loss rates is as yet unknown. The inflammatory response may be less after DSAEK due to the smaller wound, and this may be akin to the theory that chronic subclinical inflammation and/or a chronically broken-down blood-aqueous barrier may cause the increased late cell loss after (TH)PK. The differences between the wounds may also cause differences in mechanical stability of the globe and hence differences in mechanical forces, causing endothelial attrition. Finally, the edge of the DSAEK onlay graft protruding into the anterior chamber may function as a physical barrier that inhibits endothelial cell migration onto the recipient.

Endothelial cell migration does occur after DSAEK, as was recently demonstrated by Stewart et al., but this physical barrier may cause it to be slower and more fragile than after PK. After THPK, such a physical barrier for endothelial migration may be less of a factor, and the endothelial cells may migrate more freely.

Remarkably, in our THPK cohort we found that the diagnosis of PPBK was associated with a significantly lower late-phase endothelial cell loss rate as opposed to non-PPBK THPKs. This was an unexpected finding, especially in the light of the theory of redistribution of donor endothelial cells onto the recipient cornea. A possible explanation for this finding may be that one or both of the other factors perhaps responsible for higher late-phase ECD decay in THPK compared to DSAEK (e.g., the wound size/subclinical inflammation factor and the mechanical stability factor) are so strong in their effect that one or both of them dominate the effect of the redistribution at this point in the postoperative time. Redistribution-related findings after THPK may therefore not have been clear from our analysis.

In the near future, analyses of longer term results of other recent studies published on ECD loss after DSAEK will further elucidate patterns of prolonged increased endothelial cell loss and the rate of late endothelial failure after DSAEK. It will be interesting to also investigate late-phase endothelial cell loss rates and late endothelial failure rates after the newly emerged Descemet’s membrane endothelial keratoplasty (DMEK) technique. After DMEK, early endothelial cell loss due to preoperative and intraoperative tissue manipulation appears to be similar compared with that after DSAEK, but much less of a physical barrier for late endothelial migration may be present than after DSAEK.

References