Original article

Standardization of the Descemet membrane endothelial keratoplasty technique: Outcomes of the first 450 consecutive cases

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ABSTRACT

Objectives: To evaluate the clinical outcome of the first 450 consecutive cases after Descemet membrane endothelial keratoplasty (DMEK), as well as the effect of standardization of the technique.

Material and methods: Comparison between 3 groups: Group I: (cases 1–125), as the extended learning curve; Group II: (cases 126–250), transition to technique standardization; Group III: (cases 251–450), surgery with standardized technique. Best corrected visual acuity, endothelial cell density, pachymetry and intra- and postoperative complications were evaluated before, and 1, 3 and 6 months after DMEK.

Results: At 6 months after surgery, 79% of eyes reached a best corrected visual acuity of ≥0.8 and 43% ≥1.0. Mean preoperative endothelial cell density was 2530 ± 220 cells/mm² and 1613 ± 495 at 6 months after surgery. Mean pachymetry measured 668 ± 92 μm and 526 ± 46 μm pre- and (6 months) post-operatively, respectively. There were no significant differences in best corrected visual acuity, endothelial cell density and pachymetry between the 3 groups (p > 0.05). Graft detachment presented in 17.3% of the eyes. The detachment rate declined from 24% to 12%, and the rate of secondary surgeries from 9.6% to 3.5%, from group I to III respectively.

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Conclusions: Visual outcomes and endothelial cell density after DMEK are independent of the technique standardization. However, technique standardization may have contributed to a lower graft detachment rate and a relatively low number of secondary interventions required. As such, DMEK may become the first choice of treatment in corneal endothelial disease.

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La estandarización en el trasplante endotelial de membrana de Descemet: resultados de las primeras 450 cirugías

Resumen

Objetivos: Analizar los resultados de 450 casos con diferentes patologías endoteliales intervenidos mediante trasplante endotelial con la técnica de recambio de la membrana de Descemet (DMEK, por sus siglas en inglés: Descemet membrane endothelial keratoplasty) y evaluar las consecuencias de la estandarización de esta técnica.

Material y métodos: Se compararon 3 subgrupos consecutivos: el subgrupo I (casos 1-125) representaba la extensión de la curva de aprendizaje; el subgrupo II (casos 126-250) la transición a la estandarización de la técnica y el subgrupo III (casos 251-450) la estandarización propiamente dicha. Se registraron los resultados de agudeza visual mejor corregida pre- y postoperatorio, la densidad de células endoteliales, la paquimetría y las complicaciones.

Resultados: A los 6 meses de la cirugía, el 79% de los pacientes alcanzaron una agudeza visual mejor corregida ≥ 0,8 y el 43% ≥ 1. La densidad de células endoteliales media preoperatoria fue 2.530 ± 220 células/mm², y 1.613 ± 495 células/mm² al sexto mes poscirugía. La paquimetría era 668 ± 92 μm y 526 ± 46 μm pre- y postoperatoria a los 6 meses, respectivamente. No se encontraron diferencias en cuanto a la agudeza visual mejor corregida, la densidad de células endoteliales o la paquimetría entre los subgrupos (p>0,05). El desprendimiento del injerto se observó en el 17,3% de los ojos. La tasa de desprendimientos disminuyó del 24 al 12%, y el número de reintervenciones, del 9,6 al 3,5%, del subgrupo I al III respectivamente.

Conclusiones: Los resultados visuales y la densidad de células endoteliales tras DMEK son independientes de la estandarización de la técnica quirúrgica. Sin embargo, la estandarización de la técnica podría haber contribuido con un descenso en el número de desprendimientos y con un relativamente bajo número de intervenciones secundarias. A la vista de estos resultados, DMEK podría convertirse en el tratamiento de elección para las enfermedades del endotelio corneal.

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Introduction

Since the introduction in 1998 of posterior lamellar keratoplasty (PLK), also known as Deep Lamellar Endothelial Keratoplasty (DLEK), this technique has been developed and modified to become the most commonly used technique at present: DS(A)EK (Descemet Stripping (Automated) Endothelial Keratoplasty) and DMEK (Descemet Membrane Endothelial Keratoplasty). These 2 posterior lamellar techniques not only provide better visual results when compared with penetrating keratoplasty (PK) and DLEK, but also avoid the complications derived from sutures or the elevated residual astigmatism frequently observed after PK.

Even though DS(A)EK generally obtains acceptable visual results (generally better than after PK or DLEK), this technique modifies the physiological anatomy of the cornea due to the fact that, together with donor Descemet’s membrane (DM) and endothelium, the transplant also includes a stroma sheet. In other words, a posterior corneal lamella which is thicker than the physiological lamella is transplanted. This could induce optical imperfections, with the result that few patients could achieve best corrected visual acuity (BCVA) values of 1 (≥20/20, ≥1 in the Snellen scale). The introduction of the DMEK technique in 2002 signified an evolution of endothelial transplants as it enabled selectively transplanting the endothelium and DM without additional stroma insertion. Accordingly, DMEK is a “non-additive” surgery which restores physiological corneal anatomy. This translates into excellent visual results which were inconceivable with previous keratoplasty techniques.

Even though DMEK was initially regarded as more complicated to perform than DS(A)EK, the latest developments in tissue preparation and surgical technique standardization...
have made it easier to learn and to perform, \(^{19-21}\) in addition to diminishing complication rates. At present, DMEK is a technique that can be carried out without direct contact (“no-touch”) with tissue in a standardized and reproducible manner \(^{20}\) and could become the treatment of choice for corneal endothelial diseases above the rest of endothelial transplants techniques. \(^{18,22}\)

One of the objectives of the present study was to describe the results of 450 DMEK surgeries for treating Fuchs’ endothelial dystrophy, pseudophakic bullous keratopathy and graft failure after endothelial keratoplasty in terms of BCVA, graft cellularity and post-surgery complications. An additional object was to assess the effects of surgical standardization of said technique. To this end, the sample was divided into two subgroups: subgroup I included the first 125 DMEK as a representation of the learning curve extension; subgroup II included the following 125 DMEK, representing a transition toward technique standardization; and subgroup III, comprising the most recent 200 DMEK, as a sample of the standardized technique.

### Material and methods

This retrospective study included 450 consecutive eyes (55% female, 45% male) of 351 patients with a mean age (±standard deviation, range) of 67.9 (±12.5; 20–93) years. The 450 examined cases were cases 26–475 out of 475 consecutive DMEK performed by the authors of the study. The first 25 eyes were the first to be intervened with the DMEK technique (considered as the “learning curve” of the technique) and were excluded to avoid bias. \(^{15}\)

Indications for surgery comprised Fuchs’ endothelial dystrophy (n = 400), pseudophakic bullous keratopathy (n = 29), graft failure after endothelial keratoplasty (n = 13) or penetrating keratoplasty (n = 2), and other indications (n = 6) (Table 1). Out of the 450 eyes, 110 were phakic, 338 were pseudophakic and 2 aphakic. All patients underwent superior iridotomy prior to laser YAG surgery to preempt post-surgery intraocular pressure increase in case of angular closure produced by the air bubble. All patients had signed an informed consent for participating in the study, which was carried out in accordance with the guidelines of the Helsinki declaration for biomedical research.

### Donor tissue

The dissection of grafts, endothelial counts and microbiological tests were carried out in the Amritans Eyebank Rotterdam, The Netherlands. The corneoscleral rings were obtained from donor ocular globes during the first 36 h post-mortem and were preserved in a Minimally Modified Essential Medium (EMEM) (ConeaMax, Eurobio Laboratories, Les Ulis Cedex, France) at 31°C during one week. \(^{23}\) After this period, the density and morphology of endothelial cells was measured with inverted light microscope (Axiovert 40. Zeiss, Göttingen, Germany). The corneoscleral ring was placed in a vacuum-powered corneal support with the endothelial layer facing upwards and the graft was peeled by means of a standardized no-touch technique with the tissue to be transplanted. \(^{22}\)

The obtained Descemet roll was a thin 9.5 mm diameter film comprising DM and endothelium which, due to the elastic properties of DM, it rolled up on itself and presents the endothelium on the external side. Subsequently, the Descemet roll was preserved in EMEM during 5–10 days up to implantation. \(^{21}\)

### Surgical technique

All the operations were carried out applying the standardized no-touch technique of the Netherlands Institute for Innovative Ocular Surgery. \(^{20}\)

### Table 1 – Demographic data of DMEK patients.

<table>
<thead>
<tr>
<th></th>
<th>Overall group (1–450)</th>
<th>Subgroup I (1–125)</th>
<th>Subgroup II (126–250)</th>
<th>Subgroup III (251–450)</th>
</tr>
</thead>
<tbody>
<tr>
<td><strong>Number of patients</strong></td>
<td>351</td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td><strong>Mean age (±SD). In years</strong></td>
<td>68 (±12.5)</td>
<td>67 (±12)</td>
<td>67 (±12)</td>
<td>69 (±12)</td>
</tr>
<tr>
<td><strong>Gender (female/male)</strong></td>
<td>55/45% (248/202)</td>
<td>54/46% (68/57)</td>
<td>54/46% (68/57)</td>
<td>56/44% (112/88)</td>
</tr>
<tr>
<td><strong>Indications for DMEK</strong></td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>FED</td>
<td>88.9% (400)</td>
<td>92.8% (116)</td>
<td>85.6% (107)</td>
<td>88.5% (177)</td>
</tr>
<tr>
<td>BK</td>
<td>6.5% (29)</td>
<td>3.2% (4)</td>
<td>9.6% (12)</td>
<td>6.5% (13)</td>
</tr>
<tr>
<td>Failed previous keratoplasty</td>
<td>3.3% (15)</td>
<td>4.0% (5)</td>
<td>3.2% (4)</td>
<td>3.0% (6)</td>
</tr>
<tr>
<td>- Endothelial keratoplasty</td>
<td>2.8% (13)</td>
<td>3.2% (4)</td>
<td>3.2% (4)</td>
<td>2.5% (5)</td>
</tr>
<tr>
<td>- Penetrating keratoplasty</td>
<td>0.4% (2)</td>
<td>0.8% (1)</td>
<td>0.0% (0)</td>
<td>0.5% (1)</td>
</tr>
<tr>
<td>Others</td>
<td>1.3% (6)</td>
<td>0.0% (0)</td>
<td>1.6% (2)</td>
<td>2% (4)</td>
</tr>
<tr>
<td><strong>Lens</strong></td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Pseudophakics</td>
<td>75.1% (338)</td>
<td>83.2% (104)</td>
<td>72.8% (91)</td>
<td>71.5% (143)</td>
</tr>
<tr>
<td>Phakics</td>
<td>24.5% (110)</td>
<td>16.8% (21)</td>
<td>27.2% (34)</td>
<td>27.5% (55)</td>
</tr>
<tr>
<td>Aphakics</td>
<td>0.4% (2)</td>
<td>0.0% (0)</td>
<td>0.0% (0)</td>
<td>1% (2)</td>
</tr>
</tbody>
</table>

SD: standard deviation; FED: Fuchs endothelial dystrophy; DMEK: Descemet membrane endothelial keratoplasty; BK: bullous keratopathy. Number of eyes indicated between parenthesis (n).
A 3 mm limbic incision was marked at the 12 o'clock surgical position, carrying out 3 paracentesis at 10:30, 1:30 and 7:30 (4:30 in left eye) with a blade, introducing air through these to completely fill the anterior chamber (AC) utilizing a 30 G cannula. Under these conditions, a 9 mm descecmethoraxis was performed utilizing an inverted Sinskey hook (D.O.R.C. International, Zuidland, The Netherlands). Subsequently, an exhaustive examination was carried out to verify the absence of any receptor DM remains adhered to the posterior stroma, as any fragment could alter the final visual acuity (particularly in patients with Fuchs’ endothelial dystrophy) as well as being a cause for graft detachment.23–25

After achieving the full detachment of the receptor DM, the main incision was extended by means of a lamellar dissection to a depth of 50% with a blade, creating a self-sealable 3 mm tunnelized incision in the clear cornea. Subsequently, the membrane was extracted and AC was filled with air up to the implantation of the donor tissue to avoid stroma hydration.

The Descemet roll was transferred together with culture medium from the preservation flask to a crystal bowl by simple pouring. The culture medium was withdrawn with a pipette and the donor tissue was meticulously rinsed with sterile saline solution (BSS, Acon Nederland BV, Gorinchem, The Netherlands) to eliminate remains of the preservation medium. The Descemet roll was stained with 0.06% Trypan blue (VisionBlueTM, D.O.R.C. International, Zuidland, The Netherlands). By applying direct BSS flow it was possible to manipulate the DM to unroll it and create a double roll before introducing it by means of suction cups in a glass injector (surgical DMEK set, catalog number 50.2200. D.O.R.C. International, Zuidland, The Netherlands).

With prior BSS-air exchange in AC, the injector was inserted through the main incision and the Descemet roll was implanted in AC with the curls oriented toward the stroma (Fig. 1). Adequate orientation can be checked by means of the Moutsouris sign, i.e., placing a 30 G needle inside one of the lateral rolls, if the graft is correctly oriented (double roll toward the stroma, endothelium toward the iris), the end of the cannula remains inside the roll with the blue tip visible. If the graft is inverted, it can be placed in the adequate position with a small BSS injection through the paracentesis.26

An air bubble can be introduced between the 2 rolls to deploy the graft, moving it with a cannula with soft movements on the external surface of the cornea (the “Dapena maneuver”), unfolding the graft using to cannula (the “Dirisamer technique”) or applying a combination of techniques.26 Once the graft is unfolded, BSS is injected in AC to move and center the graft. A slight off-centering of the graft that covers the central corneal area is acceptable.

Once the graft has been unfolded and centered, the air bubble is increased with the purpose of flattening the graft over the iris. After approximately 10s, air was removed from AC maintaining the cannula in the center of the bubble. Still inside the AC, the cannula was slowly moved toward the end of the transplant and placed it below it. An air bubble was injected underneath the unfolded double roll to raise and place it in contact with the receptor posterior stroma.

AC was maintained completely full of air during 60 min at a pressure of 20–25 mmHg (checked by palpation with the cannula tip), followed by an air–liquid exchange with BSS to pressurize the eye (25 mmHg), to finally leave a 30% air bubble (phakic patients) or 50% (pseudophakic patients) in the AC. In the post-surgery period, 0.5% chloramphenicol and 5 mg/ml ketorolac were administered during 4 weeks, and topical steroid treatment with dexamethasone in descending pattern during one month, followed by fluoromethalone.

Data collection and analysis

In addition to age, sex and presurgery findings, the following data were collected: BCVA, endothelial cell count (ECC), pachymetry and complications. BCVA was measured pre- and postoperatively at month 1, 3 and 6. Pachymetry was assessed pre-and postoperatively at month 6 by means of Scheimpflug image analysis (Pentacam HR, Oculus Co., Wetzlar, Germany). ECC was assessed in patients at month 6 by means of mirror microscope (Topcon SP3000, Capelle a/d IJs, The Netherlands). All post-surgery complications were registered.

Statistical data was analyzed by means of the SPSS software (version 19.0. SPSS, Inc.). Anova variance analysis was carried out post hoc for the visual results, while the T for student test was applied for paired data for pachymetry and ECC. Pearson’s Chi square test was utilized for comparing the results between the 3 groups. p Values under 0.05 were considered significant.

Results

Best corrected visual acuity

Overall, 389 out of 450 eyes were included for BCVA analysis, creating 3 subgroups: subgroup I (eyes 1–125), subgroup II (126–250) and subgroup III (251–450). The study excluded eyes with ocular comorbidity which could restrict visual recovery (n = 52), eyes with graft replacement (secondary DMEK) (n = 22), eyes which required re-interventions within the first 6 months (n = 11) as well as eyes with incomplete data sets (n = 10).

Fig. 1 – Descemet membrane graft after being introduced in anterior chamber, forming a double roll. Graft endothelium is positioned in the external surface of said roll.
Presurgery BCVA was <20/40 (0.5) in 59% of patients. The majority of patients achieved useful vision before 6 months, with an observed BCVA of ≥20/40 (0.5) in 87% of patients in the first month post-surgery (86% in subgroup I, 89% in subgroup II and 86% in subgroup III), and in 96% at month 3 post-surgery (93% in subgroup I, 96% in subgroup II and 98% in subgroup III). At post-surgery month 6, 99% of all patients achieved BCVA ≥20/40 (0.5) (99% of patients with Fuchs’ disease, 94% of patients with bullous keratopathy); 79% achieved BCVA of ≥20/25 (0.8) (79% of patients with Fuchs’ disease, 72% of patients with bullous keratopathy); 43% of ≥20/20 (1.0) (44% of patients with Fuchs’ disease, 28% of patients with bullous keratopathy) and 14% of ≥24/201.2 (13.5% of patients with Fuchs’ disease, 17% of patients with bullous keratopathy) (Fig. 2 and Table 2). No statistically significant differences were observed between the subgroups (p > 0.05).

Endothelial cell count and pachymetry

The mean endothelial cell count of DMEK grafts in the presurgery period was of 2.530 ± 220 cells/mm² (n = 398), and 1.613 ± 495 cells/mm² in month 6 post-surgery (n = 398), that is a 36% reduction against presurgery values (p < 0.05). The differences between subgroups were not significant (Table 3).

Pachymetry data of only 381 patients were available. Mean corneal thickness diminished from 668 ± 92 μm presurgery to 526 ± 46 μm at post-surgery month 6 (Table 3). No significant differences were found between the subgroups.

Complications

In 24 eyes (5.3%) re-intervention was necessary within the first 6 post-surgery months. In 13 cases (2.9%) with clinically significant graft detachment, air was reinjected in AC (“re-bubbling”). In a further 10 cases, DMEK was repeated (n = 3) and one DSEK (n = 7) as secondary keratoplasty. Only one case (0.2%) underwent PK as secondary transplant. In the subgroup analysis, the number of re-interventions was 9.6% in subgroup I (n = 12), 4% in subgroup II (n = 5) and 3.5% (n = 7) in subgroup III (Fig. 3). Even though the number of complications was lower in group III and the percentage of re-interventions was nearly 3 times greater in subgroup I than in subgroup III, the differences were not significant (p > 0.05) (Table 4).

Croft detachments were observed in 78 patients (17.3%) (Fig. 3): in 44 eyes (9.7%) the detachment was of <1/3 and in 34 cases (7.5%) of >1/3 of the graft surface. Dehiscences above 1/3 of the graft surface were considered as a clinically significant detachment. The subgroups analysis revealed an important reduction in the percentage of detachments in group III when compared to group I. Even so, the difference was not significant (p = 0.06), probably due to the limited number of detachments. Table 4 comprises a detailed list of subgroups.

Primary graft failure (absence of corneal clearing despite graft adherence) occurred in only one case (0.22%).

Overall, 78 cases of intra-surgery complications were observed (17.3%), including graft implantation difficulty (n = 16), vitreous hypertension (n = 30), persistence of DM remains after descemethorraxis (n = 29) and iris hemorrhage (n = 3) (Table 4).

### Table 2 – Visual results after surgery for each subgroup and overall in post-surgery and 6 months postop.

<table>
<thead>
<tr>
<th>BCVA</th>
<th>Visual results after DMEK</th>
</tr>
</thead>
<tbody>
<tr>
<td></td>
<td>Total (cases 1–450)</td>
</tr>
<tr>
<td></td>
<td>Preop (n = 389) (%)</td>
</tr>
<tr>
<td>≥0.5</td>
<td>41</td>
</tr>
<tr>
<td>≥0.8</td>
<td>7</td>
</tr>
<tr>
<td>≥1</td>
<td>1</td>
</tr>
<tr>
<td>≥1.2</td>
<td>0</td>
</tr>
</tbody>
</table>

BCVA: best corrected visual acuity; DMEK: Descemet membrane endothelial keratoplasty.

No statistically significant differences were found in the mean BCVA (presurgery and 6 months postop) between the 3 subgroups (p > 0.05).
Table 3 - Endothelial cell count (in cells/mm²) and pachymetry (in microns) for each subgroup and overall preop, 6 months postop and differences between both periods.

<table>
<thead>
<tr>
<th>Endothelial cell count (ECC)</th>
<th>n</th>
<th>Preop ECC (cells/mm²)</th>
<th>6 m ECC (cells/mm²)</th>
<th>Δ ECC (%)</th>
</tr>
</thead>
<tbody>
<tr>
<td>All groups (1–450)</td>
<td>398</td>
<td>2530 (±220)</td>
<td>1613 (±495)</td>
<td>36 (±18)</td>
</tr>
<tr>
<td>Subgroup I (1–125)</td>
<td>107</td>
<td>2589 (±171)</td>
<td>1722 (±527)</td>
<td>34 (±19)</td>
</tr>
<tr>
<td>Subgroup II (126–250)</td>
<td>110</td>
<td>2510 (±208)</td>
<td>1606 (±512)</td>
<td>37 (±18)</td>
</tr>
<tr>
<td>Subgroup III (251–450)</td>
<td>181</td>
<td>2507 (±246)</td>
<td>1553 (±456)</td>
<td>38 (±18)</td>
</tr>
</tbody>
</table>

<table>
<thead>
<tr>
<th>Pachymetry</th>
<th>n</th>
<th>Preop pachymetry (µm)</th>
<th>6 m pachymetry (µm)</th>
<th>Δ Pachymetry (%)</th>
</tr>
</thead>
<tbody>
<tr>
<td>All groups (1–450)</td>
<td>381</td>
<td>668 (±92)</td>
<td>526 (±46)</td>
<td>20 (±11)</td>
</tr>
<tr>
<td>Subgroup I (1–125)</td>
<td>96</td>
<td>671 (±93)</td>
<td>531 (±39)</td>
<td>20 (±9)</td>
</tr>
<tr>
<td>Subgroup II (126–250)</td>
<td>107</td>
<td>667 (±96)</td>
<td>518 (±44)</td>
<td>21 (±12)</td>
</tr>
<tr>
<td>Subgroup III (251–450)</td>
<td>178</td>
<td>667 (±90)</td>
<td>527 (±49)</td>
<td>20 (±11)</td>
</tr>
</tbody>
</table>

ECC: endothelial cell count; DMEK: Descemet membrane endothelial keratoplasty.
Standard deviation shown between parenthesis.

Discussion

The present study shows the results of 450 consecutive DMEK cases of the Netherlands Institute for Innovative Ocular Surgery, without taking into account the learning curve (n = 25), retrospectively assessing the technique introduced by said institution, i.e. the standardized no-touch technique. In order to carry out an improved assessment of the technique...
standardization, the sample was divided into 3 subgroups, where subgroup I (the first 125 DMEK) represented the extension of the learning curve, whereas subgroup II (125 DMEK) and subgroup III (200 DMEK) represented the transition and standardization of the technique, respectively.

According to the results, the learning curve and standardization of said technique do not seem to influence BCVA outcome, in accordance with the observations in previously published smaller series\textsuperscript{15,27} in which visual acuity exhibited promising results. In the present study, 79% of all patients achieved BCVA of \( \geq 20/25 \) (0.8) at month 6 post-surgery, 43% of \( \geq 20/20 \) (1.0) and 14% of \( \geq 24/20 \) without evidencing significant differences in the BCVA values of the 3 subgroups. These visual results achieved through DMEK, together with the results of other published series\textsuperscript{15-19,23,27,28} have demonstrated to be significantly better than those of previous surgery techniques. In PK, only 40-50% of patients usually achieve a final BCVA \( \geq 20/40 \) (0.5)\textsuperscript{29,30} and after DS(A)EK only a few patients achieve results \( \geq 20/25 \) (0.8).\textsuperscript{10-14,16,31}

Similarly, ECC does not seem to be influenced by DMEK standardization. Mean ECC reduction in the first 6 months after DMEK is 36%, comparable to that observed after DS(A)EK.\textsuperscript{12,31} Due to the larger graft diameter (9–10 mm in DMEK against 8–9 mm in DS(A)EK and 7–8 mm in PK), in DMEK there is a higher number of transplanted endothelial cells, which could signify a longer graft life after DMEK.

Another important finding of the present study is a lower complications rate with technique standardization. The most frequent and significant complication after DMEK is persistent corneal edema due to incomplete graft adherence. In significant graft detachments (>1/3 of the graft surface or involving the visual axis), reinsertion of air in AC can achieve functional graft adherence and subsequent corneal clearing. Alternatively, keratoplasty could be repeated by means of another DMEK or a secondary DS(A)EK. The graft detachment rate after DS(A)EK has demonstrated to be highly variable according to different series, ranging between 1% and 82%, with a mean of 14.5%.\textsuperscript{31} In DMEK, the standardization of the technique diminishes graft detachment rates as can be appreciated in the present results where the overall detachment percentage was of 24% in subgroup I, diminishing to 12% in subgroup III. Even though the detachment rate differences were not statistically significant between the 3 subgroups, statistical calculations revealed less detachments than expected in group III compared with group I (data not included in Table 4). In what concerns reintervention rates, 5% of operated eyes required an additional intervention: 9.6% in subgroup I, 4% in subgroup II and 3.5% in subgroup III. Accordingly, half of the re-interventions in this series took place in the group of the first 125 DMEK. It is worth noting that the difficulty rates in graft implantation increased from 2.4% in subgroup I to 6% in subgroup III. This could be partly due to a larger range of surgery indications, i.e., due to the indication of more complex cases as surgeons gained experience.

In order to minimize graft detachment risks, in addition to surgeon experience it is important to check specific pre-, intra- and postoperative factors, such as preventing post-surgery ocular hypotension (patients who are aphakic, vitrectomized, with glaucoma drainage devices, etc.) to maintain good air pressure in AC, or measures for preventing increases in intra-surgery vitreous pressure (anti-Trendelenburg position, Honan balloon or loosening the palpebral speculum) are essential for facilitating graft adherence to the receptor stroma.\textsuperscript{32}

Glaucoma could be one of the most severe complications after keratoplasty. However, previously published data have demonstrated that the incidence of ocular hypertension in post-surgery DMEK is lower than that observed after PK and DSEK (6.5% vis-à-vis 15–30%).\textsuperscript{33} The present study gave a post-surgery ocular hypertension incidence of 9.3%, slightly above previously published results.

In conclusion, the results of the present analysis demonstrates that DMEK carried out with the no-touch standardized technique enables a fast and complete visual acuity recovery in the majority of operated eyes. Up to 80% of patients achieved BCVA \( \geq 20/25 \) (0.8) at month 6 post-surgery, while the post-DMEK endothelial cell loss rate is similar to that of other endothelial transplant techniques. These parameters are independent of the technique standardization and the learning curve. Incomplete graft adherence or detachment continue to be the most common post-DMEK complication requiring another intervention within the first 6 months in up to 5.3% of cases. This rate seems to diminish together with the increase of surgeon experience. This evidences that standardization optimizes said surgical procedure. In summary, DMEK could be the treatment of choice in Fuchs’ endothelial dystrophy and pseudophakic bullous keratopathy.

**Conflict of interest**

Dr. Melles is advisor of D.O.R.C. International/Dutch Ophthalmic USA.
The present study was carried out according to the requirements of the Institutional Review Board and Informed Consent, in accordance with the principles of the Helsinki declaration, in the Netherlands Institute for Innovative Ocular Surgery.

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Data analysis: Laurence Frank (DataSculptura-Advies voor statistische data-analyse) had full access to study data and was in charge of statistical analysis.

References
