Objective: To describe the prevention and management of various types of graft detachment after Descemet membrane endothelial keratoplasty.

Methods: In 150 consecutive eyes that underwent Descemet membrane endothelial keratoplasty, the incidence and type of graft detachment were studied at 1, 3, 6, 9, 12, and 24 months after surgery in a nonrandomized, prospective clinical study at a tertiary referral center. Four groups of detachments were identified: a partial detachment of one-third or less of the graft surface area (n=16; group 1); a partial detachment of more than one-third of the graft surface area (n=8; group 2); a graft positioned upside down (n=4; group 3); and a free-floating Descemet roll in the host anterior chamber (n=8; group 4).

Results: Partial or complete graft detachment was found in 36 cases (24%), of which 18 (12%) were clinically significant. All 24 eyes with a partial detachment (groups 1 and 2) showed spontaneous corneal clearance, and all but 6 of these eyes (75%) reached visual acuity of 20/40 or better (≥0.5). A reversed clearance pattern and interface spikes were observed in eyes with the graft positioned upside down (group 3). Eyes with a free-floating graft (group 4) showed persistent corneal edema. Detachments were associated with inward folds (12 eyes [33%]), insufficient air-bubble support (7 eyes [19%]), upside-down graft positioning (4 eyes [11%]), use of plastic materials (2 eyes [6%]), irido-graft synechiae (1 eye [3%]), poor endothelial morphology (1 eye [3%]), and stromal irregularity under the main incision (1 eye [3%]); 14 (58%) of the partial detachments were localized inferiorly.

Conclusions: Awaiting spontaneous clearance may be advocated in eyes with a partial detachment. Minor adjustments in surgical protocol as well as careful patient selection may further reduce the incidence of graft detachment after Descemet membrane endothelial keratoplasty to 4% or less.

Trial Registration: clinicaltrials.gov Identifier: NCT00521898

approved informed consent. The study was conducted according to the Declaration of Helsinki.
All eyes underwent DMEK for isolated Fuchs endothelial dystrophy as previously described. In short, from cornecoscleral buttons stored by organ culture at 31°C for 1 week, DM was stripped off so that a 9.5-mm-diameter flap of posterior DM with its endothelial monolayer was obtained. Due to its elastic properties, 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 transplantation.

In recipient eyes, a 9.0-mm-diameter descemotorhexis was created and the central portion of DM was removed from the eye. The donor Descemet roll was stained with a 0.06% trypan blue solution (VisionBlue; Dutch Ophthalmic Research Center International BV, Zuidland, the Netherlands) and sucked into a custom-made injector (Dutch Ophthalmic Research Center International BV). Using the injector, the donor Descemet roll was inserted into the anterior chamber and the graft was oriented with the endothelial side down (donor DM facing recipient posterior stroma) 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 45 to 60 minutes, followed by an air-liquid exchange to presurize the eye. All operations were recorded on DVD.

All eyes that underwent DMEK were examined before surgery and at 1, 3, 6, 9, 12, 18, and 24 months after surgery with Pentacam imaging (Oculus Optikgeräte GmbH, Wetzlar, Germany), noncontact specular microscopy (SP3000; Topcon Medical Europe, Capelle aan den IJssel, the Netherlands), anterior segment optical coherence tomography (Heidelberg Engineering GmbH, Heidelberg, Germany), confocal microscopy (ConfoScan 4; Nidek Technologies, Padova, Italy), and slit-lamp microscopy (Topcon Medical Europe).

Automated specular microscopy and confocal microscopy were used to document the presence of endothelial cells and the endothelial cell density (ECD) under a detached Descemet graft (the exposed recipient posterior stroma under a free donor Descemet flap hanging in the recipient anterior chamber). To determine the functionality of the endothelial cells, pachymetry measurements over the area with a detachment were compared with adjacent corneal quadrants.

Because the graft detachments varied in size from a loose peripheral flange to a free-floating Descemet roll in the recipient anterior chamber, the clinical relevance was graded in 2 ways. First, the detachments were divided into 4 groups that showed distinctive patterns of corneal clearance (group 1 indicated partial graft detachment of one-third or less of the graft surface area and no or minimal interference with the final visual outcome; group 2, partial graft detachment of more than one-third of the graft surface area and potentially interfering with the visual outcome; group 3, detachment with the graft positioned upside down; and group 4, complete graft detachment with severe interference with the visual outcome) (Table 1). Second, a clinically significant graft detachment was defined as a detachment requiring secondary surgical intervention (graft rebubbling or a secondary DSEK or DMEK) or reducing visual outcome.

For statistical analysis, 1-way analysis of variance was used to compare the groups (groups 1-4) with the control group of 114 eyes with a well-centered and completely attached Descemet graft, in terms of central ECD and central corneal pachymetry measurements. Contrasts (simple effects) were used to calculate statistical difference from the control group. For comparison of central corneal pachymetry measurements, only groups 1 and 3 could be included in the comparisons because of violation of the homogeneity of variance assumption in groups 2 and 4. Repeated-measures multivariate analysis of variance was used to assess the difference between central ECD and peripheral ECD adjacent to the Descemet graft between groups 1, 2, and 3. Contrasts (simple effects) were used to examine in which group(s) central corneal ECD differed significantly from peripheral ECD adjacent to the Descemet graft.

All analyses were performed with SPSS version 18.0 statistical software (SPSS Inc, Chicago, Illinois) using an α level of .05; P < .05 was considered statistically significant. All P values were corrected with the Benjamini and Hochberg correction using R version 2.12.1 statistical software (The R Foundation for Statistical Computing, Vienna, Austria) because the use of multiple tests increases the false-positive (significance) rate.

RESULTS

From a total of 150 eyes that underwent DMEK, 114 obtained complete attachment of the Descemet graft, and the transplanted cornea showed a normal corneal clearance within 1 to 3 months. Of the remaining 36 eyes, 18 (cases 17-19, 21-23, and 25-36; Table 1) showed a clinically significant detachment, ie, a detachment reducing the final visual acuity and/or necessitating secondary surgical intervention. All remaining 18 eyes showed recovery of corneal transparency and normal pachymetry results (Table 1).

Overall, 4 categories of eyes with detachments could be identified (groups 1-4) (Figure 1 and Table 1).

GROUPS

Group 1: DMEK Graft Detached Over One-Third or Less of the Graft Surface Area

Sixteen eyes (group 1, cases 1-16; Table 1) showed a partially (one-third or less) detached DMEK graft within the first weeks after surgery, sometimes with the formation of a (small) peripheral Descemet roll (Figure 1A and Figure 2A). Of these eyes, 2 (cases 5 and 16) showed a spontaneous adherence of the Descemet graft at the 3- to 6-month follow-up interval (Figure 3). In the remaining 14 eyes, complete corneal clearance of the area peripheral to the Descemet roll, ie, the area not covered by the graft, was observed within the first year and most often in about 3 months (Figure 1A and Figure 2A). Slit-lamp examination showed that the denuded posterior stromal area, devoid of either a recipient or donor DM, had a tendency to clear from the corneal periphery toward the center (Figure 1A and Figure 4). All but 2 eyes obtained best-corrected visual acuity of 20/40 (0.5) or better; 1 eye (case 1) had a poor visual acuity outcome of 20/100 (0.2) attributed to a central wrinkle in the Descemet graft, and 1 highly myopic eye (case 6) had a maximal visual acuity potential of about 20/50 (0.4).

Group 2: DMEK Graft Detached Over More Than One-Third of the Graft Surface Area

An additional 8 eyes (group 2, cases 17-24; Table 1) showed a large detachment (more than one-third) of the Descemet graft. All eyes with follow-up longer than 1 month (hence allowing re-endothelialization) showed progressive corneal clearance starting at the first months after DMEK, which was concurrent with endothelialization of the recipient denuded posterior stroma (Figure 1A...
Table 1. Descemet Membrane Endothelial Keratoplasty Graft Detachment Patient Data

<table>
<thead>
<tr>
<th>Case No. (Surgery No.)/ Sex/Age, y</th>
<th>OD/OS Localization</th>
<th>Suspected Cause</th>
<th>BCVA</th>
<th>Group 1*</th>
<th>Central Corneal ECD, Cells/mm²</th>
<th>Peripheral ECD Adjacent to Graft, Cells/mm²</th>
<th>Central Corneal Pachymetry, µm</th>
<th>Pachymetry Over Detachment Compared With Adjacent Quadrant(s), µm (Change, %)</th>
</tr>
</thead>
<tbody>
<tr>
<td>1 (15)/M/88 OD Inferior Inward fold</td>
<td>20/100 (0.2)</td>
<td>Slowly clearing cornea despite persistent detachment; central wrinkle</td>
<td>810 1150 650</td>
<td>1004–685 = 319 (+46)</td>
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<td></td>
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</tr>
<tr>
<td>2 (20)/F/58 OS Inferotemporal Traction by irido-Descemet adhesion Inward fold</td>
<td>20/25 (0.8)</td>
<td>Clear cornea despite persistent detachment</td>
<td>900 870 492</td>
<td>713–652 = 61 (+9.4)</td>
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</tr>
<tr>
<td>3 (26)/M/74 OD Inferior Inward fold</td>
<td>20/30 (0.6)</td>
<td>Clear cornea despite persistent detachment</td>
<td>1820 1560 629</td>
<td>766–638 = 128 (+20.1)</td>
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</tr>
<tr>
<td>4 (47)/F/65 OD Nasal Inward fold</td>
<td>20/23 (0.9)</td>
<td>Clear cornea despite persistent detachment</td>
<td>2350 1730 551</td>
<td>722–728 = −6 (−0.8)</td>
<td></td>
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</tr>
<tr>
<td>5 (67)/F/68 OS Inferior Unknown; spontaneous reattachment at 6 mo Inward fold</td>
<td>20/25 (0.8)</td>
<td>Clear cornea with minor detachment at inferior edge</td>
<td>1880 NA 466</td>
<td>736–748 = −12 (−1.6)</td>
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</tr>
<tr>
<td>6 (71)/F/73 OS Nasal and temporal Inward fold</td>
<td>20/50 (0.4)</td>
<td>Clear cornea despite persistent detachment; subnormal BCVA attributed to high myopia</td>
<td>2480 1820 489</td>
<td>624–697 = −73 (−10.5)</td>
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<td></td>
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</tr>
<tr>
<td>7 (80)/F/47 OD Nasal Inward fold</td>
<td>20/18 (1.2)</td>
<td>Clear cornea despite persistent detachment</td>
<td>1090 720 496</td>
<td>779–626 = 153 (+24.4)</td>
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</tr>
<tr>
<td>8 (82)/M/56 OD Inferonasal Normal cell count but poor endothelial cell morphology at 3–6 mo, with borderline decompensation at 30 mo</td>
<td>20/20 (1.0)</td>
<td>Clear cornea despite persistent detachment</td>
<td>1730 600 602</td>
<td>944–762 = 182 (+23.9)</td>
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</tr>
<tr>
<td>9 (83)/F/75 OD Inferior Inward fold</td>
<td>20/28 (0.7)</td>
<td>Clear cornea despite persistent detachment</td>
<td>1220 1140 523</td>
<td>814–800 = 14 (+1.8)</td>
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</tr>
<tr>
<td>10 (103)/M/55 OD Superior Irregular incision site</td>
<td>20/18 (1.2)</td>
<td>Clear cornea with small detachment superior</td>
<td>1600 490 559</td>
<td>851–680 = 171 (+25.2)</td>
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</tr>
<tr>
<td>11 (105)/M/51 OD Superior Inward fold</td>
<td>20/18 (1.2)</td>
<td>Clear cornea despite persistent detachment</td>
<td>1860 NA 540</td>
<td>795–712 = 83 (+11.7)</td>
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<tr>
<td>12 (106)/F/60 OD Inferior Inward fold</td>
<td>20/20 (1.0)</td>
<td>Clear cornea despite persistent detachment</td>
<td>1050 640 451</td>
<td>720–802 = −82 (−10.2)</td>
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<tr>
<td>13 (109)/F/82 OS Inferior Unknown</td>
<td>20/30 (0.6)</td>
<td>Clear cornea despite persistent detachment</td>
<td>760 350 522</td>
<td>687–712 = −25 (−3.5)</td>
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</tr>
<tr>
<td>14 (110)/M/59 OD Inferior Inward fold</td>
<td>20/20 (1.0)</td>
<td>Clear cornea despite persistent detachment</td>
<td>1570 1380 522</td>
<td>647–723 = −76 (−10.5)</td>
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</tr>
<tr>
<td>15 (122)/F/70 OD Nasal Unknown</td>
<td>20/20 (1.0)</td>
<td>Clear cornea despite persistent detachment</td>
<td>1180 1010 572</td>
<td>821–649 = 172 (+26.5)</td>
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<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>16 (123)/F/69 OS Inferior Unknown; spontaneous reattachment at 6 mo</td>
<td>20/23 (0.9)</td>
<td>Clear cornea</td>
<td>1660 1060 525</td>
<td>706–843 = −137 (−16.3)</td>
<td></td>
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</tr>
</tbody>
</table>

(continued)
<table>
<thead>
<tr>
<th>Case No. (Surgery No.)/ Sex/Age, y</th>
<th>OD/OS Localization</th>
<th>Suspected Cause</th>
<th>BCVA</th>
<th>Postoperative Findings at 6-12 mo</th>
<th>Peripheral ECD Adjacent to Descemet Graft, Cells/mm²</th>
<th>Pachymetry Over Detachment Compared With Adjacent Quadrant(s), µm (Change, %)</th>
</tr>
</thead>
<tbody>
<tr>
<td><strong>Group 2</strong></td>
<td></td>
<td></td>
<td></td>
<td>Central Corneal ECD, Cells/mm²</td>
<td>Central Corneal Pachymetry, µm</td>
<td></td>
</tr>
<tr>
<td>17 (17)/F/70 OD/OS Inferior quadrants</td>
<td>Possibly use of plastic materials</td>
<td>NA 20/40 (0.5)</td>
<td>Secondary DSEK 4 wk after DMEK</td>
<td>950 NA NA NA</td>
<td></td>
<td></td>
</tr>
<tr>
<td>18 (63)/F/82 OD Superior quadrants</td>
<td>Inadequate air-bubble support at end of surgery due to vitreous pressure</td>
<td>NA Clear cornea despite persistent detachment; BCVA not explained by cornea</td>
<td>1950 NA 558</td>
<td>845−746=99 (+13.3)</td>
<td></td>
<td></td>
</tr>
<tr>
<td>19 (64)/M/61 OD Subtotal temporal</td>
<td>Inadequate air-bubble support at end of surgery due to vitreous pressure</td>
<td>NA Corneal clearance in inferior quadrants; secondary DSEK 4 mo after DMEK</td>
<td>2270 NA 896</td>
<td>NA</td>
<td></td>
<td></td>
</tr>
<tr>
<td>20 (73)/F/75 OD Inferior quadrants</td>
<td>Unknown 20/150 (0.15)</td>
<td>Clear cornea despite persistent detachment; BCVA not explained by cornea</td>
<td>2070 NA 480</td>
<td>636−621=15 (+2.4)</td>
<td></td>
<td></td>
</tr>
<tr>
<td>21 (74)/M/75 OS Subtotal temporal</td>
<td>Inadequate air-bubble support at end of surgery due to vitreous pressure</td>
<td>CF (3/60) Corneal clearance despite persistent detachment, but wrinkled graft in corneal center; secondary DSEK 7 mo after DMEK</td>
<td>1790 NA 780</td>
<td>NA</td>
<td></td>
<td></td>
</tr>
<tr>
<td>22 (79)/F/86 OD Inferior quadrants</td>
<td>Unknown 20/40 (0.5)</td>
<td>Clear cornea despite persistent detachment</td>
<td>2070 NA 480</td>
<td>636−621=15 (+2.4)</td>
<td></td>
<td></td>
</tr>
<tr>
<td>23 (87)/F/74 OD Inferior quadrants</td>
<td>Inward fold</td>
<td>20/30 (0.6)</td>
<td>Clear cornea despite persistent detachment</td>
<td>1790 NA 780</td>
<td>NA</td>
<td></td>
</tr>
<tr>
<td>24 (150)/M/55 OS Temporal</td>
<td>Inward fold</td>
<td>20/23 (0.9)</td>
<td>Clear cornea despite persistent detachment; BCVA improved to 20/23 (0.9) at 12 mo</td>
<td>1800 1200 495</td>
<td>692−617=75 (+12.2)</td>
<td></td>
</tr>
<tr>
<td><strong>Group 3</strong></td>
<td></td>
<td></td>
<td></td>
<td>No detectable corneal clearance or re-endothelialization at 5 wk; secondary DSEK 5 wk after DMEK</td>
<td>340 560 627 725−1014=−289 (−39.9)</td>
<td></td>
</tr>
<tr>
<td>25 (19)/M/70 OD Complete (DM roll in AC) Graft positioned upside down; re-bubbling unsuccessful</td>
<td>NA</td>
<td>Clear cornea despite persistent detachment</td>
<td>340 560 627</td>
<td>725−1014=−289 (−39.9)</td>
<td></td>
<td></td>
</tr>
<tr>
<td>26 (36)/F/70 OD Subtotal nasal Graft positioned upside down</td>
<td>20/28 (0.7)</td>
<td>Clear cornea despite persistent detachment</td>
<td>340 560 627</td>
<td>725−1014=−289 (−39.9)</td>
<td></td>
<td></td>
</tr>
<tr>
<td>27 (38)/F/47 OS Subtotal inferior Graft positioned upside down</td>
<td>20/20 (1.0)</td>
<td>Clear cornea despite persistent detachment</td>
<td>340 560 627</td>
<td>725−1014=−289 (−39.9)</td>
<td></td>
<td></td>
</tr>
<tr>
<td>28 (96)/M/75 OD Inferior quadrants Graft positioned upside down</td>
<td>20/100 (0.2)</td>
<td>Corneal clearance in inferior quadrants at 3 mo; re-DMEK 6 mo after primary DMEK</td>
<td>530 490 711</td>
<td>663−810=−147 (−18.1)</td>
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<td></td>
</tr>
</tbody>
</table>

(continued)
Despite an extensive detachment, i.e., without the graft covering the optical center, 4 eyes still reached best-corrected visual acuity of 20/40 (0.5) or better at 6 months after surgery. Of the 4 remaining eyes, 2 (cases 17 and 19) did not reach the 6-month follow-up. One eye (case 21) had best-corrected visual acuity of counting fingers attributed to extensive wrinkling and/or graft contraction in the area over the pupil, and no explanation could be found for the reduced best-corrected visual acuity in case 20.

Table 1. Descemet Membrane Endothelial Keratoplasty Graft Detachment Patient Data (continued)

<table>
<thead>
<tr>
<th>Patient</th>
<th>Detachment</th>
<th>Postoperative Findings at 6-12 mo</th>
<th>Pachymetry Over Detachment Compared With Adjacent Quadrant(s), µm (Change, %)</th>
</tr>
</thead>
<tbody>
<tr>
<td></td>
<td></td>
<td>Central Corneal ECD, Cells/mm²</td>
<td>Peripheral ECD Adjacent to Descemet Graft, Cells/mm²</td>
</tr>
</tbody>
</table>

Abbreviations: AC, anterior chamber; BCVA, best-corrected visual acuity; CF, counting fingers; DM, Descemet membrane; DMEK, DM endothelial keratoplasty; DSEK, Descemet stripping endothelial keratoplasty; ECD, endothelial cell density; NA, not available; NR, not relevant.

*Group 1 indicates a Descemet graft detachment of one-third or less of the graft surface area. The mean (SD) central corneal ECD was 1500 (520) cells/mm² (n=16; P=.13 compared with control group); the mean (SD) peripheral ECD adjacent to the Descemet graft was 1040 (460) cells/mm² (n=14; P=.01 compared with corneal center); the mean (SD) central corneal pachymetry measurement was 537 (56) µm (n=16; P=.81 compared with control group); and the mean change in the pachymetry measurement from over the detachment compared with the adjacent quadrant(s) was 8.5% (n=16).

*Group 2 indicates a Descemet graft detachment of more than one-third of the graft surface area. The mean (SD) central corneal ECD was 1800 (460) cells/mm² (n=6; P=.81 compared with control group); the mean (SD) central corneal pachymetry measurement was 713 (198) µm (n=7; the variance was too high to compare with control group).

*The left eye also had detachment but is not included in this series.

dThe right eye underwent uncomplicated DMEK.

*Group 3 indicates detachment because the Descemet graft was positioned upside down. The mean (SD) central corneal ECD was 420 (100) cells/mm² (n=3; P<.001 compared with control group); the mean (SD) central corneal pachymetry measurement was 713 (198) µm (n=7; the variance was too high to compare with control group).

eGroup 4 indicates a free-floating Descemet graft.
transplanted cornea.13-16

monitor a tendency toward spontaneous clearance of the DMEK, so the postoperative interval was too short to performed within the first 3 or 4 weeks after the initial edema up to the time when a secondary DSEK was per-

Figure 2C). All of these eyes showed persistent corneal sues, in the recipient anterior chamber (Figure 1C and sensory acuity of 20/28 (0.7) or better (cases 26 and 27); 1 low-up longer than 1 month achieved best-corrected vi-

entire series of eyes that underwent DMEK with a well- oriented graft.

Despite subtotal detachment, 2 of the 3 eyes with follow-up longer than 1 month achieved best-corrected visual acuity of 20/28 (0.7) or better (cases 26 and 27); 1 eye (case 28) had best-corrected visual acuity of 20/100 (0.2), attributed to persistent central edema overlying an area where the graft was attached (Figure 5).

Figure 1. Detachment patterns observed in our study. A, In the presence of a partially detached Descemet membrane endothelial keratoplasty (DMEK) graft, the central cornea covered by the graft as well as the host peripheral stroma not covered by the graft frequently showed either spontaneous reattachment of the graft or complete clearance within 1 to 6 months. B, If the DMEK graft had been positioned upside down, a reversed clearance pattern was observed, ie, the area not covered by the graft showed complete corneal clearance within 1 to 6 months, whereas the area in which the graft was attached showed persistent edema. C, No corneal clearance was seen with a free-floating Descemet roll in the anterior chamber, ie, in the absence of a touch between the graft and the recipient cornea.

Group 4: Lack of Corneal Clearance With a Free-Floating Descemet Roll

Eight eyes (cases 29-36; Table 1) had a complete graft detachment with a free-floating Descemet roll, ie, absence of physical contact between donor and host tissues, in the recipient anterior chamber (Figure 1C and Figure 2C). All of these eyes showed persistent corneal edema up to the time when a secondary DSEK was performed, up to 4.5 months after the initial DMEK. Four of these eyes (cases 29-32; Table 1) had a secondary DSEK performed within the first 3 or 4 weeks after the initial DMEK, so the postoperative interval was too short to monitor a tendency toward spontaneous clearance of the transplanted cornea.13-16

INCIDENCE, LOCALIZATION, AND POTENTIAL CAUSES OF DESCEMET GRAFT DETACHMENT

A review of the surgical videos, sequential slitlamp photography, and clinical observation revealed several potential causes for Descemet graft detachment and its associated localization (Table 2). One-third of the detachments were attributed to the presence of an inward fold (a flange of peripheral DM sandwiched between the larger part of the graft and the cornea) at the end of surgery. Slitlamp observation showed that these inward folds had a tendency to spring away from the recipient posterior stroma, causing a larger detachment than the size of the original fold (Figure 4). A second main cause was insufficient air-bubble support of the donor tissue at the end of surgery, most frequently associated with vitreous pressure and preceding vitreoretinal surgery (causing the air to escape to the posterior segment), and/or other situations with an inadequate air fill of the anterior chamber. Other causes identified were stromal irregularity under the main incision, an irido–Descemet graft adhesion causing detachment by traction (Figure 6), poor endothelial cell morphology (Figure 7), the use of plastic materials contacting the donor tissue, and upside-down positioning of the graft. In 8 cases (22%), no cause for the detachment could be identified.

Of the 24 eyes with a partial graft detachment, 14 (58%) showed a detachment in the inferior quadrant, which may be explained by the air bubble being most effective in the superior quadrant with a 50% air fill of the anterior chamber at the end of surgery.

The incidence of graft detachment decreased with surgical experience. The number of clinically significant detachments decreased from 20% in the first 75 cases (series 1) to 4% in the next 75 cases (series 2) (Table 3). Interestingly, 2 eyes (cases 18 and 36) also had a graft detachment in the contralateral eye after DMEK. No rebubbling procedure proved (completely) successful (Figure 8).

No correlation could be found between graft detachment and recipient or donor age (P > .10).

ECD AND PACHYMETRY MEASUREMENTS

In the control group of 114 eyes with a completely attached and well-centered Descemet graft, the mean (SD) central ECD was 1750 (552) cells/mm² and the mean (SD) pachymetry measurement was 532 (42) µm. Using this group as a reference, the central ECD was not significantly lower in group 1 (graft detachment over one-third or less of the graft surface area; P = .13) (Figure 1A and Table 1). In groups 2 and 3, the central ECD represented...
re-endothelialized recipient posterior stroma because the Descemet graft was largely detached (Figure 1B). The ECD in group 2 (graft detachment over more than one-third of the graft surface area) did not differ from that of the control group \((P = .81)\), whereas the ECD was significantly lower in group 3 (mean [SD], 420 [100] cells/mm\(^2\); \(P < .001\)) (Table 1). Accordingly, central pachymetry measurements did not differ between the control group and group 1 (Figure 2 and Table 1). In group 2, the variance was too high for reliable statistical analysis. The central pachymetry measurement was significantly higher in group 3 (mean [SD], 636 [71] µm; \(P = .01\)) (Table 1). No ECD measurements could be obtained in group 4 owing to the persistent corneal edema (Figure 1C and Table 1).

The ECD under the detachment of one-third or less of the graft surface area (group 1) was lower than the central ECD \((P = .01)\) (Table 1), and the cornea in these areas was about 8% thicker compared with the opposite or adjacent quadrants without a gap or detachment (Figure 2A and Table 1). In group 3, pachymetry measurements over the area where the graft was detached were about 25% thinner than in the area showing graft attachment (Figure 2B and Table 1).

**COMPLICATIONS ASSOCIATED WITH DESCEMET GRAFT DETACHMENTS**

The only complication observed was a small corneal infiltrate in the area with edema overlying a peripheral detachment in case 6 (Figure 9). All eyes that underwent a secondary DSEK had a postoperative course and best-corrected visual acuity similar to those after primary DSEK.

**COMMENT**

Graft detachment may be the most frequently observed complication after endothelial keratoplasty. After DSEK or Descemet stripping automated endothelial keratoplasty, graft detachments may occur in up to 82% of cases (Table 4) and have been associated with lower...
ECDs. Similarly, an initial graft detachment rate of 20% to 60% has been reported after DMEK (Table 2), allowing further identification of its causes to define potential precautions as well as to determine its preferred clinical management.

First, however, it may be important to better define a graft detachment because, especially in DMEK, small and temporary detachments of a peripheral flange with little clinical significance are frequently seen. If graft detachment is defined as a lack of adherence of the donor DM to the recipient posterior stroma, reducing visual outcome and/or necessitating secondary intervention, the detachment rate in our study evaluating the first 150 consecutive DMEK eyes was 12% (18 of 150 eyes) (Table 1 and Table 3). When clinically insignificant detachments were also included, the overall detachment rate was 24% (36 of 150 eyes). Furthermore, with clinical experience, the detachment rate decreased from 20% in the first series of 75 eyes to 4% in the next series of 75 eyes (Table 3). Hence,
our study aimed to identify any factors that may aid in further reducing Descemet graft detachments as well as defining preferred treatment options.

Intuitively, rebubbling appeared to be a first treatment option with all of these detachments to again position the Descemet graft against the recipient posterior stroma. Although initially pursued in a few cases, rebubbling proved less effective than expected. In fact, some eyes showed persistent detachment of the graft in the presence of an air bubble in the recipient anterior chamber (Figure 8). Decision making on reintervention was further complicated by an unexpected spontaneous clearance in several eyes that underwent DMEK, despite the presence of a (nearly) complete graft detachment.13 While these eyes were scheduled for a rebubbling procedure, re-endothelialization of the recipient posterior stroma was observed within the first several months after surgery, with visual rehabilitation up to visual acuity of 20/20 (1.0). Given this observation, we changed our decision tree for management of detachments after DMEK, using (1) the extent of the detachment and (2) interference with the visual acuity as primary guidelines for reintervention (Figure 10).

A first group of eyes showed a peripheral detachment of one-third or less of the graft surface area, apparently without affecting the visual acuity (Table 1). At 3 to 6 months postoperatively, all of these eyes recovered with near-normal pachymetry measurements in the area overlying the detachment: either the graft reattached by itself or the recipient posterior stroma re-endothelialized (Figure 2A, Figure 3, and Figure 4). Only 1 of these eyes required additional treatment. In this eye, a small anterior corneal infiltrate developed within the still edematous area overlying the detachment (Figure 9); the corneal infiltrate quickly resolved with topical antibiotics.

For these relatively benign peripheral detachments, 2 main causes could be identified (Table 2). First, inward folds of the edge of the Descemet graft, ie, a fold sandwiched between the larger body of the graft and recipient posterior stroma (with the endothelium touching the stroma in that area), that are left in situ at termination of the surgery may be associated with peripheral detachments because the tissue tends to spring away from the stroma within the first postoperative week (Figure 4). Once recognized, this complication can easily be avoided by so-called bubble bumping during surgery or by performing Droutsas taps (applying intermittent pressure to the outer corneal surface to move the air bubble over the tissue fold

Table 2. Suspected Cause of Graft Detachment

<table>
<thead>
<tr>
<th>Suspected Cause of Graft Detachment</th>
<th>Group 1a (n=16)</th>
<th>Group 2a (n=8)</th>
<th>Group 3a (n=4)</th>
<th>Group 4a (n=8)</th>
<th>Total (n=36)</th>
</tr>
</thead>
<tbody>
<tr>
<td>Inward fold</td>
<td>9 (57)</td>
<td>2 (25)</td>
<td>0</td>
<td>1 (12.5)</td>
<td>12 (33)</td>
</tr>
<tr>
<td>Irregular incision site</td>
<td>1 (6)</td>
<td>0</td>
<td>0</td>
<td>0</td>
<td>1 (3)</td>
</tr>
<tr>
<td>Irido–Descemet graft adhesion</td>
<td>1 (6)</td>
<td>0</td>
<td>0</td>
<td>0</td>
<td>1 (3)</td>
</tr>
<tr>
<td>Poor endothelial cell morphology</td>
<td>1 (6)</td>
<td>0</td>
<td>0</td>
<td>0</td>
<td>1 (3)</td>
</tr>
<tr>
<td>Use of plastic materials contacting donor tissue</td>
<td>0</td>
<td>1 (12.5)</td>
<td>0</td>
<td>1 (12.5)</td>
<td>2 (6)</td>
</tr>
<tr>
<td>Inadequate air-bubble support due to vitreous pressure</td>
<td>0</td>
<td>3 (37.5)</td>
<td>0</td>
<td>4 (50)</td>
<td>7 (19)</td>
</tr>
<tr>
<td>Descemet graft upside down</td>
<td>0</td>
<td>0</td>
<td>4 (100)</td>
<td>0</td>
<td>4 (11)</td>
</tr>
<tr>
<td>Unknown</td>
<td>4 (25)</td>
<td>2 (25)</td>
<td>0</td>
<td>2 (25)</td>
<td>8 (22)</td>
</tr>
</tbody>
</table>

aGroup 1 indicates a Descemet graft detachment of one-third or less of the graft surface area; group 2, a Descemet graft detachment of more than one-third of the graft surface area; group 3, detachment because the Descemet graft was positioned upside down; and group 4, a free-floating Descemet graft.
inside the eye [see Figure 7 of the article by Dapena et al5] to completely unfold the donor DM. Second, a touch between the outer flange of the Descemet graft and the recipient peripheral iris may result in a progressive detachment, due to contraction of the Descemet graft after surgery that tends to stretch the detachment, making reattach-

Table 3. Incidence of Graft Detachment

<table>
<thead>
<tr>
<th>Type</th>
<th>Series 1, Cases 1-75 (n=75)</th>
<th>Series 2, Cases 76-150 (n=75)</th>
<th>Total (N=150)</th>
</tr>
</thead>
<tbody>
<tr>
<td>Partial graft detachment</td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>one-third or less</td>
<td>6 (8)</td>
<td>10 (13)</td>
<td>16 (11)</td>
</tr>
<tr>
<td>Partial graft detachment</td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>more than one-third</td>
<td>5 (7)</td>
<td>3 (4)</td>
<td>8 (5)</td>
</tr>
<tr>
<td>Graft upside down</td>
<td>3 (4)</td>
<td>1 (1)</td>
<td>4 (3)</td>
</tr>
<tr>
<td>Complete graft detachment</td>
<td>7 (9)</td>
<td>1 (1)</td>
<td>8 (5)</td>
</tr>
<tr>
<td>Total</td>
<td>21 (28)</td>
<td>15 (20)</td>
<td>36 (24)</td>
</tr>
<tr>
<td>Clinically significant</td>
<td>15 (20)</td>
<td>3 (4)</td>
<td>18 (12)</td>
</tr>
</tbody>
</table>

Figure 7. Light microscopy (A), slitlamp (B and C), and specular microscopy (D) images of a Descemet graft before (A) and after (B-D) surgery. A. Although the endothelial cell layer appears normal during preoperative evaluation in the eyebank, Fuchs dystrophy–like changes are seen across the transplant after surgery, while the cell density is virtually normal. B. The arrows indicate the area in which the graft is detached; the overlying cornea cleared despite the detachment.

Figure 8. Slitlamp photographs of an eye 1 week after Descemet membrane endothelial keratoplasty (A) and 1 day after rebubbling, 2 weeks after the initial Descemet membrane endothelial keratoplasty (B). A. The Descemet graft (arrows) is detached after surgery, and the detachment persists despite a secondary 60-minute air fill of the recipient anterior chamber followed by a 50% air fill at the first postoperative day. The air bubble seems to provide insufficient support because the detachment is visible directly over the air bubble.

Figure 9. Slitlamp photographs of an eye 5 months (A and B) and 12 months (C) after Descemet membrane endothelial keratoplasty. A and B, A small corneal infiltrate (red arrows) is visible in an area of edema over a peripheral detachment of the Descemet graft (yellow arrows). C, After treatment with a topical antibiotic, the infiltrate resolved and the area over the detachment cleared (arrow) without sequelae.
Interference with BCVA

Free Descemet

necessitating secondary intervention.

too much delay. However, if the Descemet graft shows dothelial keratoplasty, or re-DMEK performed without a secondary DSEK, Descemet stripping automated en-

to 6 to 9 months and patients may be advised to have

When a free-floating Descemet roll is observed inside the graft surface area and thereby affecting the visual acu-

air after graft positioning and the chamber angle is checked to be sure it is open over 360°. Overall, with small detach-
ments not affecting the visual acuity, awaiting spontane-
ous clearing is suggested rather than performing a sec-
ondary intervention (Figure 10).

In eyes with a detachment of more than one-third of the graft surface area and thereby affecting the visual acuity, decision making proves more complex (Table 1). When a free-floating Descemet roll is observed inside the recipient anterior chamber, corneal edema may persist up to 6 to 9 months and patients may be advised to have a secondary DSEK, Descemet stripping automated endothelial keratoplasty, or re-DMEK performed without too much delay. However, if the Descemet graft shows partial attachment, the transplanted cornea is found to clear much quicker and an acceptable visual outcome is obtained in about half of these cases (Table 1). A similar visual outcome is reached when the graft is positioned upside down, although persistent corneal edema can be seen over the area in which the graft shows attachment (Figure 5 and Table 1). Hence, large partial detach-
ments may be managed on an individual basis and ac-
ting surgery and/or improper judgment of graft orienta-
tion. Therefore, a soft eye should be obtained before commencing surgery (by performing ocular massage, applying a Honan balloon for 10 minutes, using anti-

Trendelenburg positioning, and avoiding a tight eyelid speculum) to minimize the risk of posterior pressure. The orientation of the graft can be determined by the Moutsouris sign (see Figure 6 of the article by Dapena et al3) and/or marking the graft.

We previously described that the use of plastic and/or viscoelastic materials may be avoided in DMEK to mini-
imize the risk of graft detachment. Performing the descemotorhexis under air may have the advantages that remnant host Descemet fragments are more easily identified and that the negative imbibition pressure facilitating graft adherence is better preserved (by avoiding stromal over-
hydration with the use of balanced salt solution in combi-

First postoperative day: if incomplete attachment, continue supine position for 1-2 d

First postoperative week: if incomplete attachment

Reoperation

Rebubble quickly or not at all

First postoperative day: if incomplete attachment, continue supine position for 1-2 d

First postoperative week: if incomplete attachment

No interference with BCVA

Interference with BCVA

Partial detachment

Free Descemet roll in AC

Persistent corneal edema over detachment

Stepladder approach in management of Descemet graft detachments

Check during surgery:

Descemotorhexis under air; avoid stromal overhydration

Avoid use of viscoelastic and plastic materials contacting graft

Upward orientation of Descemet graft (Moutsouris sign/tissue marking)

Proper centration of Descemet graft; avoid PAS

Complete unfolding of Descemet graft; avoid inward folds

50% Air fill in AC in pseudophakic eyes, 25% air fill in phakic eyes

Wait for 3 mo

Explain options to patients

Await spontaneous clearance

Reoperation

Rebubble quickly or not at all

DSEK or DSAEK

Re-DMEK

Persistent corneal edema over detachment

Spontaneous clearance

Spontaneous reattachment

Figure 10. Diagram displaying recommendations to prevent detachments in Descemet membrane endothelial keratoplasty (DMEK) and a decision tree in the event of a Descemet graft detachment. AC indicates anterior chamber; BCVA, best-corrected visual acuity; DSAEK, Descemet stripping automated endothelial keratoplasty; DSEK, Descemet stripping endothelial keratoplasty; and PAS, peripheral anterior synechiae.
be important: aphakic or postvitrectomy eyes or eyes with a large-sector iridectomy, glaucoma tube, extensive corneal decompensation, or tendency to have postoperative ocular hypotonia may be prone to Descemet graft detachment owing to a lack of air-bubble support and may be managed with a modified surgical technique.32

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Author Contributions: Dr Melles had full access to all of the data in the study and takes responsibility for the integrity of the data and the accuracy of the data analysis.

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REFERENCES


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