

Galvis et al also suggested automated Bowman layer preparation with a 90- to 100- μ m-thick donor lamella of anterior stroma (instead of an 8- to 12- μ m-thick isolated Bowman layer graft). In our experience, the presence of donor stroma seems to degrade the optical quality of the transplanted cornea (as Descemet stripping endothelial keratoplasty/Descemet stripping automated endothelial keratoplasty grafts containing donor stroma may perform less well than isolated Descemet membrane endothelial keratoplasty grafts or deep anterior lamellar keratoplasty with retained recipient posterior stroma as compared with deep anterior lamellar keratoplasty with bare recipient Descemet membrane).^{1,9–12} For that reason, we purposely developed a technique to manually prepare isolated Bowman layer grafts, that is, grafts with the least possible donor stroma attached,¹⁰ to obtain the highest visual outcome in this young, and therefore relatively active, patient group.

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Eventual Endothelial Failure After Initial Corneal Clearing After a Detached Endothelial Graft in Fuchs Dystrophy

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To the Editor:

We read the article by Lee et al with much interest. They recently reported a case with spontaneous resolution of cornea edema accompanied by improvement of visual recovery after a failed Descemet membrane endothelial keratoplasty (DMEK) procedure with a detached graft.¹ In the article, the authors speculated that there had been repopulation of corneal endothelial cells,

after the failed DMEK, that involved migration of the endothelial cells from the outer side of the Descemet stripping area. Borkar et al² have also previously reported spontaneous healing of corneal edema after simple stripping without keratoplasty for Fuchs dystrophy.

We propose that the corneal endothelial cells could have originated from the donor graft that had been implanted with an upside-down orientation, which partially attached to the recipient's corneal back surface on the edge of the graft. In the article, severe corneal edema in the central area immediately after surgery was reported; however, clarity of the edematous area improved 5 months after DMEK. This healing process has been reported by Dirisamer et al³ as “reverse clearance pattern after DMEK.” Although the mechanism of reverse clearance was not described in depth, they reported that it was the result of an upside-down graft insertion.

We would like to emphasize 3 points. First, the possibility of an upside-down graft insertion should be included when referring to the study by Dirisamer et al.³ Second, the authors should include the area of graft detachment and the condition of the detached graft. Scheimpflug images of the anterior chamber using optical coherence tomography of the anterior segment would be very helpful. Third, the authors should explain how they recognized the graft orientation during DMEK surgery. Did they use an S stamp⁴ or check the Moutsouris sign?⁵

If the DMEK graft is inserted in an upside-down orientation, the graft will only barely attach to the host cornea, often causing primary graft failure. However, there have been some cases with spontaneous healing after several months. We speculate that the corneal endothelial cells might have migrated from the small area that was partially folded and properly attached on the corneal stromal back surface, in the limited area on the edge of the graft. It was therefore possible to avoid surgical intervention and expect spontaneous improvement of corneal edema several weeks after the presumably failed DMEK procedure, because of upside-down insertion of the graft.

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Reply:

We appreciate the interest in our article expressed by Dr. Hayashi et al, and we would like to take the opportunity to reply to their comments. First, in regard to the possibility that the Descemet’s Membrane Endothelial

Keratoplasty (DMEK) graft was initially placed upside down, this DMEK case was performed before the common use of preprepared donor tissue. The graft was harvested in the operating room by the surgeon, and there was no S-stamp or other marking on the graft to help orient the graft. It is certainly possible that the graft was initially placed upside down in the recipient eye, causing an early detachment. Anterior segment ocular coherence tomography (OCT) was actually performed at postoperative day 1, which showed small partial detachments of the edges of the graft, and again at postoperative month 5, which showed a tightly scrolled graft in the periphery of the cornea, correlating to what was eventually visible at the slit lamp in Figure 1A of our article. We did not obtain a measurement of the exact area of graft detachment on the first postoperative day, and the cornea was too edematous to visualize the graft well enough to discern the exact degree at the slit lamp until the patient returned months later. Given the severity of corneal edema during the first postoperative week, it was assumed that the graft was completely or near-completely detached by the first week after surgery. We agree that using tools, such as an S-stamp, to verify the orientation of a DMEK graft intraoperatively is very important to the success of surgery, and we use such tools now in our refined technique.

In clinical cases such as this, there is no way to discern whether donor endothelial cells may have migrated from the scrolled graft to the host cornea at points of attachment. However, if the donor endothelial cells had successfully migrated from the graft to the host to repopulate the central cornea, then we would have expected the peripheral corneal endothelial cells to remain relatively intact, and we would not have expected eventual diffuse corneal edema suggestive of generalized reduction in endothelial cells. Therefore, we believe this argues that the host peripheral endothelial cells migrate toward the center of the cornea to repopulate the bared area. Dirisamer et al¹ in fact have also speculated that because the phenomenon of corneal clearing with Descemet membrane endothelial transfer

is not observed in eyes with pseudophakic bullous keratopathy, where there is generalized reduction in endothelial cells, but only in eyes with Fuchs dystrophy, that the host peripheral endothelium must be involved in clearance of the cornea. Related to this observation, topical application of the Rho kinase inhibitor Y-27632 in humans who underwent transcorneal freezing to lyse central corneal endothelial cells resulted in repopulation of the central cornea in cases of Fuchs endothelial dystrophy, but not in cases of bullous keratopathy.² The most logical explanation of these results would seem to be that the peripheral host cells are responsible for the endothelial cell repopulation in all of these cases.

Finally, in response to the comment about a “reverse clearance pattern after DMEK,”³ we believe that this is also better explained by peripheral host endothelial cell repopulation of corneal endothelial defects. The observation of a reverse clearance pattern made by Dirisamer et al was that when there were large DMEK detachments, the detached areas cleared before the attached areas, which suggests that the grafts were upside down because the opposite clearance pattern would be expected if the graft was correctly oriented but only partially attached. To us, the reverse clearance pattern suggests that migrating peripheral host endothelial cells are responsible for clearing the cornea in areas of graft detachment, and that in the areas where the graft is attached, but upside down, the donor endothelial cells are unable to function because they are sandwiched between the host stroma and donor Descemet membrane, and the migrating peripheral host endothelial cells are hindered from populating these areas because of the physical barrier imposed by the donor endothelial cells and Descemet membrane.

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