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COMMENT

# Endothelial keratoplasty: is Descemet membrane endothelial keratoplasty the Holy Grail of lamellar surgery? No

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Posterior lamellar surgery has transformed the management of corneal endothelial disease due to faster visual rehabilitation, minimal refractive change, and maintenance of the ocular structural integrity compared full thickness keratoplasty. Although Descemet's membrane endothelial keratoplasty (DMEK) appears to offer an anatomical repair for endothelial pathology, replacing only endothelium and Descemet's membrane without any posterior stroma,[1] it has yet to supersede Descemet's stripping endothelial keratoplasty (DSEK) and its variations; ultrathin Descemet's stripping automated endothelial keratoplasty (UT-DSAEK),[2,3] thin manual Descemet stripping keratoplasty (TMDSEK),[4] and pre-Descemet's endothelial keratoplasty (PDEK)[5] as the mainstay the treatment of Fuchs endothelial dystrophy or bullous keratopathy. The main reason for this is that DMEK is technically more challenging, requiring prolonged surgical time, associated with a steeper learning curve and possibly more potential complications.[6,7]

## Intraoperative complications

The technical challenges with DMEK initially occur at graft harvesting where rates of tissue loss and need to convert to DSEK have been reported to be between 4.2 and 8% of cases.[8,9] Melles' groups reported a higher rate (17.3%) of moderate intraocular complications such as failure of graft to unroll in the anterior chamber, persistent Descemet's membrane after Descemetorhexis and hyphaema.[10]

## Post-operative complications

The reported DMEK graft detachment rates and rebubbling rates vary in the literature. In a particular study, the rebubbling rate was as high as 62%.[8] Melles' group report a 17.3% graft detachment rate with 5.3% requiring intervention such as rebubbling (2.9%) or repeat DMEK, DSEK, or penetrating keratoplasty in 2.4% of cases.[10] Although these numbers are improved in the hands of experienced DMEK surgeons, they are still higher than complication rates reported for DSEK, UT-DSEK, TMDSEK, and PDEK.[4,5,10–12] In a comparative study, graft detachment requiring rebubbling occurred in 3.2% of DSAEK cases and 8.6% of DMEK cases.[12] The deleterious effects of rebbubling and additional surgical manipulation on the graft have been established both *in vitro* and *in vivo*.[13,14]

Primary graft failure, defined as the absence of corneal clearing despite graft adherence, has been reported with great variation between studies. Guerra *et al*[8] reported a DMEK primary graft failure rate of 8%. Conversely, Satue *et al*[10] report a lower rate of primary graft failure (0.22%) in 450 consecutive cases of DMEK. Hamzaoglu *et al*[12] reported a 5.7% rate of primary graft failure attributed to difficult surgical manipulation. In this last study, no graft failures occurred in the DSAEK group.

The rate of peri-operative problems, such as dissection failure, need for excessive tissue handling, which in turn risks graft viability, and post-operative problems, such as persistent graft folds and primary failure, is much higher in DMEK compared to DSEK and can affect graft survival and visual quality. It is also questionable if these challenges can merely be attributed to a steep learning curve or is DMEK inherently more problematic?[15]

In contrast to these intraoperative and post-operative challenges faced by the surgeon during and after DMEK surgery, a number of techniques have been described for the safe and reliable dissection of ultrathin DS(A)EK grafts.[2,4,5,16,17]

Busin *et al*[2] described a double-pass technique that allows the creation grafts with central thickness of 100 $\mu$m or less in 78.82% of cases and 130 $\mu$m or less in 95.6% of the cases. The authors reported intraoperative complications, such as difficulty in graft dissection, in 7.2% of cases and yet only 2.1% of tissue was discarded as a result. Simple technique modifications, such as eccentric punching or manual finalisation of the dissection, allowed the vast majority of the cases to be salvageable.[2]

Rosa *et al*[16] described the ultrathin $<100\,\mu$m DSAEK in 25 cases with two sequential cuts the first with a femtosecond laser and the second using a 300 $\mu$m microkeratome head. They reported no perforations or other problems during tissue preparation and a LogMar VA of 0.11 6-months post operatively.

Tsatsos *et al*[4] described a manual technique, TMDSEK, which purposely encourages and utilises temporary stromal swelling. Increased corneal stromal thickness during dissection allows for ultrathin DSEK graft creation without greatly increasing the risk of a graft perforation or button-hole creation. They reported a mean graft thickness of 90.7 $\mu$m 1-month post operatively.

Agarwal *et al*[5] described PDEK, a technique that employs pneumatic dissection rendering a thin corneal graft, much like DSEK graft which consists of endothelium, Descemet's membrane, and a predescemetic (PDL-Dua's layer) level and a mean graft thickness of 28 $\mu$m. In PDEK, the total thickness of the PDL together with the endothelium and DM is less than the overall thickness of the DSEK and UT-DSAEK graft. The sparcity or even absence of keratocytes in the central PDL tissue may also contribute to reduced haze, as air cleavage creates a smooth plane and keratocyte activity can be associated with abnormal collagen deposition and haze. The mean graft diameter obtained in PDEK is smaller than in DMEK grafts possibly due to the difficulty in the separation of the PDL in the peripheral cornea. Thus, fewer endothelial cells are transplanted in comparison with other techniques, however, this may be compensated for by reduced cell loss related to manipulation of tissue, especially during unrolling and attachment to the recipient bed.[5]

For corneal surgeons, accessibility to PDEK may be better, because preparation of the donor tissue can be done from preserved corneo–scleral rims, does not require expensive instrumentation, and is not as technically challenging as preparation and manipulation of DMEK tissue. Nevertheless, conversion of PDEK to DMEK may be required to prevent wastage of donor tissue in cases of type II bubble creation.

Large number of patients and longer follow-up periods will be required to confirm the accuracy of the above and to establish a place for PDEK in corneal transplantation surgery.

## Visual outcome

One of the greatest benefits of posterior lamellar keratoplasty is the fast visual rehabilitation and improved visual outcomes with little effect on astigmatism.[8,9,18] Some authors would argue that visual outcomes following DMEK are superior to other posterior lamellar techniques.[12,19] A 5-year prospective study by Wacker *et al*[20] reported continued visual improvement in DSEK patients over 5 years and over half the cohort with vision of 0.1 LogMar or better. The challenges when interpreting long-term data in DSEK is that the technique itself has evolved and we have been able to achieve thinner DSEK grafts more consistently.[4] Mean graft thickness in Wacker's cohort was 155 $\mu$m, which may or not be representative depending on the institution and technique employed.[20] Busin *et al*[11] reported 2-year outcomes following UT-DSAEK (mean graft thickness of 78.28 $\mu$m) with mean BSCVA at 24 months of 0.04 LogMar, with 48.8% of patients in the entire cohort achieving a visual acuity of 20/20 or better and suggested that outcomes with UT-DSAEK were comparable to DMEK.

Although DMEK offers faster visual rehabilitation compared to DSEK or DSAEK, overall performance seems to remain akin. However, the advantageous fast visual rehabilitation is also offered with other techniques such as PDEK.[5]

## Use in complex cases and one chamber eyes

Both DSEK or DSAEK and PDEK have been successfully used in aphakic or AC IOL eyes and heavily scarred host corneas.[21–24] Although there appears to be some success (limited by high rebubbling and secondary graft failure rates) with DMEK, DSEK is generally considered the preferred technique in such complex cases.[25,26] Although PDEK has not been used widely in complex cases, early results appear very promising.[24]

## Limitations of graft harvesting

DMEK graft harvesting can be at least at its initial stages very challenging.[7] For this reason, a number of useful tricks have been proposed to facilitate the harvesting process,[27,28] graft insertion, orientation, and correct placement in the host.[29] This includes the use of older donor eyes as they allow safer DMEK harvesting with less risk of endothelial rip and the easier opening of the endothelial roll inside the host's anterior chamber. This would be potentially linked to donor tissue waste, which can easily and even preferentially be averted in PDEK, as PDEK has been described in younger and even infant donor corneas.[30]

### Rejection

Endothelial graft rejection rates have been reported to be a lot higher with early DSAEK compared with DMEK. UT-DSAEK has been shown to have low rejection rates (2.8%).[8,9,31,32] This compared to the rejection rates of between 1 and 5.7% shown for DMEK at year 1 after surgery suggests a similarly low incidence of immunologic rejection seen in both UT-DS(A)EK and DMEK grafts.[8,9,32]

### Concluding remarks

It is without question that endothelial keratoplasty has transformed corneal surgery and most importantly the visual quality we can offer our patients with endothelial disease. Emerging techniques and technologies have allowed us to push the boundaries and deliver increasingly thinner grafts. DMEK offers a more anatomical correction but with it come numerous surgical challenges. The evidence regarding visual outcomes at 'end point' is similar between all techniques leading to the question 'is it worth it?' The greatest question is whether there is still a role for DSEK and DSAEK? To which the evidence suggests that there is both as a primary procedure or rescue procedure. To answer the question 'Has DMEK taken over?' the answer is no, or at least, not yet.

### Conflict of interest

The authors declare no conflict of interest.

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