**Title:** Thinning rate over 24 months in ultrathin DSAEK

**Subtitle**: Thinning rate in UT-DSAEK

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**Abstract**

**Aim**: To describe the changes in corneal thickness following ultrathin Descemet’s Stripping Automated Endothelial Keratoplasty (UT-DSAEK) from pre- to post-operative visits over 24-month period.

**Methods**: In this retrospective single-centre case series, patients who received eye bank prepared tissues for UT-DSAEK surgery were included. Pre-operative and post-operative graft thickness measurements was determined in the eye bank and in clinic using anterior segment optical coherence tomography (AS-OCT) images. Percentage of graft thickness change between pre-operative values and values at 1 day, 1 week and 1, 6, 12, 24 months were calculated.

**Results**: 47 eyes of 47 patients with a mean age of 69 ± 11 years (29 males) were included. 23 patients had Fuchs (49%) and the remaining 24 had PBK (51%). 29/47 eyes underwent UT-DSAEK alone (62%) and 18/47 received combined cataract surgery as a triple procedure (38%).

Pre-operative donor graft thickness measured was 92 ± 28μm. Compared to preoperative values, graft thickness resulted to be increased to 194 ± 101.3μm at day 1, 151.1 ± 71.4μm at 1 week, 108.4 ± 52.5μm at 1 month. Graft thickness continued to gradually decrease over time until 6 months (-91.7 ± 33.6μm), and then plateaued at 12 months 83.9 ± 25.0μm), showing minimal changes at 2 years (101.4± 37.5μm).

**Conclusion**: Better knowledge of rate of post-operative corneal graft thickness deturgescence will allow for more targeted graft preparation and selection, whilst also giving the surgeon a better understanding of expected corneal thickness at nodal post-operative time-points.

**Keywords:** UT-DSAEK; DSAEK; thinning rate; Eye bank prepared tissue; ultrathin

It will provide a better knowledge of the post-operative DSAEK graft deturgescence, giving the surgeon the expected corneal thickness at nodal post-operative time-points

**Introduction**

Endothelial keratoplasty (EK) techniques has emerged since its introduction by Melles on posterior lamellar keratoplasty (PLK) in 1997 or Terry and Ousley’s deep lamellar endothelial keratoplasty (DLEK) (1–6). Improvement in interface architecture from DLEK to Descemet stripping automated endothelial keratoplasty (DSAEK) resulted in substantial improvement in visual acuity (VA) (6–11). Notwithstanding the growing interest in Descemet membrane endothelial keratoplasty (DMEK) as a result of its better visual outcomes (12–14), DSAEK still remains the most popular treatment of choice for endothelial pathology (15).

It is known that DSAEK provides faster visual rehabilitation, reduced surgically induced regular or irregular astigmatism and preserves biochemical corneal strength compared to penetrating keratoplasty (PK) (4–7,9,10,16–18). Yet, visual outcome is often sub-optimal regardless of the clarity of the graft and less patients than expected achieve full visual recovery (19–22). Several reasons have been considered responsible for this outcome, which includes graft irregularities and differences in graft thickness, high order aberrations, donor-recipient interface and anterior stromal fibrosis (20,21,23). Growing interest has developed in investigating graft thickness, with consensus suggesting better visual outcomes with thinner grafts after DSAEK (4,16,24–27).

Several authors have observed that the thickness of the donor button measured pre-operatively did not correspond with that measured post-operatively (11,28,29). A correlation between pre-operative and post-operative central corneal thickness has been shown, with a growing interest in nanothin (<50um) and ultrathin (approx. <100um) DSAEK techniques (3,11,18,27,30–32). Only a few studies have evaluated changes in DSAEK graft thickness over time to date, with most of them failing to provide information after the 6th postoperative month.

In this case series, we aimed to describe the relation between pre-operative DSAEK graft thickness and post-operative thickness at different time-points, with a follow-up up to 24 months.

**Methods**

Retrospective single-centre case series where patients who underwent UT-DSAEK with Eye bank prepared tissues between April 2017 and July 2019 were included. Both types of EKs graft were precut or preloaded at Eye Bank and shipped to The Royal Liverpool University Hospital (Liverpool, UK). The retrospective data collection followed the tenets of the Declaration of Helsinki and was approved by the local Institutional Review Board (A0002786). Patients included had undergone UT-DSAEK surgery for corneal decompensation due to pseudophakic bullous keratopathy (PBK) or Fuchs’ endothelial dystrophy (FED). Both patients who received UT-DSAEK alone or combined phacoemulsification plus intraocular lens insertion (IOL) and UT-DSAEK (triple surgery) were included in the study. Patients were excluded if no post-operative graft thickness measurements were present or if the graft had failed.

Donor corneas were prepared at the Venice or Monza Eye Bank and shipped to the Royal Liverpool University Hospital as either pre-cut only or pre-loaded tissues. Time from tissue preparation to tissue usage was recorded. Donor characteristics and graft details such as donor age, gender, endothelial cell density (ECD), graft diameter, graft thickness as reported by the eye bank and type of tissue received (pre-cut only or pre-loaded) were recorded.

Clinical data collected were age, gender, indication for surgery, pre-operative best corrected visual acuity (BCVA), procedure type (UT-DSAEK only or triple procedure), post-operative complications and occurrence of re-bubbling procedures. Post-operative BCVA and post-operative graft thickness were also obtained. Pre-operative and post-operative graft thickness was measured using anterior segment optical coherence tomography (Casia AS-OCT, Tomey). High-resolution corneal scans centred on the corneal apex were selected. Axial optical resolution was 10um. The horizontal cross-sectional image, from 180 to 0 degrees was selected. The interface was manually identified and central corneal graft thickness was determined on the central point of the selected images. Peripheral measurements were not recorded. All measurements were taken by trained operators.

Measurements were taken postoperatively, where available, at 1 day, 1 week, 1 month, 2 months, 6 months, 12 months and 24 months. Percentage of graft thickness change between pre-operative values and values at each time point were calculated.

Data is presented as mean ± standard deviation and percentages for graft thickness change. BCVA was converted into LogMAR. Pre-operative and post-operative values were compared with paired t-test.

**Results**

47 eyes from 47 patients who underwent DSAEK surgery were included in the study. The mean patient age at the time of surgery was 69 ± 11 years and 29 were males (62%). Indication for surgery was FED in 23 cases (49%) and BK in 24 (51%). 29/47 eyes underwent DSAEK alone (62%) and 18/47 received combined cataract surgery as a triple procedure (38%). Surgery was performed in the right eye in 51% of cases (24/47).

Average time from tissue preparation to tissue usage was 2.8 ± 0.8 days. Mean preoperative ECD was 2572 ± 134 cells/mm2.

Pre-operative donor graft thickness measured 92.3 ± 28.2μm. Compared to preoperative values, graft thickness resulted to be increased by 99 ± 69% at day 1 (194.0 ± 101.3μm)(n=11)(p=0.003), by 48.2 ± 50.7% at 1 week (151.1 ± 71.4μm)(n=13)(p=0.004), by 19.5 ± 30% at 1 month (108.4 ± 52.5μm)(n=12)(p=0.06). Graft thickness continued to gradually decrease over time, slowly re-assuming pre-operative thickness values. From 2 months onwards, percentage of change in graft thickness compared to pre-operative values always showed to be within approximately 10%; specifically, graft thickness was increased by 3.9 ± 27% at 2 months (99.38 ± 24.0μm)(n=8) (p=0.88), decreased by 11.5 ± 28.6% at 6 months (91.7 ± 33.6μm)(n=14) (p=0.27), decreased by 2.7 ± 27% at 12 months (83.9 ± 25.0μm)(n=15) (p=0.88) and increased by 7.0 ± 24.0% at 24 months (101.4± 37.5μm)(n=11) (p=0.33). In general, a significant amount of increase in graft thickness was observed on day 1, which progressively reduced until the second months, when the graft thickness was back to preoperative values, then it reached its minimum at 6 months, while it showed a minimal upwards trend at 12 and 24 months. Figure 1 shows graft thickness at different follow-up, while figure 2 the percentual change of graft thickness compared to baseline.



Figure 1 – Bar graph showing graft thickness at baseline and at different follow up time. Graft thickness at day 1 is doubled from the preoperative and progressively reverts back to preoperative values within the first 2 months. It remains stable at 6 and 12 months, while at 24 months it shows a minimal increase in thickenss.



Figure 2 – Bar graph showing percentage of graft thickness at different follow up time compared to preoperative thickness value. At day 1, the thickness is almost double the preoperative, and in the first 2 months there is the most significant reduction brings it to similar value of the baseline. At 6 months there is the minimum graft thickness reached and then there is a slow but progressive upward trend.

We analyzed the ratio between the graft thickness and the recipient cornea (figure 3). This ratio started at 0.28 ± 0.14 at day 1 and progressively reduced at 1 week (0.24 ± 0.12, p=0.12) and at 1 month (0.19 ± 0.08, p=0.08). Then it stabilized reaching a plateau at 12 months (0.17 ± 0.04) and started to show a minimal upwards trend at 24 months (0.2 ± 0.07).

We also analysed the ratio between the graft and the recipient cornea thickness at different follow-ups. This is expressed by the following mathematical equation:

*Ratio of DSAEK to Cornea= 0.35+0.00018(days) - 0.0737(days)0.2*





Figure 3 – (Top) Bar graph showing ratio of graft thickness divided by the recipient cornea thickness. At day 1, the ratio 0.28 and it reduces significantly within the first month, reaching 0.19. Then it plateaus until 12 months (0.17) and starts to show a minimal upwards trend at 24 months, which may represent an early graft failure in some patients. (Bottom) Graphical representation of the mathematical equation that expresses the ratio of graft thickness divided by the recipient cornea thickness. Ratio graft thickness/corneal thickness = 0.533102+0.000114(day) - 0.29308(day)0.1 + 0.0399368(day)0.2

Preoperative BCVA was 1.1 ± 0.7 LogMAR and it improved significantly at 12 months follow-up after surgery to 0.34 ± 0.3 LogMAR (p<0.0001).

Nine patients required re-bubbling within one week after surgery (19%). Although graft thickness was increased at day 1 (+114 ± 68.5% vs +93.5 ± 74%; thickness of detached vs non-detached grafts compared with pre-operative graft thickness, respectively) and in the first week after surgery (+70 ± 50% vs. +37.2 ± 50%, respectively), this difference was not significant (p=0.41 and p=0.23, respectively). All grafts were successfully attached at subsequent follow-up visits.

**Discussion**

In the current study we evaluated central UT-DSAEK graft thickness change over time in comparison with pre-operative graft thickness measurements. Our results show an initial marked increase in central corneal graft thickness within the first weeks after surgery, which gradually reduced over the first 6 post-operative months. At 6 months, graft thickness values become similar to those measured pre-operatively by the eye bank and beyond this time point they tend to plateau, showing a minimal increase at 2 years. This study attempted to make a further step in the direction of being able to predict the UT-DSAEK graft thickness one would expect at a given period if prior knowledge of the baseline graft thickness is known.

Previous studies on DSAEK have shown varying degrees of thinning over time, with thicker grafts undergoing greater reduction of thickness (11,29). Woodward et al. reported a mean thinning rate of 17% at 6 months, similar to results from Mater et al., showing a reduction of 12% (11,12). Similarly, Romano et al. reported a 15% thinning at 3 months post-operatively when making use of thinner grafts (28). In agreement, our data showed a significant reduction in the graft thickness within the first 6 months and a graft thickness within 5% of the original pre-operative baseline graft thickness measurements thereafter.

It is known that corneal deturgescence begins almost immediately (11), with central deturgescence rate peaking after 1 week (33). Pogorelov et al. found that the thickness of the donor corneal lenticule decreases rapidly after DSAEK in almost a linear fashion. They suggested that stabilisation of the total central corneal thickness and graft thickness was achieved by 8 weeks (26) and similarly, Ahmed et al. suggested that graft thickness stabilized at 3 months after surgery (34). In contrast, longer DSAEK graft thinning times were shown by Di Pasquale et al., who found that total corneal thickness and central graft thickness reached a steady state between 6-9 months, even showing a mild increase in corneal thickness between 6 and 9 months post-operatively. Those results might however be affected by the fact that only 43% of the cohort were used at this nodal point (33), yet no further decrease was noticed after 6 months.

Similarly, in our cohort of patients, there is a speculation that after the initial 6 months there is a slight increase in average graft thickness which might represent a very initial sign of graft decompensation. However, within our follow up time of 2 years we didn’t assist to any graft with obvious decompensation, therefore no clear conclusion can be drawn on this.

Most patients undergoing UT-DSAEK surgery fail to achieve 6/6 vision post-operatively (4,7,33), with 6/12 vision often used as a benchmark. Studies vary drastically, with results varying in a range of 26% and 70% (4,7). Whilst VA in this study was significantly improved post-operatively (p<0.01), the average post-operative VA was worse than 6/12. We feel this in part was may be due to the fact that patients were not excluded if they had underlying amblyopia, macular pathology, dense vision-limiting PCO or any other corneal pathology. Furthermore, there have only been a handful of studies capable of demonstrating a correlation between better visual acuity and lower total corneal thickness (4,16,24,26,27,35). Most others have however failed to show any significant correlation (7,8,35–41,12,13,15,16,26,31,33,34). There is no randomized control study to date to assess the impact of DSAEK graft thickness on VA. Unfortunately, we are unable to comment on this because the retrospective nature of the study did not allow for a correlation to be made since VA and graft thickness were not available at each nodal time point.

As partially highlighted above, our study is not without limitations. It is retrospective in nature with caveats in serial post-operative BCVA and AS-OCT measurements at expected nodal points. The literature shows considerable variability in graft thickness amongst conventional DSAEK techniques, ranging between 78um to 259um (7,8,26,33,34,39), further emphasising the importance behind this decision. That being said, our study only assessed central donor disc corneal thickness and not the peripheral thickness. Having said that, whilst central thickness may vary significantly from peripheral thickness, this does not have any statistically significant influence on postoperative VA (31). Similarly, since graft thickness varies in all directions from the centre (16,42,43), our measurements were taken from a single central point. Lastly, our graft thickness measurements were taken using AS-OCT.

A better understanding of the UT-DSAEK graft thinning rate requires better co-operation with eye banks when ordering pre-cut corneal tissue, especially ultrathin pre-cut DSAEK grafts. Knowledge of the continual remodelling of corneal interfaces, as well as the slow and gradual change in corneal thickness with time provides us with a better understanding of what to expect after DSAEK surgery. A better understanding of the relationship between graft thickness and visual acuity should be achieved and further studies with longer follow up could help clarify whether this slight increase in graft thickness after the first 6 months that we found could be representative of an early graft decompensation.

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**Authors’ contribution**: All authors equally contributed to study design, data collection, statistical analysis, drafting of the manuscript and reviewing it.

**Data availability statement:** Raw data were generated at Royal Liverpool University Hospital. Derived data supporting the findings of this study are available in the supplementary material.

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