

## ARTICLE



# Thinning rate over 24 months in ultrathin DSAEK

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**AIM:** To describe the changes in corneal graft thickness following ultrathin Descemet's Stripping Automated Endothelial Keratoplasty (UT-DSAEK) comparing pre- and postoperative values over a 24-month period.

**METHODS:** In this retrospective single-center case series, patients who received eye bank-prepared tissues for UT-DSAEK surgery were included. Preoperative and postoperative graft thickness measurements were determined in the eye bank and in clinic using anterior segment optical coherence tomography (AS-OCT) images. Graft thickness measurements and their percentage change between preoperative values and values at 1 day, 1 week and 1, 6, 12, 24 months were calculated.

**RESULTS:** In total, 47 eyes of 47 patients with a mean age of 69 ± 11 years (29 males) were included. Twenty-three patients had Fuchs' endothelial dystrophy (49%) and the remaining 24 had pseudophakic bullous keratopathy (51%). In total, 29/47 eyes underwent UT-DSAEK alone (62%) and 18/47 received combined cataract surgery as a triple procedure (38%). Preoperative donor graft thickness was 92 ± 28 µm. Compared to preoperative values, where graft thickness increased to 194 ± 101.3 µm at 1 day, 151.1 ± 71.4 µm at 1 week, and 108.4 ± 52.5 µm at 1 month. Graft thickness continued to gradually decrease over time until 6 months (91.7 ± 33.6 µm), and then plateaued at 12 months (83.9 ± 25.0 µm), showing minimal changes at 2 years (101.4 ± 37.5 µm).

**CONCLUSION:** Preoperative DSAEK graft thickness measurements as reported by the eye bank are a valid approximation of DSAEK graft thickness at 6 months after surgery and these measurements tend to stabilize over time up to 2 years after surgery.

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## INTRODUCTION

Endothelial keratoplasty techniques started with the introduction by Melles of posterior lamellar keratoplasty in followed by Terry and Ousley's deep lamellar endothelial keratoplasty (DLEK) in 2001 [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 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 [4–7, 9, 10, 16–18]. Yet, visual outcome is often sub-optimal regardless of the clarity of the graft and fewer patients than expected achieve full visual recovery [19–22]. There are several possible reasons for this outcome, which include 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].

There is conflicting evidence that the thickness of the donor button measured pre-operatively corresponds with that measured

postoperatively [11, 28, 29]. There is a growing interest in nanothin (<50 µm) and ultrathin (~ <100 µm) DSAEK techniques [3, 11, 18, 27, 30–32]. Only a few studies have evaluated changes in DSAEK graft thickness over time, with the majority only measuring up to the 6th postoperative month [11, 33, 34].

In this case series, we aimed to describe the relationship between preoperative DSAEK graft thickness and postoperative thickness at various time-points, with a follow-up of up to 24 months.

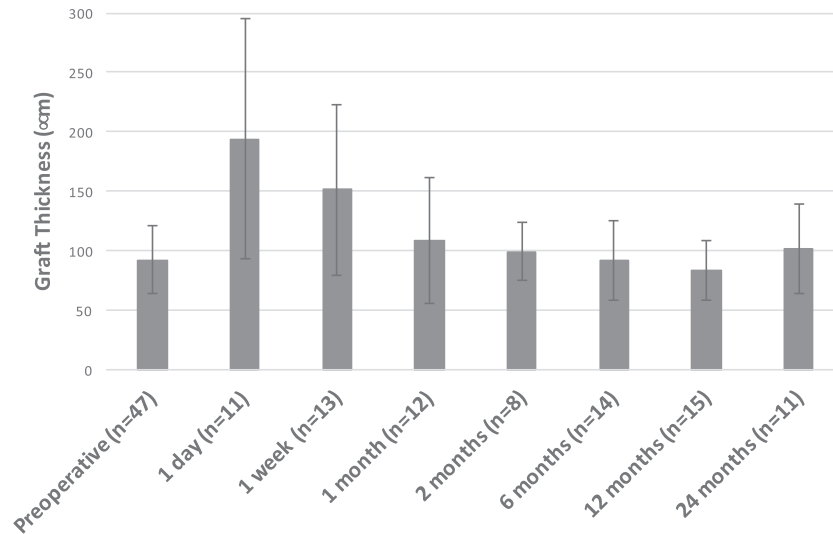
## METHODS

Retrospective single-center 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 pre-cut or pre-loaded at the 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 and UT-DSAEK (triple surgery) were included in the study. Patients were excluded if no postoperative 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

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**Fig. 1 Graft thickness at baseline and at different follow up times.** 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 thickness.

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, preoperative best corrected visual acuity (BCVA), procedure type (UT-DSAEK only or triple procedure), postoperative complications and occurrence of re-bubbling procedures. Postoperative BCVA and postoperative graft thickness were also obtained. Preoperative and postoperative graft thickness was measured using anterior segment optical coherence tomography (Casia AS-OCT, Tomey). High-resolution corneal scans centered on the corneal apex were selected. Axial optical resolution was 10 µm. 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 preoperative values and values at each time point were calculated.

Data are presented as mean ± standard deviation and percentages for graft thickness change. BCVA was converted into LogMAR. Preoperative and postoperative values were compared using a paired *t*-test.

## RESULTS

Forty-seven 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 PBK in 24 (51%). In total, 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/mm<sup>2</sup>.

Preoperative donor graft thickness measured 92.3 ± 28.2 µm [min 42; max 166]. Compared to preoperative values, graft thickness increased by 99.1 ± 69.1% at day 1 (194.0 ± 101.3 µm, min 82, max 347, *n* = 11, *p* = 0.003), by 50.7 ± 49.2% at 1 week (151.1 ± 71.4 µm, min 52, max 316, *n* = 13, *p* = 0.004), and by 19.5 ± 29.9% at 1 month (108.4 ± 52.5 µm, min 57, max 242, *n* = 12, *p* = 0.06). Graft thickness continued to gradually decrease over time, slowly re-assuming preoperative thickness measurements. From 2 months onwards, percentage of change in graft thickness compared to preoperative values was always within ~10%; specifically, graft

thickness was increased by 3.9 ± 26.7% at 2 months (99.38 ± 24.0 µm, min 68, max 144, *n* = 8, *p* = 0.88), decreased by 11.4 ± 28.6% at 6 months (91.7 ± 33.6 µm, min 53, max 151), *n* = 14, *p* = 0.27), decreased by 2.7 ± 26.9% at 12 months (83.9 ± 25.0 µm, min 46, max 124, *n* = 15, *p* = 0.88) and increased by 7.2 ± 24.1% at 24 months (101.4 ± 37.5 µm, min 57, max 170, *n* = 11, *p* = 0.33). In general, a significant increase in graft thickness was observed on day 1, which progressively reduced until the second month, 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 times, while Fig. 2 shows the percentage change of graft thickness compared to baseline.

We analyzed the ratio between the graft thickness and the recipient cornea (Fig. 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 analyzed the ratio between the graft and the recipient cornea thickness at different follow-up times. This is expressed by the following mathematical equation:

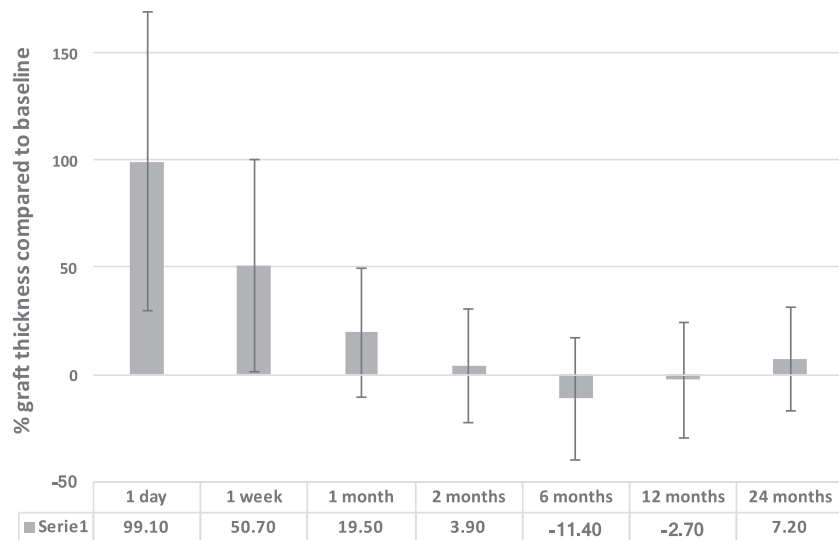
$$\text{Ratio of DSAEK to Cornea} = 0.35 + 0.00018(\text{days}) - 0.0737(\text{days})^{0.2}$$

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 1 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 preoperative 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 this study we evaluated central UT-DSAEK graft thickness change over time in comparison with preoperative graft thickness measurements. Our results show an initial marked increase in central corneal graft thickness within the first weeks after surgery,



**Fig. 2** Percentage of graft thickness at different follow up times compared to preoperative thickness values. At day 1, the thickness is almost double the preoperative, and in the first 2 months there is the most significant reduction bringing it to a similar value as the baseline. At 6 months there is the minimum graft thickness reached and then there is a slow but progressive upward trend.

which gradually reduced over the first 6 postoperative months. At 6 months, graft thickness values were similar to those measured pre-operatively by the eye bank and beyond this time point they tended to plateau, showing a minimal increase at 2 years.

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 postoperatively in patients with 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 preoperative 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 stabilization 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 [35]. In contrast, longer DSAEK graft thinning times were shown by Di Pasquale et al. [33], 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 postoperatively.

Similarly, in our cohort of patients, after the initial 6 months there is a slight increase in average graft thickness and we can speculate that this may represent a very early sign of graft decompensation. However, within our follow up time of 2 years we did not witness 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 postoperatively [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% of patients achieving more than 6/12 [4, 7]. Whilst VA in this study was significantly improved postoperatively ( $p < 0.01$ ), the average postoperative VA was worse than 6/12. We feel this in part was perhaps due to the fact that patients were not excluded if they had underlying amblyopia, macular pathology, dense vision-limiting posterior capsule opacification or any other corneal pathology. Furthermore, there have only been a handful

of studies capable of demonstrating a correlation between better VA and lower total corneal thickness [4, 16, 24, 26, 27, 36]. Most others have however failed to show any significant correlation [7, 8, 36–42, 12, 13, 15, 16, 26, 31, 33, 35]. There has been 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.

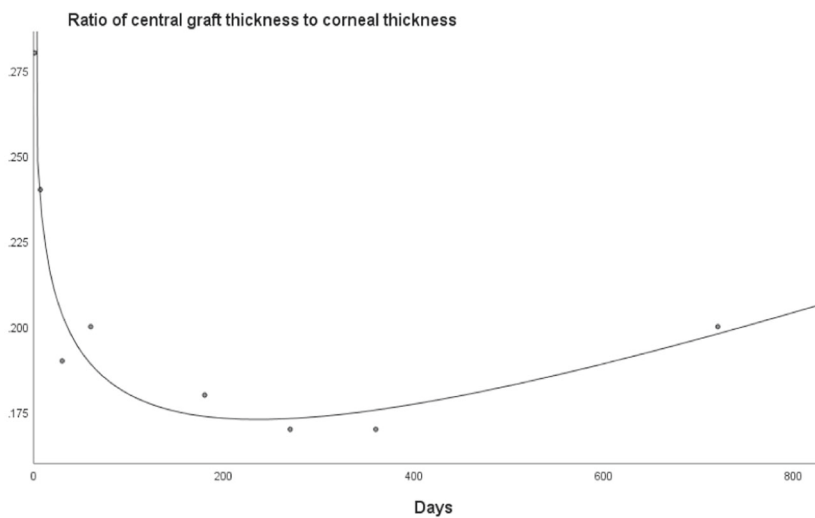
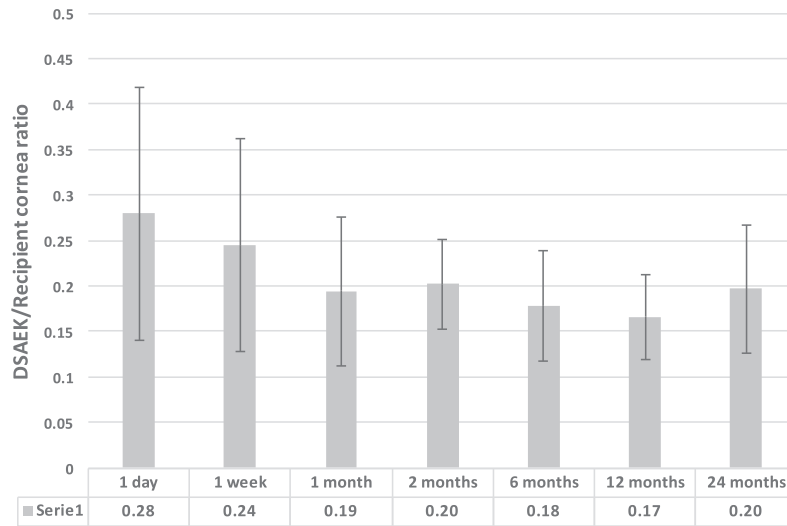
As partially highlighted above, our study is not without limitations. It is retrospective in nature with caveats in serial postoperative BCVA and AS-OCT measurements at expected nodal points, which in some patients were not available. The literature shows considerable variability in graft thickness amongst conventional DSAEK techniques, ranging between 78 to 259  $\mu\text{m}$  [7, 8, 26, 33, 35, 40], while in our case we opted to only consider bank-prepared DSAEK in order to increase reproducibility. That being said, our study only assessed central donor disc corneal thickness and not the peripheral thickness [43–49]. However, whilst central thickness may vary significantly from peripheral thickness, this does not have any statistically significant influence on postoperative VA [31]. Lastly, our graft thickness measurements were taken manually on an image acquired using AS-OCT, which might result in a less reliable measurement.

In conclusion, this study aimed to determine whether prior knowledge of the baseline UT-DSAEK graft thickness allows prediction of graft thickness at a given time point postoperatively. We found that preoperative DSAEK graft thickness as reported by the eye bank is a valid approximation of DSAEK graft thickness at 6 months and up to 2 years after surgery. A better understanding of the relationship between graft thickness and VA would be beneficial and further studies with longer follow up could help clarify whether the slight increase in graft thickness seen after the first 6 months could be representative of an early graft decompensation.

## SUMMARY

What was known before

- Postoperative DSAEK graft thickness tends to decrease with time.



**Fig. 3 (Top) 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.  $\text{Ratio graft thickness/corneal thickness} = 0.533102 + 0.000114(\text{day}) - 0.29308(\text{day})0.1 + 0.0399368(\text{day})0.2$ .

#### What this study adds

- This study highlights the rate of change in the postoperative corneal graft thickness deturgescence, giving the surgeon a better understanding of expected corneal thickness at nodal postoperative time-points.

#### DATA AVAILABILITY

Raw data were generated at Royal Liverpool University Hospital. Derived data supporting the findings of this study are available in the Supplementary Material (see Supplementary Table 1).

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#### AUTHOR CONTRIBUTIONS

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

#### COMPETING INTERESTS

The authors declare no competing interests.

#### ADDITIONAL INFORMATION

**Supplementary information** The online version contains supplementary material available at <https://doi.org/10.1038/s41433-022-02011-8>.

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