Ultrathin Descemet's Stripping Automated Endothelial Keratoplasty Using the Double-pass Technique with the Microkeratome versus Standard Descemet's Stripping Automated Endothelial Keratoplasty

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Purpose
The aim of the present study was to compare the results of Descemet's stripping automated endothelial keratoplasty (DSAEK) and ultrathin Descemet's stripping automated endothelial keratoplasty (UT-DSAEK) that were performed with a standardized technique at a single institution.
Design
The present study was designed as a single-center, prospective, randomized nonblinded study.
Participants and methods
Sixty-one and 51 eyes underwent DSAEK and UT-DSAEK, respectively, for any endothelial disease at the 'Villa Igea' Center. Patients with pre-existing ocular comorbidity that impacted visual potential such as macular degeneration, amblyopia, advanced glaucoma, and other optic neuropathies were excluded from the study.

Best-corrected visual acuity (BCVA) (in Snellen acuity chart) was obtained and specular microscopy of donor corneal tissue was performed before surgery. Postoperative complications, BCVA, and the percent of endothelial cell loss (ECL) recorded at 1, 3, 6 months, and 1 year were compared.
Main outcome measures
Visual acuity improvement, ECL, intraoperative postoperative complications, iatrogenic primary graft failure, and rebubbling were the main outcome measures in this study.
Results
Mean ± SD BCVA improved from 0.17 ± 0.13 and 0.19 ± 0.13 before surgery to 0.75 ± 0.18 and 0.88 ± 0.19 at 1 year after DSAEK and UT-DSAEK, respectively (P = 0.001). ECL was 33.88 ± 17.74% after DSAEK and 36.37 ± 13.10% after UT-DSAEK (P = 0.4080). There were no iatrogenic primary graft failures after the two procedures but there were two late endothelial failures after DSAEK. Rebubbling was performed for four of 51 eyes after UT-DSAEK and for none after DSAEK (P = 0.04).
Conclusion
Compared with DSAEK, UT-DSAEK provided better visual recovery and comparable ECL. The UT-DSAEK group had a higher percentage of rebubbling procedures but less rejection and failure rate.

Keywords:
DSAEK, endothelial, fuch's, keratoplasty, ultrathin DSAEK

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Introduction

Penetrating keratoplasty (PK) was the only procedure available for decades for the therapy of patients with vision loss due to endothelial disease. This made the primary decision for the corneal transplant easy for the surgeon, with decisions of trephination size, suturing style, and other technique-specific decisions to be made secondarily. Over the past decade, however, the field of endothelial keratoplasty (EK) has evolved, making the process of deciding what to do for the specific patient more complicated. Volumes of data over the past 10 years have demonstrated that all the posterior lamellar techniques of endothelial replacement yield far superior results compared with PK [1,2].

In the last few years, EK has established itself as the gold standard for the treatment of endothelial failure of

various origins [2]. As early as 2007, 85% of the donor corneas provided by the Eye Bank Association of America for patients with endothelial dysfunction were used in the EK procedures (2007 Eye Banking Statistical Report, available from the Eye Bank Association of America at: *http://www.restoresight.org*) and EK amounted to about 40% of all cornea grafts performed since 2009 [1]. Descemet's stripping automated endothelial keratoplasty (DSAEK) is by far the most popular technique to replace the diseased endothelium.

Contrasting evidence has linked postoperative vision to the thickness of DSAEK grafts [3–8]. In 2011, Neff *et al.* [3] reported post-DSAEK visual results to be better than those of the post-descemet membrane endothelial keratoplasty (DMEK) ones in patients with grafts thinner than 131 μm, thus correlating the first-time postoperative vision to the morphologic characteristics of the DSAEK tissue transplanted.

We compared herein the results of a prospective study investigating the outcomes of DSAEK procedures employing donor tissue prepared with the microkeratome-assisted double pass technique [ultrathin Descemet's stripping automated endothelial keratoplasty (UT-DSAEK)] with conventional DSAEK, as published previously [9].

Participants and methods

The study included 112 eyes that were divided into two groups (DSAEK and UT-DSAEK). Sixty-one and 51 eyes underwent DSAEK and UT-DSAEK procedure, respectively. All were operated on by the same surgeon (M.B.) using the conventional DSAEK and microkeratome-assisted double-pass technique at 'Villa Igea' Private Hospitals (Forli, Italy) from January 2012 until December 2015, and were included in a prospective, randomized, nonblinded comparative study aimed at evaluating the outcomes of the two techniques.

Patients with endothelial dysfunction resulting from causes other than Fuch's corneal dystrophy were included but patients with prior ocular surgery other than cataract surgery were excluded to limit confounding variables. Failed PK and ocular comorbidity that may affect visual potential such as macular degeneration, amblyopia, advanced glaucoma, and other optic neuropathies were excluded.

The study followed the tenets of the 1964 Declaration of Helsinki and was approved by the local ethics committee; detailed informed consent was signed by all patients undergoing UT-DSAEK. Preoperatively, all patients underwent a complete ophthalmological examination, including the slit-lamp examination, uncorrected, and best spectacle-corrected visual acuity, manifest refraction, applanation tonometry, fundoscopy, and B-scan ultrasound (if required).

Donor preparation

Descemet's stripping automated endothelial keratoplasty

The donor cornea was mounted on an artificial anterior chamber (AAC) of the ALTK System (Moria, Antony, France). One pass was done using a Carriazo-Barraquer microkeratome with a 300-μm head. Pressure in the system was standardized by raising the infusion bottle to a height of 120 cm above the level of the AAC and then by clamping the tube at 50 cm from the entrance to the AAC.

Ultrathin Descemet's stripping automated endothelial keratoplasty

The donor cornea was mounted on an AAC of the ALTK System (Moria). The central corneal thickness was measured using ultrasound pachymetry (Alcon, Fort Worth, Texas, USA). An initial debulking was carried out using a Carriazo-Barraquer microkeratome with a 300 μm head. A second microkeratome-assisted refinement dissection was carried out according to the thickness measured by ultrasound pachymetry according to the Busin nomogram Table 1. Pressure in the system was standardized by raising the infusion bottle to a height of 120 cm above the level of the AAC and then clamping the tube at 50 cm from the entrance to the AAC.

Recipient preparation

Surgery was performed using peribulbar anesthesia in all cases. The surgery was performed using the standard DSAEK technique previously describe d [10] with the following modifications in UT-DSAEK [9]. The graft was inserted using the pull-through technique with the modified mini-Busin glide. The graft was allowed to unfold spontaneously under continuous irrigation from the anterior chamber maintainer.

Table 1 Busin's nomogram

Thickness of residual stromal bed	Head used for second microkeratome pass
<151 μm	No second cut
151–190 μm	50 μm
191–210 μm	90 μm
211–230 μm	110 μm
>230 μm	130 μm

For patients undergoing a triple procedure (UT-DSAEK and phacoemulsification with intraocular lens [IOL] implantation), phacoemulsification and IOL implantation were carried out before UT-DSAEK surgery. No viscoelastics were used throughout the procedure. Capsulorrhexis was performed using a bent needle mounted on a syringe filled with saline to maintain a closed system, whereas the IOL was implanted under continuous irrigation from an anterior chamber maintainer placed at the 12 O'clock position. Intracameral acetylcholine chloride was used to constrict the pupil before UT-DSAEK surgery.

After surgery, patients were instructed to lie supine for at least 2 h. All patients were examined about 3 h after the surgery at the slit-lamp and some air was removed if no aqueous had entered the anterior chamber from behind the iris through the peripheral inferior iridotomy.

Postoperatively, all patients were given topical tobramycin 0.3%, and dexamethasone 0.1%, and suspension combination therapy every 2 h for 2 weeks, and then every 3 h for 2 additional weeks. Treatment was switched to pure steroidal eye drops (dexamethasone 0.1%) four times daily for 1 month, three times daily for 1 month, twice daily for 1 month, and then finally daily, which was continued indefinitely unless the patient was phakic or steroid responder. All sutures were removed in all cases between 4 and 6 weeks from the surgery.

Outcome analysis

Each patient underwent a complete ophthalmological examination 1, 3, 6, and 12 months after undergoing the two procedures, including the slit-lamp examination, best-corrected visual acuity (BCVA), manifest refraction, and applanation tonometry. Baseline donor endothelial cell density was measured by the provider eye bank using specular microscopy. Postoperative endothelial cell density was measured using a noncontact specular microscopy (EM-3000; Tomey, Tennenlohe, Germany). In addition, 1 year postoperatively, graft thickness was measured in each patient centrally using the anterior segment optical coherence tomography (OCT) (Spectralis HRA +OCT; Heidelberg Engineering, Heidelberg, Germany). BCVA was measured using Snellen acuity.

Statistical analyses

Statistical analyses were performed using the SPSS software (version 20.0; SPSS Inc., Chicago, Illinois, USA). Statistical significance between preoperative and postoperative values was tested using the Student *t*-test. A value below 0.05 was considered statistically significant. Normal distribution of values was reported as mean ± SD. For normally distributed data, groups were compared using the Student *t*-test and χ^2 analysis.

Results

Demographics

Mean ± SD patient ages were 65.7 ± 13.5 and 70.7 ± 8.7 years for the DSAEK and UT-DSAEK groups, respectively ($P=0.085$). Transplantation with concurrent cataract surgery (triple procedure) was performed in 31 (50.8%) eyes in the DSAEK group and 25 (49%) eyes in the UT-DSAEK group ($P=0.456$). The remaining eyes were pseudophakic at the time of their initial evaluation. Indications of DSAEK and UT-DSAEK were Fuchs' dystrophy, pseudophakic bullous keratopathy, posterior polymorphous dystrophy, herpetic endotheliitis, and failed DSAEK. The predominant preoperative indications for both groups were Fuchs' dystrophy and pseudophakic bullous keratopathy. There was no statistical significance among the two groups (Table 2).

Visual outcomes

Mean ± SD BCVA improved from 0.17 ± 0.13 and 0.19 ± 0.13 before surgery to 0.75 ± 0.18 and 0.88 ± 0.19 at 1 year after DSAEK and UT-DSAEK, respectively. There was no significant difference in mean preoperative visual acuity. However, there was a significant difference in the mean postoperative visual acuity between DSAEK and UT-DSAEK eyes (Table 3 and Fig. 1).

At 1 year, in the DSAEK group, a total of 91.8% of eyes reached a BCVA of 0.5 or better, 60.7% of eyes reached a visual acuity of 0.8 or better, and 11.5% of eyes reached a visual acuity of 1.0 at 1 year after surgery.

Table 2 Indications of ultrathin Descemet's stripping automated endothelial keratoplasty and Descemet's stripping automated endothelial keratoplasty

Indications	DSAEK ($n=61$) [*n* (%)]	UT-DSAEK ($n=51$) [*n* (%)]
Fuchs dystrophy	42 (70)	43 (84.3)
Pseudophakic/aphakic corneal edema	15 (25)	4 (7.8)
Decompensated EK	1 (1.7)	2 (3.9)
Herpetic endothelitis	1 (1.7)	0
Posterior polymorphous dystrophy	1 (1.7)	2 (3.9)

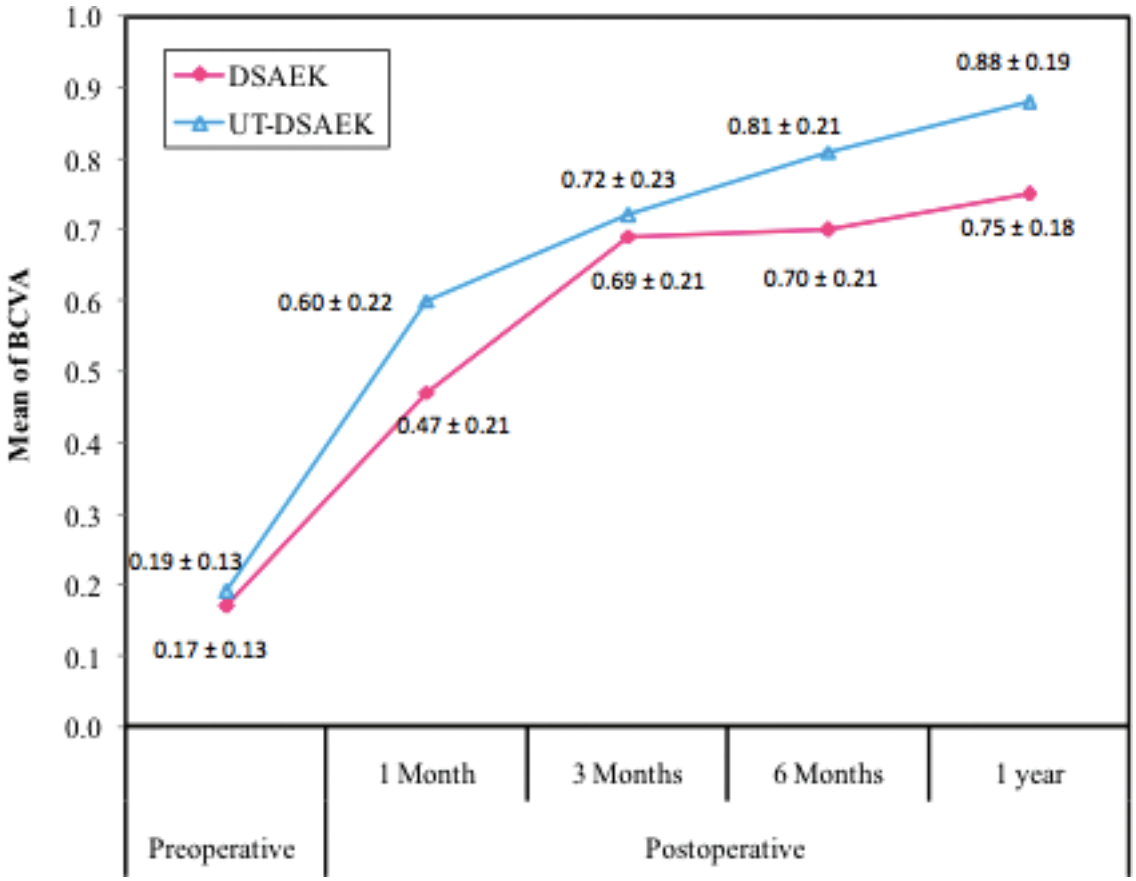
DSAEK, Descemet's stripping automated endothelial keratoplasty; EK, endothelial keratoplasty; UT-DSAEK, ultrathin Descemet's stripping automated endothelial keratoplasty.

Table 3 Best-corrected visual acuity results after ultrathin Descemet's stripping automated endothelial keratoplasty and Descemet's stripping automated endothelial keratoplasty in all eyes without comorbidities

	Best spectacle-corrected visual acuity (mean ± SD)		*P*-value (*t*-test)
	DSAEK (Snellen)	UT-DSAEK (Snellen)	
Preoperative	0.17 ± 0.13	0.19 ± 0.13	0.348
Month 1	0.47 ± 0.21	0.60 ± 0.22	0.001
Month 3	0.69 ± 0.21	0.72 ± 0.23	0.297
Month 6	0.70 ± 0.21	0.81 ± 0.21	0.015
Year 1	0.75 ± 0.18	0.88 ± 0.19	0.001

DSAEK, Descemet's stripping automated endothelial keratoplasty; UT-DSAEK, ultrathin Descemet's stripping automated endothelial keratoplasty.

Figure 1



UCVA before surgery and at different follow up periods at the 2 study groups.

In the UT-DSAEK group, all eyes reached a BCVA of 0.5 or better, 78.4% of eyes reached a visual acuity of 0.8 or better, and 43.1% of eyes reached a visual acuity of 1.0 at 1 year after surgery (Table 4 and Fig. 2).

Endothelial cell loss

Mean ± SD endothelial cell loss percentage (ECL%) at 1 month after DSAEK and UT-DSAEK surgeries was 24.4 ± 11.2 and 27.6 ± 11.7%, respectively (P = 0.595). At 3 months, the mean ± SD ECL% after DSAEK and UT-DSAEK surgeries was 29.1 ± 15.0 and 31.1 ± 12.4%, respectively (P = 0.153). Mean ± SD ECL% at 6 month after DSAEK and UT-DSAEK surgeries was 31.9 ± 16.9 and 30.2 ± 13.6%, respectively (P = 0.653). At 1 year, the mean ± SD ECL% after DSAEK and UT-DSAEK surgeries was 33.9 ± 17.7 and 36.4 ± 13.1%, respectively (P = 0.408) (Fig. 3).

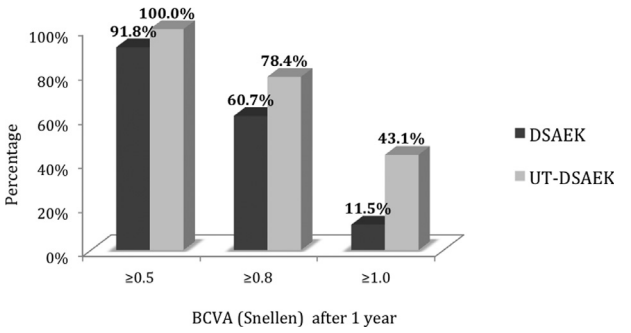
Graft thickness

Average postcut donor corneal thickness at 1 month after DSAEK and UT-DSAEK surgeries was 163.40 ± 44.13 and 89.25 ± 40.22 µm, respectively (P < 0.001). At 3 months, the average postcut donor corneal thickness after DSAEK and UT-DSAEK surgeries

was 150.10 ± 37.28 and 78.41 ± 29.64 µm, respectively ($P < 0.001$). Average postcut donor corneal thickness at 6 month after DSAEK and UT-DSAEK surgeries was 152.68 ± 35.22 and 79.82 ± 29.52 µm, respectively ($P < 0.001$). At 1 year, the average postcut donor corneal thickness after DSAEK and UT-DSAEK surgeries was 143.25 ± 29.91 and 76.04 ± 30.28 µm, respectively ($P < 0.001$).

In the DSAEK group, at 1 year, 37 eyes had a central graft thickness (GT) above 130 µm (73.8%). Twenty-four (39.3%) eyes had a central GT below 130 µm, and one (1.6%) eye had a central GT below 100 µm. None of the grafts had GT below 80 µm. In the UT-DSAEK group, at 1 year, only two grafts had a central GT above 130 µm (3.9%). Forty-nine (96.1%) eyes had a central GT below 130 µm, 43 (84.3%) eyes below 100 µm, and 29 (59.6%) eyes below 80 µm.

Figure 2



BCVA of both study groups.

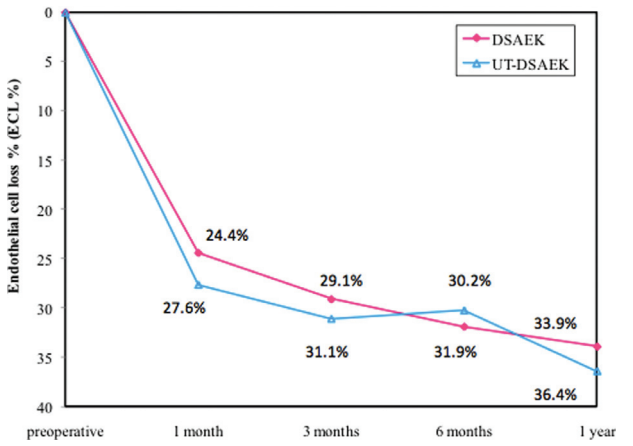
Complications

Postoperative complications are summarized in Table 5. Rebubbling was carried out in four eyes with total detachment after UT-DSAEK ($P = 0.04$) and none after DSAEK. All detachments in the UT-DSAEK group resolved after one air injection and none of them failed.

There were two immunologic graft rejections for the 12 months in the UT-DSAEK group. Four eyes in the DSAEK group had an immunologic rejection episode in this period. All rejections in the two groups resolved completely with topical steroid therapy.

There were no cases of iatrogenic primary graft failure in the two groups. There were two late endothelial failures in the DSAEK group.

Figure 3



Comparison between endothelial cell loss in both groups.

Table 4 Best-corrected visual acuity results after ultrathin Descemet's stripping automated endothelial keratoplasty and Descemet's stripping automated endothelial keratoplasty in all eyes without comorbidities

Snellen acuity	Best-corrected visual acuity (%)							
	1 month		3 months		6 month		1 year	
	DSAEK	UT-DSAEK	DSAEK	UT-DSAEK	DSAEK	UT-DSAEK	DSAEK	UT-DSAEK
≥0.5	42.6	72.5	85.2	86.3	83.6	98.0	91.8	100
≥0.8	9.8	25.5	41.0	54.9	47.5	62.7	60.7	78.4
≥1.0	1.6	7.8	16.4	13.7	13.1	31.4	11.5	43.1

DSAEK, Descemet's stripping automated endothelial keratoplasty; UT-DSAEK, ultrathin Descemet's stripping automated endothelial keratoplasty.

Table 5 Complications after ultrathin Descemet's stripping automated endothelial keratoplasty and Descemet's stripping automated endothelial keratoplasty

	DSAEK [*N* (%)]	UT-DSAEK [*N* (%)]	*P*
PCO	8 (13.1)	6 (11.8)	0.830
Rejection	4 (6.6)	2 (3.9)	0.687
Failure	2 (3.3)	0 (0.0)	0.500
Graft detachment	0 (0.0)	4 (7.8)	0.040
Perforation with microkeratome	0 (0.0)	2 (3.9)	0.205
Hand refined	0 (0.0)	1 (2.0)	0.455

DSAEK, Descemet's stripping automated endothelial keratoplasty; PCO, posterior capsule opacification; UT-DSAEK, ultrathin Descemet's stripping automated endothelial keratoplasty.

Two perforations occurred during donor preparation in the UT-DSAEK group. It occurred while using the 50 μm head in the second pass.

Discussion

Many authors claim that the final visual acuity following DSAEK is suboptimal, with fewer eyes than expected achieving 20/20 vision, possibly because of the presence of a stromal interface [3–8]. In comparison with most of the DSAEK series published to date, DMEK has shown a decisive improvement in terms of speed of visual recovery, percentage of patients achieving 20/20 vision, and rate of immunologic rejection [11–13]. However, ease of graft preparation, manipulation, delivery and attachment, and feasibility of the procedure for eyes with complicated anatomy or poor intraoperative visualization limit the use of DMEK even in the hands of an experienced corneal surgeon.

Ideally, every surgeon would like to use grafts that can be manipulated as easily as DSAEK ones are, but produce the same visual results of DMEK grafts.

No standardized method to obtain DSAEK grafts of a required thickness was available. All the reports published to date on this topic analyzed retrospectively the correlation between graft thickness and postoperative visual performance, thus strongly affecting its significance. We recently developed a technique aimed at reproducibly preparing what was named UT-DSAEK grafts – that is, DSAEK grafts thinner than 131 μm, with a double microkeratome pass – and could therefore undertake a prospective evaluation of the influence of DSAEK graft thickness on visual outcomes [9].

In our prospective study, it was found that visual recovery is significantly faster and better in the UT-DSAEK group as can be seen in Tables 3 and 4 and Figs. 1 and 2. This coincides with the results published in a study by Busin *et al.* [9], in which they found that the visual results after UT-DSAEK almost overlap with DMEK throughout the entire follow-up period, whereas the results of conventional DSAEK remains at a lower level.

Various studies have reported mean BCVA of 20/40 at 3–6 months postoperatively, with the average ranging from 0.6 to 0.3 and the follow-up ranging from 3 to 30 months [10,14–24]. Our results for the two groups (UT-DSAEK and DSAEK) showed better visual acuity than those in other studies, as we excluded visual comorbidities (e.g. retinal disease and glaucoma) from our visual analysis.

In this study, a reliable double-pass microkeratome-assisted dissection of donor tissue was obtained, creating consistently thin and symmetric grafts with minimal loss of tissue, with a mean ± SD thickness of 76.04 ± 30.28 μm.

Using the past technique, the only major limitation of microkeratome dissection was its poor accuracy in determining the final thickness of the dissected tissue. As the head size increases, there seems to be a greater variation in the resulting thicknesses cut. Therefore, using a cutting head of 450 or 500 μm would increase the risk of perforation of the residual stromal bed with poor reproducibility of results. Thus, to prevent perforation, the tissue for DSAEK is cut with heads 300 or 350 μm, often resulting in a donor button with a significant amount of residual deep stroma [9,25–27].

In our technique, to standardize microkeratome dissection of donor tissue, the pressure was set in the ALTK System at a fixed level by clamping the infusion tube at 50 cm from its entrance to the artificial chamber system. The 'closed system' condition obtained in this way guarantees homogeneous pressure in the system throughout the dissection and is easily reproducible. In addition, to minimize the risk for perforation, we used a double-cut type of preparation [25]. If a single cut is performed using microkeratome heads with slits wider than 350 μm, the actual thickness of the excised lamellae can vary from the intended thickness of 100 μm or more [26].

Busin *et al.* [9] showed that after bringing down the thickness of the donor tissue to less than 200 μm with the first debulking dissection, a second cut can be made safely using microkeratome heads with narrow slits (e.g. 130 μm), which allow for more limited variations in the thickness of the excised lamella. They also demonstrated in his study that the risk for perforation increases if both dissections are started at the same site, probably because the microkeratome blade reaches the deepest point in the tissue at the beginning of the cut. Therefore, they recommended rotating the dovetail by 180° and therefore starting the second dissection from the other side. We carried out the intended procedure successfully in all the tested corneas, independently of the technique used. This was also demonstrated in another study [26], in which, according to the precut corneal thickness, the researchers chose the heads used in the first and

second cut but they used the anterior segment OCT in measuring corneal thickness in both cuts [25].

Tissue loss due to central perforation during preparation of UT-DSAEK grafts (two cases; 2.1%) occurred less often than during the preparation of DMEK grafts (3.9%), always with the use of a 50 µm microkeratome head to perform the second cut in a residual bed of central thickness below 190 µm. Inaccuracy in the evaluation of the residual bed thickness by means of ultrasonic pachymetry could explain this complication, particularly if inadvertently measurements were taken paracentrally. The use of an anterior segment OCT to evaluate the residual bed after the debulking cut could prove essential in avoiding even this low percentage of central perforations. This was confirmed in a study by Busin *et al.* [9,25], in which he recommended not using the 50 µm head for the same reason.

Mean ± SD ECL% at 1 year was 33.88 ± 17.74 and 36.37 ± 13.10% in the DSAEK and UT-DSAEK groups, respectively. There was no significant difference in the ECL between the UT-DSAEK and DSAEK groups in our study (Fig. 3). This proves that the double-pass technique did not lead to any further increase in the ECL. We found the ECL to be greater at 3 months, which stabilized afterwards.

Six-month ECL for DSAEK ranged from 13 to 54% [14,21,28–32] and ECL at 1 year ranged from 15.6 to 61% [15,28,31] (Table 32). This further confirms our findings that most of the ECL in DSAEK occurs more in the first 3 months.

This is also consistent with an earlier finding that cell loss in DSAEK patients plateaus more quickly than in those who undergo PK for similar moderate risk indications in a 1-year study in which the endothelial cell density images were analyzed by a central microscopy reading center [33].

Higher ECL after EK surgery can be attributed to the technically challenging donor preparation and insertion techniques, especially in the early learning phase [31]. Most reports of cell loss in DSAEK involved early cases where techniques were still relatively primitive, and as techniques have improved, cell loss has decreased [1]. That was one of the reasons that the ECL in both groups was considered lower than what had been reported in other studies, as the surgeon in this study had passed the learning curve in DSAEK surgery and UT-DSAEK technique did not differ much from the conventional DSAEK surgery.

In this study, the Busin glide was used for the insertion of the DSAEK and UT-DSAEK graft. Most important advantage of this approach is that the donor endothelium remains protected during the entire procedure. Possibly damaging maneuvers such as folding the graft, squeezing the tissue through the surgical wound with a forceps, or touching the endothelial surface with various instruments while trying to unfold the graft are eliminated. In addition, the persistence of a viscoelastic coating on the internal surface of the graft protects the endothelium if the edges curl over each other while the tissue roll flattens and is dragged through the incision [10,25].

Although postoperative graft dislocation was higher after UT-DSAEK (four eyes; 7.8%) and none after DSAEK, it was still much less than that reported after DMEK by Price *et al.*[34] (63%), Guerra *et al.*[13] (60%), and Laaser *et al.*[35] (92%). UT-DSAEK grafts, not different from DSAEK ones, have a shape of their own. Partial UT-DSAEK or conventional DSAEK graft detachments, therefore, do not need rebubbling because they usually zip down on their own over time [20,30,34].

Donor dislocation rates reported after DSAEK vary from as low as 0% to as high as 82% (Table 32) [10,14–18,28,29,36]. To attach the graft, it should be in mechanical contact with the recipient cornea for a long period of time after surgery with no fluid in the interface [2].

It was found that leaving full air tamponade and tight wound closure for 2 h postoperatively is sufficient for graft attachment as it squeezes the fluid out of the interface, which is also suggested by another study where high intraocular pressure was needed to achieve graft attachment [37]. In this study, there were no cases with pupillary block syndrome after both UT-DSAEK or DSAEK because a peripheral inferior iridotomy was always performed and air was removed after 2 h to leave a level above the inferior iridotomy.

In our study, we did not repeat any procedure because of poor BCVA in either groups, which was similar to the findings of other studies [9,10,25]. Yet, the numbers in our study are small and need further investigation.

In our study, none of the cases experienced primary graft failures after UT-DSAEK and DSAEK procedures, maybe because we excluded all eyes with

comorbidities – for example, previous PK failure, glaucoma surgery, and aphakic eyes, which make the procedure more difficult, and due to the surgeon experience in the procedure before, which is an important factor leading to graft failure.

Primary graft failure is considered the third most common DSAEK complication in the reviewed literature, with a range of 0–29% and an average primary graft failure rate of 5% among all published studies [1]. In comparison, Mead *et al.*[38] found a primary failure rate of 2.7% in 778 PK eyes, whereas Wilhelmus *et al.*[39] found a 2% primary graft failure rate in a review of the Adverse Reaction Registry of the Eye Bank Association of America, which included 7240 donor corneas undergoing PK. In their study, de Freitas *et al.*[40] found a 17% primary graft failure rate in 213 eyes that underwent PK, performed by cornea experts, likely reflecting the increased endothelial trauma from surgeon inexperience with technique and tissue handling. Terry [41], Chen *et al.*[42] proposed that the same scenario may occur in DSAEK and cautioned that poor surgical technique, excessive tissue handling, and the use of specific surgical steps that are inherently more traumatic are all associated with a higher risk for primary graft failure.

Although our study had limited number of participants and a relatively shorter follow-up, the graft survival in our study after DSAEK and UT-DSAEK at 1 year was 96.7 and 100%, respectively, which is close to what has been reported in the previous studies [10,14,15,18,27,31,43–47]. There was no statistical significance between the two groups ($P=0.5$).

One-year graft survival rates for DSEK have ranged from 55 to 100%. After exclusion of the reports of surgeons during their early learning curve, the range of clear DSAEK grafts at 1 year is 94–100% [10,14,15,18,27,31,43–47]. Busin *et al.*[9] reported a graft survival probability of UT-DSAEK at 1, 3, 6, 12, and 24 months as 98.6, 98.2, 97.8, 97.8, and 96.2%, respectively. We could not confirm these findings in our series, probably because of the small number of failed grafts, as well as the relatively short follow-up time.

Rejection rates after DSAEK was double to that after UT-DSAEK at 1 year of follow-up, but this was not statistically significant ($P=0.687$) due to limited number of the study and limited number of follow-up. Similarly, Busin *et al.*[9] reported a Kaplan–Meier cumulative probability for a rejection episode after UT-DSAEK at 3, 6, 12, and 24 months of 0, 0.4, 2.4, and 3.3, respectively. Anshu *et al.*[11] have reported the Kaplan–Meier cumulative probability of a rejection episode at 1 and 2 years to be 1 and 1%, respectively, for DMEK; 8 and 12%, respectively, for DSAEK; and 14 and 18%, respectively, for PK. In a different study, Guerra *et al.*[13] found the rejection rate to be 5.7% 1 year after DMEK. In another series, evaluating rejection after DSAEK, Li *et al.*[48] found that the estimated probability of a rejection episode was 6% by 1 year and 10% by 2 years after DSAEK. From these findings, it is clear that immunologic rejection can complicate the postoperative course of UT-DSAEK in a much lower percentage of cases than that of DSAEK and slightly higher than DMEK.

A limitation of this study was that most of the eyes in this study were treated for Fuchs' dystrophy; additional studies on larger cohorts with bullous keratopathy and with pre-existing glaucoma would be valuable. A larger number of participants and a longer follow-up would be helpful to compare between the two groups to confirm our results.

In conclusion, our series indicated that UT-DSAEK as a procedure shares the improved visual outcome and lower immunologic rejection rate of DMEK over DSAEK, while minimizing all types of postoperative complications. In addition, similar to DSAEK and unlike DMEK, UT-DSAEK can be performed in all types of eyes, even in those with complicated anatomy (i.e. free communication between anterior chamber and vitreous cavity as in aphakia, presence of anterior chamber IOLs, etc.) or poor anterior chamber visualization. Finally, UT-DSAEK grafts can be routinely dissected even by relatively inexperienced eye bank technicians, and can be easily evaluated, thus reducing tissue waste and further improving the quality of the tissue to be transplanted.

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Conflicts of interest
Massimo Busin receives travel expenses reimbursement and royalties from Moria (Antony, France). For the remaining authors there are no conflicts of interest.

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