Ultrathin Descemet's Stripping Automated Endothelial Keratoplasty with the Microkeratome Double-Pass Technique

Two-Year Outcomes

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Purpose: To evaluate the outcomes and graft survival rates after ultrathin (UT) Descemet's stripping automated endothelial keratoplasty (DSAEK) using the microkeratome-assisted double-pass technique.

Design: Prospective, consecutive, interventional case series.

Participants: Patients with endothelial decompensation of various causes (Fuchs endothelial dystrophy, pseudophakic or aphakic bullous keratopathy, failed previous graft, herpetic endotheliitis, or buphthalmus; n = 285 grafts).

Intervention: Donor preparation was performed using the microkeratome-assisted double-pass technique. Stripping of the Descemet's membrane was performed under air and the graft was delivered into the anterior chamber using the pull-through technique through a 3-mm clear-cornea incision using a modified Busin glide.

Main Outcome Measures: Best spectacle-corrected visual acuity (BSCVA), manifest refraction, endothelial cell density, and graft thickness (GT).

Results: Excluding all eyes with pre-existing ocular comorbidities, mean BSCVA at 3, 6, 12, and 24 months was 0.16, 0.11, 0.08, and 0.04 logarithm of the minimum angle of resolution units, respectively. The percentage of patients achieving BSCVA of 20/20 or better at 3, 6, 12, and 24 months was 12.3%, 26.3%, 39.5%, and 48.8%, respectively. A statistically significant ($P < 0.0001$) hyperopic shift of 0.78 ± 0.59 diopters (D; range, −0.75 to 1.75 D) was found at 1 year. The endothelial cell loss at 3, 6, 12, and 24 months was 29.8 ± 14.3%, 33 ± 15.5%, 35.6 ± 14.1%, and 36.6 ± 16.0%, respectively. The mean central GT recorded 3 months after surgery was 78.28 ± 28.89 μm. Complications included microkeratome failure to achieve perfect dissection in 21 donor tissues (7.2%), with 6 (2.1%) being discarded; total graft detachment in 11 cases (3.9%); primary failure in 4 cases (1.4%); and secondary failure in 4 additional cases (1.4%). Kaplan-Meier cumulative probability of a rejection episode at 3, 6, 12, and 24 months was 0%, 0.4%, 2.4%, and 3.3%, respectively.

Conclusions: The visual outcomes of UT DSAEK are comparable with those published for Descemet's membrane endothelial keratoplasty and better than those reported after DSAEK in terms of both speed of visual recovery and percentage of patients with 20/20 final visual acuity. However, unlike with Descemet's membrane endothelial keratoplasty, preparation and delivery of donor tissue are neither difficult nor time consuming. Complications of UT DSAEK do not differ substantially from those recorded with standard DSAEK but are much less frequent than those reported after Descemet's membrane endothelial keratoplasty.

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In the last few years, endothelial keratoplasty has established itself as the gold standard for the treatment of endothelial failure of various origins.[1] 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 endothelial keratoplasty procedures (2007 Eye Banking Statistical Report, available from the Eye Bank Association of America at www.restoresight.org; accessed April 20, 2012), and endothelial keratoplasty amounted to approximately 40% of all cornea grafts performed since 2009.[2] Descemet's stripping automated endothelial keratoplasty (DSAEK) is by far the most popular technique to replace diseased endothelium.[1,2] Descemet's stripping automated endothelial keratoplasty is an onlay posterior lamellar keratoplasty procedure that foresees transplantation of donor Descemet's membrane and endothelium attached to a layer of deep stroma. As a result, a stromal interface is created between donor tissue and recipient stroma, which has been held responsible by some authors for the suboptimal

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visual results obtained in a variable percentage of patients undergoing this type of surgery.[3,4]

To improve the results of endothelial keratoplasty further, a newer method was introduced in 2002 by Melles et al,[5] who named it Descemet's membrane endothelial keratoplasty (DMEK) because the donor graft consisted of only Descemet's membrane and endothelium. In comparison with conventional DSAEK, DMEK has shown faster visual recovery, better visual outcomes, and reduced rejection rates.[6–8] However, as Terry[9] recently explained in a thorough editorial, DMEK has not gained popularity over DSAEK mainly because it is technically much more demanding than DSAEK and complications both during and after surgery occur much more frequently with this technique. In addition, although more than 40% of patients undergoing DMEK in the absence of comorbidities could achieve 20/20 vision, still more than 50% could not do so, which suggests factors other than the presence of a stromal interface as possible determinants for the final visual performance.[6,8]

In 2011, Neff et al[4] reported post-DSAEK visual results to be better than the post-DMEK results in patients with grafts thinner than 131 μm, thus correlating for the first time postoperative vision to the morphologic characteristics of the DSAEK tissue transplanted. Whereas surgeons in the past had simply removed "most" of the anterior stroma from the donor cornea and transplanted "what was left behind," the debate was then open regarding whether an attempt should be made to optimize the shape and thickness of DSAEK grafts to minimize postoperative refractive change and, most of all, to maximize postoperative visual performance. Subsequently, contrasting evidence has linked postoperative vision to the thickness of DSAEK grafts.

This article reports the results of a prospective study investigating the outcome of ultrathin (UT) DSAEK procedures using donor tissue prepared with the microkeratome-assisted double-pass technique and intended to be thinner than 130 μm, as published previously.[10]

Patients and Methods

All consecutive patients operated on by the same surgeon (M.B.) using the microkeratome-assisted double-pass technique[10] at Villa Serena-Villa Igea Private Hospitals, Forlì, Italy, from January 2010 through December 2011 were included in a prospective study aimed at evaluating the outcomes of this technique.

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

Each patient also underwent a complete ophthalmologic examination 1, 3, 6, 12, and 24 months after DSAEK, including slit-lamp examination, BSCVA, manifest refraction, and applanation tonometry. Baseline donor endothelial cell density was measured by the provider eye bank by means of specular microscopy. Postoperative endothelial cell density was measured with noncontact specular microscopy (EM-3000; Tomey GmbH, Erlangen, Germany), starting from the 3-month examination. In addition, 3 months after surgery, graft thickness was determined in each patient both centrally and at 2.5 mm from the center nasally and temporally using anterior segment optical coherence tomography (Spectralis HRA+OCT; Heidelberg Engineering, Heidelberg, Germany).

Snellen BSCVA was converted into the logarithm of minimum angle of resolution units for statistical analysis. Patients with pre-existing comorbidities in whom penetrating keratoplasty (PK) had failed were excluded from visual outcomes analysis. Statistical significance between preoperative and postoperative values was tested using a Student t test. A P value less than 0.05 was considered statistically significant. Normally distributed values were reported as mean±standard deviation. Kaplan-Meier analysis was used to calculate graft survival probability and cumulative probability of a rejection episode.

Donor Preparation

The donor cornea was mounted on an artificial anterior chamber (AAC) of the ALTK system (Moria, Antony, France). The central corneal thickness of the donor was measured during surgery using ultrasound pachymetry (SP-3000; Tomey GmbH). An initial debulking cut was performed using a Carriazo-Barraquer microkeratome (Moria) with a 300-μm head. After turning the dovetail of the AAC 180°, a second microkeratome-assisted dissection (refinement cut) was carried out from the direction opposite to the one of the first cut. The head used for this step was selected according to a nomogram developed by Busin (personal data; Table 1, available at http://aaojournal.org), foreseeing leaving behind a residual bed with a central thickness of approximately 100 μm. 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 tubing at 50 cm from the entrance into the AAC. In addition, maximum care was taken to maintain a uniform, slow movement of the hand-driven microkeratome, requiring a time between 4 and 6 seconds for each of the 2 dissections in all cases. Figure 1 shows the optical coherence tomography images of donor tissue before (Fig 1A) and after (Fig 1B) both the debulking and the refinement cut (Fig 1C).

Surgical Technique

After administering peribulbar anesthesia (10 ml L-bupivacaine 0.75% combined with 100 IU hyaluronidase), surgery was performed with the surgeon sitting at the 12-o'clock position. The DSAEK procedure was performed according to a standard technique previously described,[11] except for the following modifications (Videos 1, 2, 3, 4, 5, 6, and 7, available at http://aaojournal.org, demonstrate the surgical procedure). The side platform of a modified Busin glide was used to scoop the tissue floating on a balanced salt solution cushion in the hollow of the punching block (Fig 2A); the graft then was delivered into the anterior chamber with the pull-through technique through a 3-mm clear-cornea wound (Fig 2B). Because the funnel of the modified glide is smaller than the conventional glide, the tip could be inserted into the wound during delivery, thus preventing squeezing of the tissue while entering the anterior chamber through the corneal incision. In patients undergoing a triple procedure, phacoemulsification and intraocular lens implantation were performed before UT DSAEK surgery.

After surgery, patients were instructed to lie supine for at least 2 hours and then were examined approximately 3 hours after

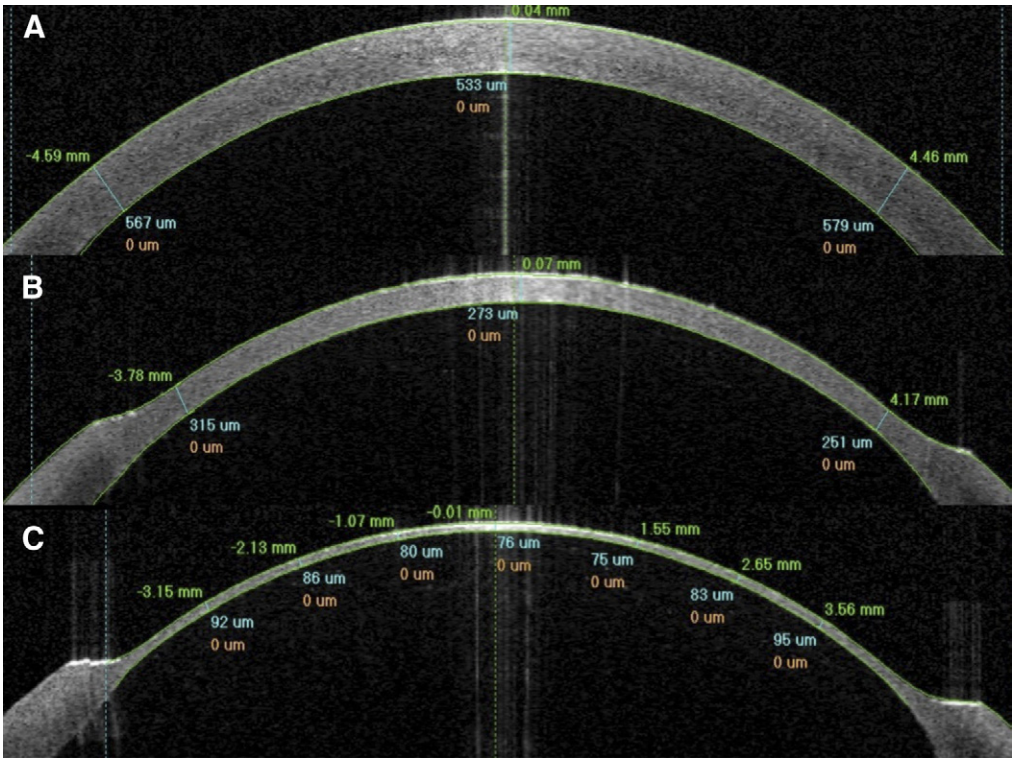

Figure 1. Optical coherence tomography images of donor tissue obtained (**A**) before debulking cut, (**B**) after debulking cut, and (**C**) after refinement cut. Note that peripheral thickness differs by 64 μm from one extremity to the other in (**B**) (315 vs. 251 μm), whereas in (**C**), the values are almost identical (92 vs. 95 μm).

surgery at the slit lamp; some air was removed only if no aqueous had entered the anterior chamber from behind the iris through the peripheral iridotomy. After surgery, all patients were given topical tobramycin 0.3%, dexamethasone 0.1%, and suspension combination therapy (TobraDex, Alcon, Italia) every 2 hours for 2 weeks, then every 3 hours for 2 additional weeks. Treatment was switched to dexamethasone 0.1% 4 times daily for 1 month, thrice daily for 1 month, twice daily for 1 month, then finally once daily to be continued indefinitely unless the patient was phakic or responded to steroids. All sutures were removed from all patients between 4 and 6 weeks after surgery.

Results

Two hundred eighty-five UT DSAEK procedures performed in 279 eyes (6 repeat UT DSAEK procedures) of 250 patients were included in the study. Demographics and indications for surgery

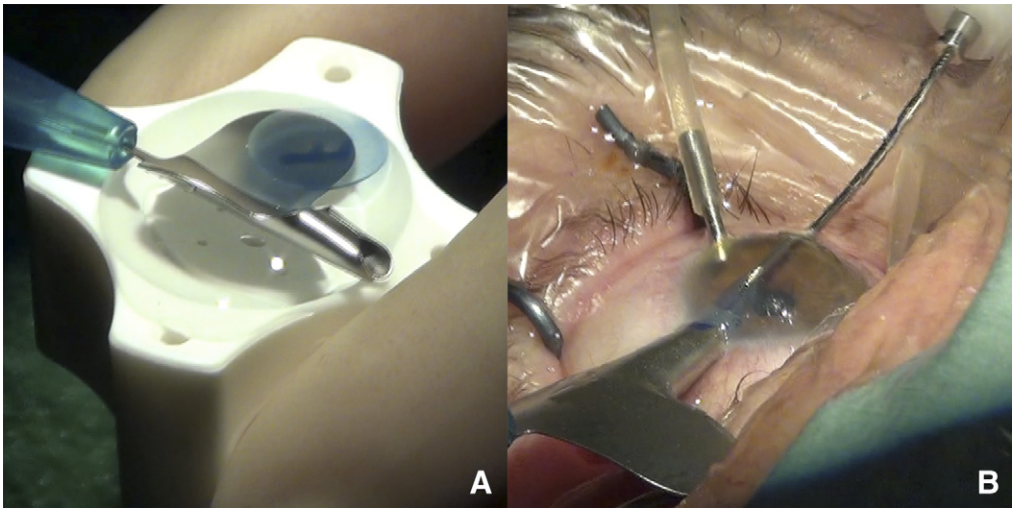

Figure 2. Photographs showing (**A**) tissue being scooped with modified Busin glide and (**B**) delivered using the pull-through technique.

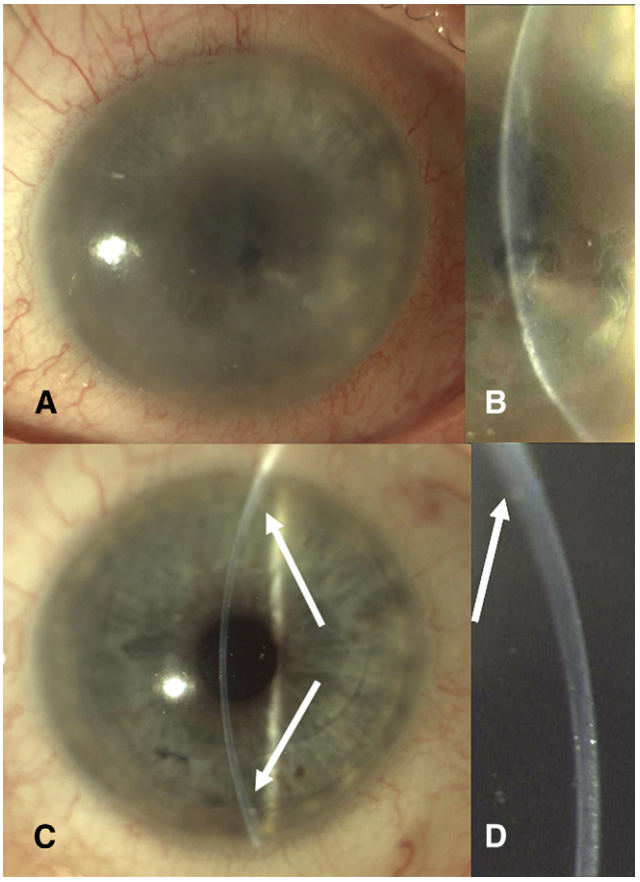

Figure 3. Images from an eye with pseudophakic bullous keratopathy (**A**, **B**) before and (**C**, **D**) after ultrathin Descemet's stripping automated endothelial keratoplasty (UT DSAEK). The UT DSAEK graft is barely visible in its peripheral portion (arrows).

are shown in detail in Table 2 (available at http://aaojournal.org). An example of pseudophakic bullous keratopathy is shown in Figure 3A, B. All phakic patients with a perfectly clear crystalline lens underwent simple DSAEK, whereas even minimal lens changes in elderly patients (age >60 years) were sufficient to pose the indication for combined cataract surgery. Table 3 (available at http://aaojournal.org) lists all types of UT DSAEK procedures performed, as well as procedures combined with UT DSAEK. All grafts were clear by the 1-month follow-up (Fig 3C, D [the same patient as in Fig 3A, B]), except for 4 cases. All eyes were examined 1 month after UT DSAEK, but 20 grafts (7%) were lost to follow-up later on. Follow-up examinations were performed in 272, 242, 181, and 62 eyes at 3, 6, 12, and 24 months, respectively.

Seventy-six eyes (27%) were excluded from the analysis of visual outcomes because of pre-existing ocular comorbidities, including retinal disease (n = 38), advanced glaucoma (n = 20), amblyopia (n = 12), and recipient corneal scarring (n = 6). All 15 eyes with graft decompensation occurring after PK were excluded as well because of the unpredictable effect on vision of the possibly irregular cornea. Figure 4 and Table 4 illustrate the postoperative BSCVA Snellen values recorded at 1, 3, 6, 12, and 24 months after UT DSAEK. Before surgery, 175 of 188 eyes (93%) had visual acuity of less than 20/40. As early as 1 month after surgery with all sutures still in place, BSCVA of 20/20 or better was recorded in 11.7% and BSCVA of 20/40 or better was recorded in 63.8% of all eyes. The BSCVA kept improving over time, with 48.8% of patients seeing 20/20 or better 2 years after UT DSAEK. In particular, phakic patients (Table 5) performed best, with 76.5% of them reaching a BSCVA of 20/20 or better as early as 6 months after UT DSAEK. The mean logarithm of minimum angle of resolution BSCVA values recorded at different times after UT DSAEK in eyes without comorbidities are shown in Figure 5, where they are compared with the values reported in the past for conventional DSAEK[12] and DMEK.[8] The curve obtained for the UT DSAEK values shows a steep, continuous improvement in average logarithm of minimum angle of resolution BSCVA and almost overlaps the DMEK curve, whereas the DSAEK one remains parallel at all times, but at a clearly lower level.

Refractive outcomes could be considered only for those eyes that could be refracted reliably before surgery (n = 108). In these eyes, the mean refractive cylinder increased from 1.1±1.1 diopters (D; range, 0–4 D) before to 1.2±1.1 D (range, 0–3.25 D) 1 year after surgery. This difference was not statistically significant (P = .7593). In the 58 eyes that underwent a stand-alone UT DSAEK procedure, the average spherical equivalent (SE) increased from −0.76±1.69 D before surgery to 0.01±1.84 D 1 year after surgery, resulting in a mean hyperopic shift of 0.78±0.59 D (range, −0.75 to 1.75 D) that was statistically significant ($P < 0.0001$).

The mean endothelial cell density in the donor corneas was 2510±154 (range, 2100–3000 cells/mm^2). The mean endothelial cell loss at 3, 6, 12, and 24 months was 29.8±14.3, 33±15.5, 35.6±14.1, and 36.6±16.0%, respectively, showing substantial stabilization of cell loss as early as 1 year after UT DSAEK (Fig 6, available at http://aaojournal.org). At 1 year, there was no statistically significant difference between medically treated (n = 23) or postsurgical glaucomatous patients (trabeculectomy, n = 14; shunt, n = 3) and nonglaucomatous patients (n = 141). However, 2 years after UT DSAEK, the endothelial cell loss in glaucomatous patients with previous trabeculectomy (n = 7) or shunts (n = 1) was significantly higher (P = 0.0041) than in nonglaucomatous patients (n = 48). In addition, only postsurgical glaucomatous patients seemed to lack stabilization in their cell loss 2 years after UT DSAEK, although statistical analysis did not show any significance for this trend, probably as a consequence of the small numbers involved (n = 8 at 2 years vs. n = 17 at 1 year).

According to the Busin nomogram (Table 1, available at http://aaojournal.org), the second cut was performed with a 130-μm head in 100 cases (34.3%), with a 90-μm head in 113 cases (38.8%) a 50-μm head in 61 cases (20.9%). No second pass was required (measurement of residual bed thickness less than 150 μm) in 17 cases (5.8%). Hand-refined grafts were excluded from the thickness analysis (see "Complications" below). All eyes had a

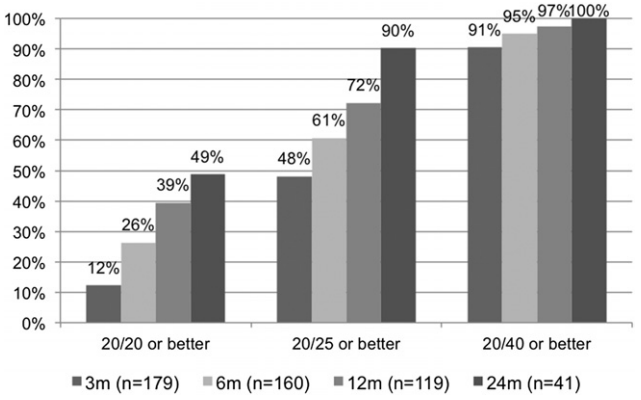

Figure 4. Bar graph showing distribution of best spectacle-corrected visual acuity after ultrathin Descemet's stripping automated endothelial keratoplasty over time. M = months.

Table 4. Best Spectacle-Corrected Visual Acuity Results after Ultrathin Descemet's Stripping Automated Endothelial Keratoplasty in All Eyes without Comorbidities

		Best Spectacle-Corrected Visual Acuity				
	No.	*Mean Logarithm of the Minimum Angle of Resolution*	*Mean Snellen*	*≥20/20 (% eyes)*	*≥20/40 (% eyes)*	**P Value (*t* test)**
Preoperative	188	0.76 ± 0.49	20/115	0.00	6.91	
Month 1	188	0.35 ± 0.40	20/45	11.70	63.83	<0.0001
Month 3	179	0.16 ± 0.13	20/29	12.29	90.50	<0.0001
Month 6	160	0.11 ± 0.12	20/26	26.25	95.00	0.0024
Year 1	119	0.08 ± 0.12	20/24	39.50	97.48	0.0063
Year 2	41	0.04 ± 0.09	20/22	48.78	100.00	0.0251

central graft thickness (GT) of less than 151 μm, 260 eyes (95.6%) had a central GT of less than 131 μm, and 213 eyes (78.3%) had a central GT of less than 101 μm. Three months after surgery, the mean central GT±standard deviation was 78.28 ± 28.89 μm, and the mean peripheral GT was 92.30 ± 38.04 μm nasally and 97.77 ± 35.66 μm temporally. Peripheral GT was significantly higher than central GT ($P < 0.0001$) but did not differ statistically between the temporal and nasal side ($P = 0.0842$).

Complications

Most complications (Table 6) occurred during preparation of donor tissue. Microkeratome-related complications occurred in 21 (7.2%) of all the dissections performed; all but 1 occurred during the first year of the study. All complications occurred during the second pass. In 10 cases (3.4%), buttonholing caused incomplete central dissection of the donor tissue, which was used anyway in all cases after refinement by hand. Perforation occurred in 9 cases, with tissue being discarded in 6 (2.1%) and used anyway in 3 (1%) by punching the tissue eccentrically on the rather peripheral site of the perforation. Finally, in 2 cases, dissection was not complete at the end of the cut but was outside of the area required for punching the tissue to the desired size.

None of the second cuts performed with the 130-μm head were complicated. There were 6 complications with the use of the 90-μm head and 15 with the use of the 50-μm head (buttonhole, n = 3 and n = 7, respectively; perforation, n = 2 and n = 7, respectively; cut incomplete peripherally, n = 1 and n = 1, respectively). Two of the 15 grafts used despite complicated dissection failed primarily and 3 failed at a later time.

After surgery, complete graft detachment was seen in 11 cases (3.9%) and was always managed successfully by rebubbling (single injection, n = 8; double injection, n = 3). In 2 additional cases, the graft detached only in a limited portion of its periphery with no interference with vision and was not treated. None of these cases progressed to total detachment or failure during the time of follow-up.

Graft Survival

Eight grafts failed. Four grafts did not clear the cornea by the 1-month examination and were considered primary failures (1.4%). Four additional grafts cleared primarily but showed late endothelial decompensation and had to be exchanged, and thus were considered secondary failures (1.4%). Two of the grafts that failed primarily and 3 of those that failed at a later stage had necessitated hand refinement during preparation. Kaplan-Meier graft survival probability at 1, 3, 6, 12, and 24 months was 98.6%, 98.2%, 97.8%, 97.8%, and 96.2%, respectively (Fig 7, available at http://aaojournal.org). All failed grafts were regrafted successfully with UT DSAEK.

The risk for immunologic rejection was high in 21 eyes because of previous PK surgery. Endothelial rejection was documented in 6 eyes (2.1%), of which only 1 eye was at high risk. All rejection episodes were reversed with corticosteroids except for 1 case, possibly a consequence of the late referral of this patient, 1 week after onset of the rejection. Kaplan-Meier cumulative probability of a rejection episode at 3, 6, 12, and 24 months was 0%, 0.4%, 2.4%, and 3.3 %, respectively.

Discussion

Many authors claim that final visual acuity after DSAEK is suboptimal, with fewer eyes than expected achieving 20/20 vision, possibly because of the presence of a stromal interface.[1–3,13] 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

Table 5. Best Spectacle-Corrected Visual Acuity Results after Ultrathin Descemet's Stripping Automated Endothelial Keratoplasty in Phakic Eyes without Comorbidities

		Best Spectacle-Corrected Visual Acuity				
	No.	*Mean Logarithm of the Minimum Angle of Resolution*	*Mean Snellen*	*≥20/20 (% eyes)*	*≥20/40 (% eyes)*	**P Value (*t* test)**
Preoperative	18	0.55 ± 0.43	20/71	0.00	28.78	
Month 1	18	0.07 ± 0.07	20/24	22.22	100.00	<0.0001
Month 3	18	0.06 ± 0.09	20/23	38.89	100.00	0.42
Month 6	17	0.01 ± 0.05	20/21	76.47	100.00	0.02
Year 1	13	0.03 ± 0.08	20/21	69.23	100.00	0.80
Year 2	7	0.03 ± 0.12	20/22	85.71	100.00	0.75

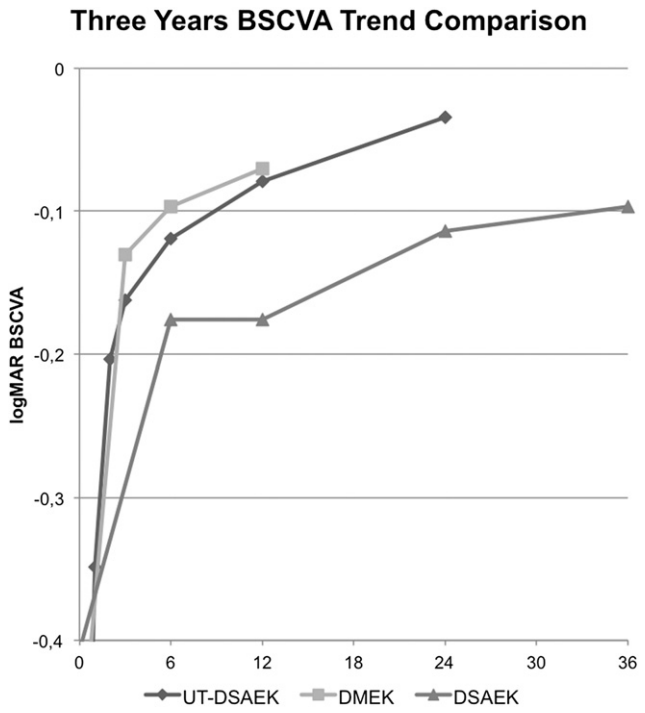

Figure 5. Graph showing postoperative best spectacle-corrected visual acuity (BSCVA) obtained after ultrathin Descemet's stripping automated endothelial keratoplasty (UT DSAEK) compared with Descemet's membrane endothelial keratoplasty (DMEK) (Guerra et al[8]), and Descemet's stripping automated endothelial keratoplasty DSAEK (Li et al).[13] logMAR = logarithm of the minimum angle of resolution.

patients achieving 20/20 vision, and rate of immunologic rejection.[6–8] However, ease of graft preparation, manipulation, delivery, and attachment, as well as feasibility of the procedure for eyes with complicated anatomic features or poor intraoperative visualization limit the use of DMEK even in the hands of experienced corneal surgeons.[9]

Ideally, every surgeon would like to use grafts that can be manipulated as easily as DSAEK ones are but that produce the same visual results of DMEK grafts. In fact, 20/20 vision after DSAEK is well possible, as reported in a variable percentage of patients,[12] thus demonstrating that the procedure itself is compatible with optimal visual results. Among the factors that may make a DSAEK procedure work like a DMEK procedure, graft thickness has been debated most with contrasting evidence.[4,14] In particular, Neff et al[4] and other investigators showed that 20/20 vision could be obtained in approximately 71% of the eyes of very selected patients with a DSAEK graft thinner than 131 μm. However, because 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 we have termed *UT DSAEK* grafts, that is, DSAEK grafts thinner than 131 μm, with a double microkeratome pass,[10] and therefore could undertake a prospective evaluation of the results of transplantation of thin DSAEK grafts.

As shown in Table 4, the number of eyes recovering at least 20/20 BSCVA after UT DSAEK increased over time in this study. At 6 months, 1 year, and 2 years, the percentage over the total of eyes with no comorbidities was 26.3%, 39.5%, and 48.8%, respectively. When comparing these results from UT DSAEK with those published after DSAEK[13] and DMEK[8] in the series with the longest available follow-up, quite strikingly, the curves of UT DSAEK and DMEK almost overlap throughout the entire follow-up period considered, whereas the curve of DSAEK remains constantly at a lower level (Fig 5). Other DMEK studies[15,16] showed higher percentages (30% and 47%) of eyes achieving 20/20 vision, but the follow-up was limited to 6 months.

The speed of visual recovery after UT DSAEK is somewhat slower than that recorded after DMEK,[16,17] but as early as 1 year after surgery, the percentage of eyes with BSCVA of 20/20 or better are similar.[2,8] However, the delay in recovery of BSCVA after UT DSAEK could be just a consequence of the substantially lower preoperative visual acuity in this series in comparison with the DMEK series published to date.[8,18,19]

Instead, Li et al[12] reported 13.9%, 34.3%, and 47.2% of eyes with 20/20 BSCVA 1, 2, and 3 years after conventional DSAEK, respectively. Based on this report, in terms of 20/20 visual recovery, UT DSAEK compares favorably with conventional DSAEK as early as 1 year in the postoperative course, with approximately 3 times as many patients achieving 20/20 or better vision.

We also analyzed separately the visual outcome of patients undergoing phakic UT DSAEK (Table 5), who, with rare exceptions (i.e., buphthalmic eyes), have the best prognosis among all indications because they are young (younger than 50 years) and have never undergone any type of ophthalmic surgery. A BSCVA of at least 20/40 was recorded in all eyes of this series as early as 1 month after UT DSAEK. In addition, a BSCVA of 20/20 or better was obtained in approximately 76.5% of eyes at 6 months,

Table 6. Intraoperative and Postoperative Complications of Ultrathin Descemet's Stripping Automated Endothelial Keratoplasty

Complication	No. of eyes (%)
Microkeratome-related complication	21 (7.2)
Tissue loss	6 (2.1)
Hand refinement of the donor tissue	15 (5.2)
Graft detachment treated with air injection	11 (3.9)
Graft failure	8 (2.8)
Primary	4 (1.4)
Secondary	4 (1.4)
Endothelial immunologic rejection	6 (2.1)
Reversed with treatment	5 (1.7)
Not reversed with treatment	1 (0.3)
Cystoid macular edema	5 (1.7)
Interface infection	2 (0.7)
Persistent epithelial defect	1 (0.3)
Urrets-Zavalia syndrome	1 (0.3)
Persistent interface haze	1 (0.3)
Postoperative cataract	2 (8.3 of phakic eyes)

approximately 3 times as many as in the general population of eyes with no comorbidity. These data confirm the experience of Shamie N, et al and other authors reporting that eyes with better preoperative visual acuity and younger age tend to achieve a better final vision in a shorter period (Shamie N, et al. Descemet's-stripping automated endothelial keratoplasty: predictive factors for good visual acuity. Poster presented at: AAO Annual Meeting, November 13, 2007; New Orleans, Louisiana).

Although the visual outcome recorded after UT DSAEK compares favorably with that obtained after DSAEK and is no different than after DMEK, the percentage of eyes without comorbidities recovering 20/20 vision is lower than expected.[2,6,8,15,16,19] This indicates that other factors besides the presence of a stromal interface of any type likely can determine the final visual result of endothelial keratoplasty. As indicated by Patel et al,[20] recovery of normal stromal architecture in corneas with long-standing edema may require a prolonged period, during which vision would be affected negatively. If this were true, the excellent results obtained in eyes of younger patients undergoing phakic UT DSAEK would be a simple consequence of a so-called better recipient cornea.

After UT DSAEK, a statistically significant ($P < 0.001$) hyperopic shift of approximately 0.78 ± 0.59 D was found. Several authors have reported a substantially higher significant hyperopic shift (up to 1.5 D after DSAEK).[1,2] In a previous series of DSAEK eyes,[21] the authors hypothesized that the change in posterior corneal curvature caused by the attachment of a meniscus-shaped donor graft was the main cause of the hyperopic shift recorded. The presence of a hyperopic shift after UT DSAEK correlates to a lesser extent with the reduced but still significant difference between central and peripheral GT. However, a statistically significant hyperopic shift in the SE also has been reported after DMEK,[6,16] and corneal deturgescence alone has been held responsible for this.[22] This mechanism could well contribute to the presence of a hyperopic shift after UT DSAEK, despite the use of thin, fairly plano grafts.

The negative cylinder remained practically unchanged after UT DSAEK (0.1 D of difference 1 year after surgery), similar to what is recorded after DMEK.[6,8] Instead, a significant induced cylinder (up to 0.6 D) has been reported after DSAEK by several authors.[1,2] The most probable explanation for this is in the different size of the wound used for graft delivery with the different techniques. In UT DSAEK, grafts can be delivered through a 3-mm wound by means of a modified Busin glide without squeezing the tissue, whereas this is less possible for thicker grafts. For this reason, most DSAEK surgeons prefer to use a 5-mm wound, which induces more postoperative astigmatism than a smaller wound.

The mean endothelial cell loss of approximately 35% recorded 1 year after UT DSAEK is similar to that recorded after DSAEK[1,2,11,23] and DMEK,[2,8,24] showing that a double microkeratome pass does not affect endothelial survival. Also, as shown in Figure 6 (available at http://aaojournal.org), stabilization of cell loss is achieved as early as 1 year after UT DSAEK, in accordance with what is seen after DSAEK. Cell loss is significantly more pronounced in glaucomatous patients who have undergone surgery. Although this also was reported after DSAEK,[25] the explanation for an increased cell loss remains unclear. The physical presence of a shunt in the anterior chamber may contribute to mechanical damage of the donor tissue, but normal levels of intraocular pressure controlled after filtering surgery should be compatible with normal endothelial survival. In the present series, the number of patients with shunts or previous trabeculectomy was too small to allow a meaningful analysis of the endothelial cell loss in these 2 separate subgroups.

Table 6 lists all UT DSAEK complications encountered both during and after surgery in this study. Tissue loss resulting from a central perforation during preparation of UT DSAEK grafts occurred relatively rarely (6 cases [2.1%]), always with the use of a 50-μm microkeratome head to perform the second cut in a residual bed of central thickness of less than 190 μm. Inaccuracy in the evaluation of the residual bed thickness by means of ultrasonic pachymetry may explain this complication, particularly if measurements were obtained inadvertently paracentrally. The use of anterior segment optical coherence tomography to evaluate the residual bed after the debulking cut may prove useful in avoiding even this low percentage of central perforations. In the 3 cases with peripheral perforation, the donor tissue was used anyway after eccentric punching. The explanation for peripheral perforation is more difficult because the residual bed is thicker peripherally compared with centrally. However, in all 3 cases of this series, entanglement of the dissected tissue into the microkeratome head-slit occurred during dissection, possibly resulting in malfunctioning of the device. None of these 3 cases failed, and neither was their final BSCVA or endothelial cell density affected substantially, showing that peripheral perforations can be managed successfully with no loss of tissue.

Postoperative graft dislocation occurred in 11 eyes after UT DSAEK (3.9%), much less often than that reported after DMEK by Price et al[6] (63%), Guerra et al[8] (60%), Laaser et al[17] (92%), and even Dirisamer et al[18] (9%). The UT DSAEK grafts, not unlike DSAEK grafts, have a shape on their own, making them much more stable than the Descemet's-endothelial roll of DMEK. Partial UT or conventional DSAEK graft detachments therefore do not need rebubbling because they usually zipper down on their own over time, whereas the edges of DMEK detachments have a tendency to curl under, maintaining the cleft.[6,8]

Graft survival probability of UT DSAEK at 1, 3, 6, 12, and 24 months was 98.6%, 98.2%, 97.8%, 97.8%, and 96.2%, respectively. To date, no data are available regarding DMEK graft survival probability. One-year graft survival for DSAEK in series excluding the initial learning curve of surgeons has been reported to vary between 94% and 100%.[1,2,11,23,26,27] Price et al[23] reported recently a DSAEK graft survival rate at 5 years of 93%, with a significantly higher value for Fuchs patients (95%) than for patients with pseudophakic bullous keratopathy (76%) or previous glaucoma surgery (40%). These data could not be confirmed in the present series, probably because of the small number of failed grafts as well as the limited

Table 7. Outcomes after Ultrathin Descemet Stripping Automated Endothelial Keratoplasty, Descemet Stripping Automated Endothelial Keratoplasty and Descemet Membrane Endothelial Keratoplasty in Comparison

	UT-DSAEK (%)	DSAEK[1,2] (%)	DMEK[6–8] (%)
Tissue loss	2.8	N/A	4.2
Air reinjection	3.9	0–35	62
Primary failure	1.4	0–29	8.1
Rejection rate at 1 yr	2.8	2–18	5.1
ECL at 1 yr	35	24–57	36

UT-DSAEK = Ultrathin Descemet stripping automated endothelial keratoplasty, DSAEK = Descemet stripping automated endothelial keratoplasty, DMEK = Descemet membrane endothelial keratoplasty, N/A = Not Available, ECL = endothelial cell loss.

follow-up time. However, the significantly higher postoperative endothelial cell loss in patients with previous glaucoma surgery recorded in this series indicates that they are clearly at risk for long-term graft failure.

The Kaplan-Meier cumulative probability of a rejection episode at 1, 3, 6, and 12 months after UT DSAEK was 0%, 0.3%, 2.4%, and 3.3%, respectively. Anshu et al[7] 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 report, Guerra et al[8] found the rejection rate to be 5.7% at 1 year after DMEK. In another series evaluating rejection after DSAEK, Li et al[28] found that the estimated probability of a rejection episode was 6% by 1 year and 10% by 2 years after DSAEK. From these data, it seems that immunologic rejection can complicate the postoperative course of UT DSAEK in a much lower percentage of cases than that of DSAEK. Instead, contradictory results at 1 year in different articles (higher rejection probability of 2.44% for UT DSAEK versus 1% for DMEK, but similar rejection rate of 2.8% for UT DSAEK versus 1% to 5.7% for DMEK) indicate a comparably low incidence of immunologic rejection with UT DSAEK and DMEK.

These results indicate that UT DSAEK is a procedure that shares the improved visual outcome and lower immunologic rejection rate of DMEK over DSAEK, while minimizing all types of postoperative complications (Table 7). In addition, similar to DSAEK and unlike DMEK, UT DSAEK can be performed safely in all types of eyes, even in those with complicated anatomic features (e.g., free communication between anterior chamber and vitreous cavity as in aphakia, presence of anterior chamber intraocular lenses) or poor anterior chamber visualization.[6,8] Finally, unlike DMEK grafts, UT DSAEK grafts can be dissected routinely even by relatively inexperienced eye bank technicians and can be evaluated easily, thus reducing tissue waste and further improving the quality of tissue to be transplanted. However, despite all the above-mentioned advantages of UT DSAEK, a dedicated randomized study is necessary to produce the scientific evidence required to confirm the significance of different outcomes obtained with different endothelial keratoplasty techniques.

References

1. Lee WB, Jacobs DS, Musch DC, et al, Ophthalmic Technology Assessment Committee Cornea and Anterior Segment Disorders Panel. Descemet's stripping endothelial keratoplasty: safety and outcomes: a report by the American Academy of Ophthalmology. Ophthalmology 2009;116:1818–30.
2. Anshu A, Price MO, Tan DT, Price FW Jr. Endothelial keratoplasty: a revolution in evolution. Survey Ophthalmol 2012;57:236–52.
3. Letko E, Price DA, Lindoso EM, et al. Secondary graft failure and repeat endothelial keratoplasty after Descemet's stripping automated endothelial keratoplasty. Ophthalmology 2011; 118:310–4.
4. Neff KD, Biber JM, Holland EJ. Comparison of central corneal graft thickness to visual acuity outcomes in endothelial keratoplasty. Cornea 2011;30:388–91.
5. Melles GR, Lander F, Rietveld FJ. Transplantation of Descemet's membrane carrying viable endothelium through a small scleral incision. Cornea 2002;21:415–8.
6. Price MO, Giebel AW, Fairchild KM, Price FW Jr. Descemet's membrane endothelial keratoplasty: prospective multicenter study of visual and refractive outcomes and endothelial survival. Ophthalmology 2009;116:2361–8.
7. Anshu A, Price MO, Price FW Jr. Risk of corneal transplant rejection significantly reduced with Descemet's membrane endothelial keratoplasty. Ophthalmology 2012;119:536–40.
8. Guerra FP, Anshu A, Price MO, et al. Descemet's membrane endothelial keratoplasty: prospective study of 1-year visual outcomes, graft survival, and endothelial cell loss. Ophthalmology 2011;118:2368–73.
9. Terry MA. Endothelial keratoplasty: why aren't we all doing Descemet membrane endothelial keratoplasty? Cornea 2012; 31:469–71.
10. Busin M, Patel AK, Scorcia V, Ponzin D. Microkeratome-assisted preparation of ultrathin grafts for Descemet stripping automated endothelial keratoplasty. Invest Ophthalmol Vis Sci 2012;53:521–4.
11. Busin M, Bhatt PR, Scorcia V. A modified technique for Descemet membrane stripping automated endothelial keratoplasty to minimize endothelial cell loss. Arch Ophthalmol 2008;126:1133–7.
12. Li JY, Terry MA, Goshe J, et al. Three-year visual acuity outcomes after Descemet's stripping automated endothelial keratoplasty. Ophthalmology 2012;119:1126–9.
13. Price MO, Price FW Jr. Descemet's stripping with endothelial keratoplasty: comparative outcomes with microkeratome-

dissected and manually dissected donor tissue. Ophthalmology 2006;113:1936–42.
14. Ahmed KA, McLaren JW, Baratz KH, et al. Host and graft thickness after Descemet stripping endothelial keratoplasty for Fuchs endothelial dystrophy. Am J Ophthalmol 2010;150:490–7.
15. Ham L, Balachandran C, Verschoor CA, et al. Visual rehabilitation rate after isolated Descemet membrane transplantation: Descemet membrane endothelial keratoplasty. Arch Ophthalmol 2009;127:252–5.
16. Ham L, Dapena I, van Luijk C, et al. Descemet membrane endothelial keratoplasty (DMEK) for Fuchs endothelial dystrophy: review of the first 50 consecutive cases. Eye (Lond) 2009;23:1990–8.
17. Laaser K, Bachmann BO, Horn FK, et al. Donor tissue culture conditions and outcome after Descemet membrane endothelial keratoplasty. Am J Ophthalmol 2011;151:1007–18.
18. Dirisamer M, Ham L, Dapena I, et al. Efficacy of Descemet membrane endothelial keratoplasty: clinical outcome of 200 consecutive cases after a learning curve of 25 cases. Arch Ophthalmol 2011;129:1435–43.
19. Tourtas T, Laaser K, Bachmann BO, et al. Descemet membrane endothelial keratoplasty versus Descemet stripping automated endothelial keratoplasty. Am J Ophthalmol 2012;153:1082–90.
20. Patel SV, Baratz KH, Hodge DO, et al. The effect of corneal light scatter on vision after Descemet stripping with endothelial keratoplasty. Arch Ophthalmol 2009;127:153–60.
21. Scorcia V, Matteoni S, Scorcia GB, et al. Pentacam assessment of posterior lamellar grafts to explain hyperopization after Descemet's stripping automated endothelial keratoplasty. Ophthalmology 2009;116:1651–5.
22. Kwon RO, Price MO, Price FW Jr, et al. Pentacam characterization of corneas with Fuchs dystrophy treated with Descemet membrane endothelial keratoplasty. J Refract Surg 2010;26:972–9.
23. Price MO, Fairchild KM, Price DA, Price FW Jr. Descemet's stripping endothelial keratoplasty: five-year graft survival and endothelial cell loss. Ophthalmology 2011;118:725–9.
24. Ham L, van Luijk C, Dapena I, et al. Endothelial cell density after Descemet membrane endothelial keratoplasty: 1- to 2-year follow-up. Am J Ophthalmol 2009;148:521–7.
25. Kim P, Amiran MD, Lichtinger A, et al. Outcomes of Descemet stripping automated endothelial keratoplasty in patients with previous glaucoma drainage device insertion. Cornea 2012;31:172–5.
26. Terry MA, Shamie N, Chen ES, et al. Endothelial keratoplasty: the influence of preoperative donor endothelial cell densities on dislocation, primary graft failure, and 1-year cell counts. Cornea 2008;27:1131–7.
27. Price MO, Price FW Jr. Endothelial cell loss after Descemet stripping with endothelial keratoplasty: influencing factors and 2-year trend. Ophthalmology 2008;115:857–65.
28. Li JY, Terry MA, Goshe J, et al. Graft rejection after Descemet stripping automated endothelial keratoplasty: graft survival and endothelial cell loss. Ophthalmology 2012;119:90–4.

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