ENDOTHELIAL KERATOPLASTY: A COMPARISON OF COMPLICATION RATES AND ENDOTHELIAL SURVIVAL BETWEEN PRECUT TISSUE AND SURGEON-CUT TISSUE BY A SINGLE DSAEK SURGEON

BY **Mark A. Terry MD***

ABSTRACT

Purpose: Descemet stripping automated endothelial keratoplasty (DSAEK) can be performed with donor tissue prepared with a microkeratome either by the surgeon at the time of surgery or by a technician in the eye bank days before surgery. Are the complications and endothelial survival affected by donor preparation by a surgeon vs a technician?

Methods: A single surgeon at a referral practice performed 225 DSAEK procedures for Fuchs endothelial dystrophy using a similar surgical technique for all cases. Surgeon-cut tissue was used in 49 cases (group 1), and precut tissue was used in 176 cases (group 2). Retrospective analysis was done from a prospectively collected database for donor dislocations, iatrogenic primary graft failure (IPGF), and 6- and 12-month postoperative central endothelial cell density (ECD).

Results: There were no dislocations in group 1 and 3 dislocations in group 2 ($P = .224$). There were no IPGFs in group 1 and one IPGF in group 2. The preoperative donor ECD was 2948 ± 382 for group 1 and 2728 ± 269 for group 2. ($P < .001$). The cell loss at 6 months was 33% ± 14% for group 1 and 27% ± 13% for group 2 ($P = .01$), and cell loss at 12 months was 34% ± 13% for group 1 and 27% ± 14% for group 2 ($P = .01$). Six-month cell loss for 8.0-mm grafts (n=127) was 30% ± 16% and for larger grafts (n=98) was 27% ± 12% % ($P = .296$).

Conclusions: Precut tissue for DSAEK does not increase the risk of the acute complications of graft dislocation or IPGF. Early endothelial cell loss may be less with precut tissue. Larger graft sizes did not result in significantly higher cell counts at 6 months.

Trans Am Ophthalmol Soc 2009;107:184-193

INTRODUCTION

Endothelial keratoplasty (EK) has now become the standard of care for the treatment of visual loss due to corneas with the primary etiology of endothelial dysfunction. While the first successful human case of EK was reported by Charles Tillet in 1956,[1] the modern technique of sutureless endothelial replacement was developed by Dr Gerrit Melles of the Netherlands in 1999.[2,3] After a year of laboratory work to modify and simplify the posterior lamellar keratoplasty procedure, I performed the first EK procedure in the United States in March 2000 and renamed it deep lamellar EK (DLEK).[4-6] Over the past 9 years, we have continued data collection in a prospective manner as this exciting new surgical procedure has evolved in our practice from DLEK,[7-9] to Descemet stripping automated EK (DSAEK),[10-15] and now, in laboratory work, to Descemet membrane EK (DMEK) (Terry MA, Stoeger C, Holiman JD, Saad HAH, Davis-Boozer, D. Descemet's membrane endothelial keratoplasty (DMEK): tissue wastage and endothelial damage when stripping donor tissue. Paper presented at: annual meeting of the American Society of Cataract and Refractive Surgery; April 3, 2009; San Francisco, California).

One of the advances in EK that has enabled more surgeons to embrace this procedure is the introduction of donor corneal tissue that has been "precut" with an automated microkeratome by an eye bank technician prior to being shipped to the surgeon for transplantation. The use of precut tissue has eliminated the need for the occasional transplant surgeon to invest in expensive technology for relatively few DSAEK cases per year and has reduced the operative time required for DSAEK performed by novice and experienced surgeons alike. Although some surgeons have expressed concern that precut tissue would not perform as well as tissue that is cut at the time of DSAEK surgery by the surgeon,[16] our clinical experience with precut tissue at the Devers Eye Institute in Portland, Oregon, has been quite gratifying.[17-19]

We previously reported the early complications, as well as the 6- and 12-month clinical results, of our first 100 consecutive cases of DSAEK surgery using precut tissue.[17,18] These cases also included eyes that did not have Fuchs dystrophy as the underlying etiology of their endothelial demise, and the procedures were performed by multiple surgeons. We have also published the early complication rate and clinical results of our first 315 consecutive cases of DSAEK in eyes with Fuchs endothelial dystrophy.[15] However, in all of these cases, the surgery was performed by more than one surgeon, with multiple "novice" surgeons performing the DSAEK procedure, and these cases were a mixture of surgeon-cut and precut donor tissue.

This report presents a retrospective analysis of our prospectively collected database and selected DSAEK cases for analysis that were performed by one surgeon (M.A.T.). These represent my first DSAEK cases and are consecutive cases in which DSAEK surgery was performed strictly for the preoperative diagnosis of Fuchs endothelial dystrophy. Eyes that had endothelial dysfunction from other causes (eg, pseudophakic bullous keratopathy from surgical trauma), and did not have Fuchs as an underlying condition, were excluded. Eyes with other anterior segment abnormalities, such as filtering tubes and blebs, or with an anterior chamber intraocular lens (IOL) in place were also excluded in order to minimize the presence of confounding variables.

I evaluated this unique uniform subset of DSAEK cases and asked the question, Does tissue that is precut by a technician increase the complication rate of DSAEK surgery, and does this donor manipulation by a technician affect the donor endothelial survival over the first 12 months? By limiting the cases examined to a single surgeon and by minimizing the confounding variables, I hoped to determine the value (or liability) of this latest modification in the EK field.

From the Devers Eye Institute, Portland, Oregon.
*Presenter.
Bold type indicates AOS member.

MATERIALS AND METHODS

PROTOCOL

An institutional review board–approved and Health Information Portability and Accountability Act–compliant clinical protocol and surgical consent form for EK were developed in March 2000, and enrollment for our entire EK study was initiated for patients with endothelial dysfunction due to Fuchs endothelial dystrophy, pseudophakic bullous keratopathy, or endothelial failure following penetrating keratoplasty and without significant stromal haze. Our first DSAEK procedure was performed in September 2005, and the technique remains largely the same to the current time. Over the years, that technique has been utilized for the ongoing study by one experienced surgeon (M.A.T.) and 5 novice surgeons.

The data reported in this report emanate from a retrospective review of our database in which I selected the first consecutive Fuchs dystrophy eyes that underwent DSAEK surgery by a single surgeon (M.A.T.) at our center from September 2005 to November 2008. Fuchs dystrophy eyes with a posterior chamber IOL in place from prior cataract surgery or with the native crystalline lens in place (with or without cataract formation) qualified for this analysis. Eyes that had confounding variables, such as an altered anterior segment from prior glaucoma procedures (tubes and blebs) or presence of an anterior chamber IOL, were excluded. There were 225 eyes that met these criteria.

The two groups to be compared were those eyes that received a donor cornea that was prepared for DSAEK surgery by the surgeon at the time of surgery (group 1, n = 49) and those eyes that received a donor cornea that was prepared with precutting by an eye bank technician (group 2, n = 176). The surgeon-cut tissues were used for my very first 49 cases of DSAEK in Fuchs dystrophy eyes, and the 176 precut corneas were used for subsequent cases that I performed for a similar cohort of Fuchs dystrophy patients.

The specific outcomes to be analyzed included the immediate postoperative complications of donor tissue dislocation requiring intervention, primary graft failure (called "iatrogenic" by our group, or IPGF), and the survival of the donor endothelium from preoperatively to 6, 12, and 24 months postoperatively, as measured by central endothelial cell density (ECD) determined by noncontact specular microscopy.

No specific requests were made of the eye banks to provide tissue for EK with any donor characteristics different from what we normally request for our full-thickness penetrating keratoplasty tissue. We typically accept donor tissue with an ECD greater than 2,000 cells/mm^2, any age between 4 and 75 years old, and death to transplantation time of up to 12 days. For consistency in calculating ECD changes preoperatively to postoperatively, only the donor specular ECD that was done *prior* to microkeratome cutting was used as the specified "preoperative ECD," and cell counts done on precut tissue *after* the microkeratome cut were not used for calculations of postoperative cell loss.

TISSUE PREPARATION

Surgeon preparation of tissue was performed in the operating room just prior to beginning the DSAEK procedure, and the operating microscope was used extensively for the donor tissue preparation. A Moria microkeratome and artificial anterior chamber system (Moria Inc, Doylestown, Pennsylvania) were used for tissue preparation. The tissue was mounted onto the artificial anterior chamber after thoroughly coating the endothelium with the cohesive viscoelastic Healon (Advanced Medical Optics, Santa Ana, California). The specific cutting procedure is detailed more thoroughly in previous publications.[12,13] The Healon was removed from the endothelium with gentle irrigation of Optisol GS after carefully dismounting the tissue from the artificial anterior chamber device. Following trephination of the tissue, a thin strip of Healon was reapplied to the endothelium prior to folding the tissue on the Teflon trephination block (Barron punch trephine system, Katena Products Inc, Denville, New Jersey) into a 60%/40% taco shape. The remainder of the DSAEK procedure was identical to our previous detailed report[13] and to the DSAEK technique for cases using precut tissue.[17,18]

Precut tissue was obtained primarily from the Lions Eye Bank of Oregon (n= 161), but for some of the initial cases, precut tissue was obtained from the North Carolina Eye Bank (n= 15). Tissue was prepared at these sites utilizing a Moria microkeratome and artificial anterior chamber system (Moria Inc). Of note, the eye bank technicians did not use a microscope for donor tissue preparation, and they also used an "inversion" technique in which the artificial anterior chamber is turned upside down with irrigation from the attached line of balanced salt solution. This technique is more practical for technicians working under an aseptic hood and eliminates the need for Healon coating of the endothelium to protect against trauma from the dismount of the tissue. After successful precutting, the resected corneal cap was placed back onto the stromal bed, the corneal-scleral donor tissue was placed back into Optisol GS in the viewing chamber, and then the tissue underwent postcutting slit-lamp and specular microscopy evaluation.

Preoperative specular microscopy was performed at the eye banks utilizing their standard operating procedure, and this has been more extensively described in previous reports.[12,14,15,18] Of note, precutting of the tissue and placement back into the viewing chamber filled with Optisol allowed evaluation by the eye bank personnel of the tissue after microkeratome manipulation, and tissue was not shipped to the surgeon if slit-lamp examination showed that it may be damaged or had a postcut ECD that fell below 2,000 cells/mm^2. Precut tissue that passed examination and specular microscopy standards was then transported to our surgical site in the viewing chamber filled with Optisol GS using standard shipping protocol.

SURGICAL PROCEDURE

DSAEK was performed in our standard technique as previously described.[13] A video of this DSAEK technique using precut donor tissue is available at http://aaojournal.org.[17]

Briefly, a 5.0-mm scleral tunnel approach was used for entry into the anterior chamber. The Descemet membrane was stripped to a previously determined size of 8.0 to 9.0 mm using Healon (Advanced Medical Optics) for maintenance of the anterior chamber, followed by scraping of the peripheral recipient bed with a Terry scraper (Bausch & Lomb, St Louis, Missouri) to promote donor adhesion.[11] The Healon was completely removed with automated irrigation and aspiration.

Attention was then directed to the donor table, and the operating microscope was used for all donor tissue manipulations. The surgeon microkeratome tissue was prepared as described above. All surgeon-prepared tissue was trephinated and then folded into the 60%/40% taco shape on the trephine block. The block was brought into the operative field over the patient's eye, and the tissue was grasped with Charlie insertion forceps (Bausch & Lomb) and then inserted into the anterior chamber and unfolded in a controlled fashion using our standard technique.[13]

When precut tissue was used, the operating microscope was also moved over to the separate donor table and used for all donor examination, marking, and trephination. The donor tissue with its wide scleral rim was placed endothelial side down onto a lint-free surface with the convex shape of the tissue elevating and protecting the endothelium from the donor table surface. The corneal surface of the precut tissue was examined and the bed of resection measured to ensure adequate size. The bed was greater than 8.5 mm in all cases, allowing safe trephination of a minimum donor size of 8.0 mm. The peripheral gutter of the microkeratome cut was gently dried and then marked with a gentian violet marker. A centering mark was also placed on the epithelial cap. These marks were placed in all cases except for the first case. A donor trephine size was chosen in every case to fit within the prior precut resection area, and no tissue required additional peripheral dissection. The tissue was then placed endothelium side up onto a Teflon block, and a donor punch of the same size as the Descemet stripping was used for trephination. The donor rim was examined for retention of the peripheral gutter markings to ensure that the punch was centered within the microkeratome resection bed. Centration of trephination within the resection bed was confirmed in all cases of this report. A thin strip of Healon was then placed along the central endothelial surface, and the tissue was folded into a 60/40 overfolded "taco" configuration. Of note, in January 2007, we changed our folding technique in order to further minimize endothelial trauma.[20] After January 1, 2007, we folded the tissue on the trephination block into a 40%/60% underfold technique to avoid overhang of the tissue edge and possible exposure of the donor endothelium to the plastic block surface. This technique change was performed in all but 14 of the precut donors and none of the surgeon-cut donors.

After donor manipulation at the donor table in either precut or surgeon-cut tissues, the remainder of the operation was identical. The donor tissue was grasped utilizing single-point fixation Charlie forceps (Bausch & Lomb), inserted into the anterior chamber with the 60% side of the tissue anterior, and the graft was unfolded in the anterior chamber with a combination of balanced saline solution (BSS, Alcon Laboratories, Fort Worth, Texas) and air. Once the graft was open and centered, residual interface fluid was removed using the Cindy Sweeper (Bausch & Lomb) for surface compression and stroking, moving from the center of the graft to the periphery while the anterior chamber is completely filled with air. No corneal stab "venting" incisions were utilized to evacuate any suspected interface fluid in any cases. The tissue was then left completely undisturbed for 10 minutes to promote attachment of the graft. Dilating drops of cyclopentolate 1% and phenylephrine 2.5% were placed during this time. Once this time had passed, the air was nearly totally exchanged for BSS and then a freely mobile, residual air bubble of 5 to 9 mm was reinjected to support the graft postoperatively.

STATISTICAL ANALYSIS

For normally distributed data, groups were compared using the Student *t* test and chi-square analysis. SPSS Version 12.0 (SPSS Inc, Chicago, Illinois) was used for all statistical testing.

COMPLICATIONS

The complication of IPGF was defined as any graft that had to be replaced with a new graft within 1 year of surgery.The complication of graft dislocation was defined as any transplant that required another reinjection of an air bubble to ensure adhesion. Grafts that had interface fluid of any amount at any time after surgery but were still in position on the recipient bed were observed. If the surgeon opted to place a second air bubble for support, that case was designated as a "dislocation" and recorded as a complication. Grafts floating freely in the anterior chamber were obviously designated as a dislocation.

RESULTS

From September 2005 to November 2008, 225 cases of DSAEK surgery for the indication of Fuchs endothelial dystrophy were performed by a single surgeon. In 49 cases the tissue was surgeon-cut with the microkeratome at the time of DSAEK surgery, and in 176 cases the donor tissue was precut by a trained eye bank technician at a time ranging from less than an hour to up to 5 days before the DSAEK surgery (mean time from precutting to surgery, 28.86 hours ± 18.86 hours; range, 0.17 hours to 120 hours). Demographics of the patients in this series are presented in Table 1. Because our cornea service is a national tertiary referral center for DSAEK and other surgery, nearly one third of the patients in this study live outside the state of Oregon, reducing our ability to obtain postoperative specular microscopy results on a sizable number of this study group, but this did not affect our ability to document for the entire group the incidence of donor tissue dislocation or IPGF.

Preoperatively, every patient had a diagnosis of Fuchs endothelial dystrophy with clinically evident stromal edema with subjective complaints of reduced visual function. Cataract surgery was concurrently performed if the patient had visually significant cataract or mild cataract with expectation of progression and minimal remaining accommodative amplitude. In 157 cases (70%) phacoemulsification cataract surgery with IOL implantation was performed at the same time as the DSAEK surgery. For group 1, 75% of the eyes had concurrent cataract surgery, and for group 2, 67% of the eyes had concurrent cataract surgery.

TABLE 1. DEMOGRAPHICS AND COMPLICATIONS OF DSAEK SERIES

DONOR TISSUE	GENDER	AGE	CONCURRENT PHACO	GRAFT SIZE	DISLOCATION	IPGF
Precut (n=176)	F 54% M 46%	68 ± 10	75%	45% 8.0 mm 56% >8.0 mm	2%	<1%
Surgeon-cut (n=49)	F 60% M 40%	66 ± 11	67%	96% 8.0 mm 4% >8.0 mm	0%	0%

DSAEK, Descemet stripping automated endothelial keratoplasty; IPGF, iatrogenic primary graft failure; Phaco, phacoemulsification.

COMPLICATIONS

For the 49 cases using surgeon-cut tissue (group 1), there were no cases of dislocation and no cases of IPGF.

For the 176 cases using precut tissue (group 2), there were 3 dislocations, representing a dislocation rate of 1.7%, which was not statistically different from the 0% dislocation rate in group 1 (*P* = .224). There was one recent case of IPGF in group 2. This was due to surgeon error in unfolding the tissue and a break in established technique, which caused the tissue to unfold upside down. Subsequent intraoperative manipulations to correct the orientation of the tissue were extensively traumatic to the donor endothelium, and therefore the tissue was replaced 3 days after the original surgery. This case was also one of the 3 dislocations recorded for this series.

DONOR ENDOTHELIAL CELL DENSITIES AND CELL LOSS

The preoperative and the 6-, 12-, and 24-month postoperative specular ECD results from DSAEK surgery are displayed in Table 2. Of note, the preoperative ECD was 2948 ± 382 for group 1 and 2728 ± 269 for group 2, representing a highly significant difference in the preoperative donor cell counts between the two groups (P < .001). However, subsequent postoperative ECD measurements were not statistically different between the two groups. The 6-month postoperative ECD was 1849 ± 436 for group 1 (n = 42) and 1995 ± 341 for group 2 (n = 94) (P = .641). The 12-month postoperative ECD was 1875 ± 365 for group 1 (n = 41) and 2036 ± 371 for group 2 (n = 63) (P = .122). Finally, at 24 months postoperatively, the ECD was 2043 ± 438 for group 1 (n = 34) and 2115 ± 486 for group 2 (n = 17) (P = .602).

TABLE 2. ENDOTHELIAL CELL DENSITY AND CELL LOSS BY GROUP

DONOR TISSUE	ENDOTHELIAL CELL MEASUREMENTS, cells/mm^2 (range)			
	PREOP	6 MONTHS	12 MONTHS	24 MONTHS
Precut (n=176)	2728 ± 269 (2042-3553)	1995 ± 341 (1100-2825) 27% cell loss n=94	2036 ± 371 (1020-2924) 27% cell loss n=63	2115 ± 486 (1397-2874) 26% cell loss n=17
Surgeon-cut (n=49)	2948 ± 382 (2341-4209)	1849 ± 436 (1126-2803) 33% cell loss n=42	1875 ± 365 (1116-2680) 34% cell loss n=41	2043 ± 438 (1094-2924) 32% cell loss n=34

Because of the statistically higher preoperative cell counts for the surgeon-cut tissue vs the precut tissue, and despite the similar absolute ECD postoperatively for the two groups, there was a trend toward greater percentage decrease of cell density for the surgeon-cut tissue when compared to the precut tissue cases. The central endothelial cell loss at 6 months was 33% ± 14% for group 1 and 27% ± 13% for group 2 (P = .014), and the endothelial cell loss at 12 months was 34% ± 13% for group 1 and 27% ± 14% for group 2 (P = .01). Because the number of cases to reach the 2-year postoperative visit is relatively small for the precut tissue group, the difference of cell loss between the 32% for the surgeon-cut tissue and the 26% for the precut tissue did not reach statistical significance (P = .241).

ANALYSIS AND RESULTS OF SPECIAL SUBGROUPS

Several other factors, in addition to the use of surgeon-cut vs precut tissue, can influence postoperative endothelial cell counts, and therefore a special subgroup to eliminate these other variables was identified. From the overall group of 225 cases of DSAEK performed by a single surgeon, evaluation was further restricted to only those eyes that had a 60%/40% overfold technique and only those eyes that had an 8.0-mm-diameter donor trephination. Also removed from analysis were any eyes that had any episode of rejection during the follow-up period as well as the 3 cases of dislocation that had further surgical manipulation postoperatively.

The preoperative and the 6-, 12-, and 24-month postoperative specular ECD results from this special subgroup of DSAEK surgery are displayed in Table 3. As can be seen, the elimination of these other variables (especially the underfold cases) reduces the overall number of eyes available for analysis considerably, leaving just 32 eyes of the surgeon-cut group and 9 of the precut tissue group available for the 6-month postoperative ECD analysis, and even fewer for longer-term analysis. Also of interest, the preoperative previously higher cell count of the surgeon-cut tissue (n = 38) was now on par with the precut tissue (n = 14), now demonstrating no significant difference in preoperative ECD between the two groups (*P* = .323). In accordance with this comparable preoperative ECD between the two groups, the percentage drop in ECD at all postoperative time points was now statistically equivalent between the groups as well.

TABLE 3. ENDOTHELIAL CELL DENSITY OF SPECIAL SUBGROUP OF 8.0-MM GRAFTS USING OVERFOLD TECHNIQUE AND ELIMINATING THE REJECTION EYES AND DISLOCATION EYES

DONOR TISSUE	ENDOTHELIAL CELL MEASUREMENTS, cells/mm^2 (range)			
	PREOP	6 MONTHS	12 MONTHS	24 MONTHS
Precut (n=14)	2874 ± 284 (2544-3553)	1785 ± 328 (1269-2146) 38% cell loss n=9	1912 ± 395 (1304-2315) 33% cell loss n=7	1911 ± 378 (1468-2404) 34% cell loss n=7
Surgeon-cut (n=38)	2983 ± 385 (2341-4209)	2005 ± 380 (1239-2803) 38% cell loss n=32	1923 ± 354 (1116-2680) 36% cell loss n=30	2048 ± 475 (1094-2924) 33% cell loss n=26

An analysis of endothelial survival was also done comparing the eyes that received an 8.0-mm-sized donor and those eyes that received a larger-sized donor (ie, 8.5 mm or 9.0 mm). Data from this analysis is summarized in Table 4. In the entire series of 225 Fuchs dystrophy eyes, 127 eyes received an 8.0-mm graft and 98 eyes received a larger DSAEK graft. The average percentage cell loss of the 8.0-mm grafts at 6 months was 30% ± 16%, and the average percentage cell loss of the larger grafts at 6 months was 27% ± 12% (*P* = .296). Comparing just the 8.0-mm grafts between the two groups, there were 47 grafts in group 1 and 80 grafts in group 2. The average percentage cell loss of the group 1 grafts at 6 months was 33% ± 15%, and the average percentage cell loss of the group 2 same-size grafts at 6 months was 27% ± 16%, which represented a significant difference (*P* = .041) in cell loss between the two groups when only 8.0-mm grafts were analyzed.

TABLE 4. ENDOTHELIAL CELL LOSS BY GRAFT SIZE

DONOR TISSUE	ENDOTHELIAL CELL MEASUREMENTS, cells/mm^2 (range)			
	PREOP	6 MONTHS	12 MONTHS	24 MONTHS
8.0-mm Precut (n=80)	2714 ± 290 (2042-3553)	1989 ± 355 (1100-2825) 27% cell loss n=51	1997 ± 353 (1054-2924) 28% cell loss n=34	2086 ± 433 (1468-2660) 27% cell loss n=11
8.0-mm Surgeon-cut (n=47)	2968 ± 394 (2341-4209)	1960 ± 416 (1126-2803) 33% cell loss n=41	1919 ± 359 (1116-2680) 34% cell loss n=40	2043 ± 438 (1094-2924) 32% cell loss n=34
>8.0-mm Precut (n=96)	2744 ± 245 (2201-3465)	2003 ± 328 (1174-2740) 27% cell loss n=43	2081 ± 392 (1020-2801) 25% cell loss n=29	2167 ± 614 (1397-2874) 25% cell loss n=6
>8.0-mm Surgeon-cut (n=2)	3123 ± 86 (3062-3184)	2088 32% cell loss n=1	2353 23% cell loss n=1	NA

NA, not available.

DISCUSSION

As the field of EK evolves, it is important to determine those factors that contribute to postoperative complications as well as donor endothelial survival. The benefits of any change in technique or tissue processing for EK surgery have to be balanced against the measurable risks of those changes.

The ability to precut the donor tissue in the eye bank facility offers significant advantages for the patient and the DSAEK surgeon. Precut tissue can be examined at the slit lamp after the microkeratome procedure, and the central ECD can be quantified by specular microscopy. This offers the surgeon a level of quality control and assurance that healthy tissue is being transplanted. This is in stark contrast to the surgeon-cut tissue, where evaluation of the tissue after cutting is not practical, leaving the surgeon to assume that the cutting process was without detrimental effect to the donor endothelium.

This study evaluated 225 cases of DSAEK surgery performed by a single surgeon (M.A.T.) for the select population of Fuchs endothelial dystrophy patients. There was no difference in complication rate between the 49 cases where I prepared the tissue minutes prior to transplantation of the tissue and those 176 cases where the tissue was prepared by an eye bank technician hours or days prior to the surgery. Clearly, in this report and as we have shown in prior publications,[14,15,17,19] tissue cut by a technician poses no greater risk of complications than tissue cut by this surgeon, and storage of precut donor tissue does not contribute to the events of dislocation or graft failure. The comparable complication rate between the two groups is even more remarkable in that the procedures with the surgeon-prepared tissue were performed as my initial "novice surgeon" DSAEK cases, and one would expect a higher complication rate during the learning curve of this unique surgery. This low complication rate is also a testament to the specific surgical technique we have developed for DSAEK surgery, as it compares quite favorably to the reported initial dislocation rates of 6.5% to 23% reported by other experienced DSAEK surgeons[21,22] and the 3.5% to 17% rate of IPGF reported by experienced DSAEK surgeons.[22,23] This very large retrospective series described here comparing surgeon-cut to technician-cut tissue also compares well to the small pilot prospective study by Price and coworkers,[24] which reported a 10% dislocation rate in both their precut tissue group and their surgeon-cut tissue group of DSAEK surgeries.

The endothelial survival after DSAEK surgery is the most important postoperative outcome parameter for analysis and yet also one of the most elusive to document and compare. It is known that dislocations can cause further donor endothelial cell loss[12,21,25] and also that insertion of tissue through smaller, more compressive entrance wounds can devastate the endothelium.[26] However, whether tissue that has been precut offers any benefits or detriment to endothelial survival has not been previously firmly established. In this report, we demonstrate that tissue can be stored for a day or more after precutting with at least a comparable degree of donor endothelial survival as tissue that is cut minutes before surgery.

For the overall group of 225 cases, the endothelial cell loss after DSAEK surgery with precut tissue was actually statistically less than that after using tissue that was cut by the surgeon. There can be several explanations for that finding.

The most likely possible cause for the difference in endothelial cell loss found between the groups was the change in our technique for donor folding between surgeon-cut and precut tissue groups. The surgeon-cut tissue used almost exclusively a 60%/40% overfold technique, whereas in the cases using precut tissue, we used predominantly an underfold technique. This change in technique of folding the tissue into a 40%/60% underfold on the trephine block prior to grasping with insertion forceps eliminated the possibility of donor peripheral edge endothelial touch to the trephine block, and this may have allowed less peripheral cell loss prior to tissue insertion. The endothelial-sparing advantage of this single technique change has been documented previously.[20] Indeed, when those cases of precut tissue that had this advantage of "underfolding" are eliminated, the significance of the disparity in ECD loss between the two groups disappears.

Another difference between the two groups was the number of donors that were greater than 8.0 mm in diameter. In our initial DSAEK series, which was predominantly surgeon-cut tissue, we routinely used a donor trephination size of 8.0 mm. Only later in our series did we begin to trephinate our tissue to the larger diameter size of 8.5 mm or 9.0 mm. In the surgeon-cut tissue series, there were 2 donors (4%) that were greater than 8.0 mm in diameter, and in the precut tissue group, there were 96 donors (56%) that were greater than 8.0 mm in diameter. It has been suggested that a larger-diameter donor button carries a greater total number of donor endothelial cells and therefore a greater likelihood of higher central ECD postoperatively.[27] This concept has not been proven by controlled clinical trial, and as Table 4 demonstrates, there was no significant difference in the cell loss between precut tissue that was 8.0 mm in diameter and tissue that was 8.5 mm or 9.0 mm in diameter at any time point, suggesting that donor diameter may not matter in regard to ECD up to at least 1 year after surgery. In addition, when we limited our analysis to only those eyes that were 8.0 mm in size in each group, the significance of the disparity in ECD loss between the two groups remained, again indicating that a factor other than tissue size influenced the differences in cell loss between our precut and our surgeon-cut groups.

The technique of cutting the tissue was different between the surgeon-cut and the precut groups. The difference in postoperative cell loss between the groups may have represented a greater damage to the donor tissue using the specific technique of surgeon tissue preparation. Another possibility for greater cell damage in the surgeon-cut group was the fact that the initial DSAEK cases performed by the surgeon were the cases where the tissue was prepared by the surgeon. It is possible that I was still experiencing a "learning curve" of DSAEK surgery and so performed the entire DSAEK surgery more traumatically in my earlier cases than in my later cases, and it is this learning curve that accounts for the difference in cell loss between the two groups.

Finally, the difference in postoperative cell loss between the two groups may represent a selection bias in favor of the precut tissue. Because the precut tissue undergoes examination and specular microscopy following the microkeratome cutting and dismounting manipulations, any tissue that has undergone significant endothelial damage from microkeratome precutting is eliminated from

distribution and from subsequent transplantation for this study. On the other hand, surgeon-cut tissue does not undergo slit-lamp examination, and even significant central or peripheral endothelial damage from cutting or dismount would be missed and the partially damaged tissue transplanted. If this scenario is correct, then it is a strong argument for the use of validated precut tissue rather than traumatically suspect surgeon-cut tissue. This argument for precut tissue for DSAEK is accentuated as we move into the possibility of DMEK surgery. Although there is now some evidence that DMEK surgery may offer even faster rates of visual rehabilitation and even higher rates of 20/25 or better visual acuity following DMEK than DSAEK,[28] the issue of donor tissue quality and validation becomes paramount. It is not possible to evaluate the fragile donor tissue of DMEK prior to transplantation. Neither slit-lamp examination nor specular microscopy is possible once the donor Descemet membrane has been stripped, as it rolls up like a rug, with the endothelium facing outward, and is implanted in this form. With a current published graft replacement rate of 20% with DMEK,[28] it is not possible to know if the surgeon is implanting tissue that is already severely damaged from the stripping preparation or if the tissue is damaged beyond survival by the surgical transplantation itself. Until precut donor tissue for DMEK can be evaluated by the distributing eye bank similar to what is currently done with DSAEK, it is unlikely that this latest iteration of EK surgery can become as safe and as widespread as DSAEK.

Any discussion of the relative merits and/or disadvantages of using precut tissue for DSAEK surgery should also include the financial considerations of surgeon-cut vs precut tissue. The current additional processing charge for precutting tissue by an eye bank is, on average, about $800 per donor tissue. A new CPT code (65757) has recently been created for performing “back-bench” cutting of tissue in the operating room by the surgeon. The reimbursement for this surgeon work is currently not uniform across states nor across insurance carriers but appears to be substantially lower than the $800 charged by eye banks. As a practical matter, the financial circumstances surrounding the microkeratome cutting of donor EK tissue would appear to favor this step of tissue processing to be carried out in the operating room by the surgeon.

The results of this analysis of DSAEK surgery in Fuchs endothelial dystrophy by a single surgeon demonstrate that the use of technician precut tissue has a low complication rate similar to that with surgeon-cut tissue and has at least as high a percentage of endothelial survival in the first 2 years following surgery. With the ability to examine and validate the tissue following microkeratome cutting, as well as the savings in operating room time, the use of precut tissue may offer significant clinical advantages for the surgeon performing DSAEK surgery. However, practice patterns in this regard may be substantially influenced by the current reimbursement system for this microkeratome step of tissue processing.

ACKNOWLEDGMENTS

Funding/Support: Supported by the Lions Eye Bank of Oregon through the Lions Eye Bank of Oregon Vision Research Laboratory, Portland.

Financial Disclosures: Dr Terry has a financial royalty interest in the Bausch & Lomb specialized instruments that he designed and that were used in this surgery. Bausch & Lomb Surgical, St Louis, Missouri, manufactured and supplied the specially designed instruments free of charge for this project.

Conformity With Author Information: The study was reviewed and approved by the Institutional Review Boards of Legacy Health System and of Providence Health System, Portland, Oregon.

Other Acknowledgments: Daniel J. Friend, MS, of the Lions Eye Bank of Oregon Vision Research Laboratory, performed all of the relevant data retrieval from our project database and performed the data statistical analysis in this study. I thank him for his very hard work.

REFERENCES

1. Tillett CW. Posterior lamellar keratoplasty. *Am J Ophthalmol* 1956;41:530-533.
2. Melles GR, Eggink FA, Lander F, et al. A surgical technique for posterior lamellar keratoplasty. *Cornea* 1998;17:618-626.
3. Melles GR, Lander F, Beekhuis WH, et al. Posterior lamellar keratoplasty for a case of pseudophakic bullous keratopathy. *Am J Ophthalmol* 1999;127:340-341.
4. Terry MA, Ousley PJ. Endothelial replacement without surface corneal incisions or sutures: topography of the deep lamellar endothelial keratoplasty procedure. *Cornea* 2001;20:14-18.
5. Terry MA, Ousley PJ. Deep lamellar endothelial keratoplasty in the first United States patients: early clinical results. *Cornea* 2001;20:239-243.
6. Terry MA, Ousley PJ. Replacing the endothelium without surface corneal incisions or sutures: first US clinical series with the deep lamellar endothelial keratoplasty procedure *Ophthalmology* 2003;110:755-764.
7. Terry MA. Deep lamellar endothelial keratoplasty (DLEK): pursuing the ideal goals of endothelial replacement. *Eye* 2003;17:982-988.
8. Terry MA, Ousley PJ. Deep lamellar endothelial keratoplasty (DLEK): visual acuity, astigmatism, and endothelial survival in a large prospective series. *Ophthalmology* 2005;112:1541-1549.
9. Terry MA. Endothelial keratoplasty: clinical outcomes in the two years following deep lamellar endothelial keratoplasty (an American Ophthalmological Society thesis). *Trans Am Ophthalmol Soc* 2007;105:530-563.
10. Terry MA. Endothelial keratoplasty (EK): history, current state, and future directions [editorial]. *Cornea* 2006;25:873-878.
11. Terry MA, Hoar KL, Wall J, Ousley PJ. The histology of dislocations in endothelial keratoplasty (DSEK and DLEK): prevention of dislocation with a laboratory-based surgical solution in 100 consecutive DSEK cases. *Cornea* 2006;25:926-932.

12. Terry MA, Chen ES, Shamie N, Hoar KL, Friend DF. Endothelial cell loss after Descemet's stripping endothelial keratoplasty in a large prospective series. *Ophthalmology* 2008;115:488-496.
13. Terry MA, Shamie N, Chen ES, Hoar KL, Friend DF. Endothelial keratoplasty: a simplified technique to minimize graft dislocation, iatrogenic graft failure and pupillary block. *Ophthalmology* 2008;115:1179-1186.
14. Terry MA, Shamie N, Chen ES, Hoar KL, Phillips PM, Friend DJ. Endothelial keratoplasty: the influence of pre-operative donor endothelial densities on dislocations, primary graft failure, and one year cell counts. *Cornea* 2008;27:1131-1137.
15. Terry MA, Shamie N, Chen ES, et al. Endothelial keratoplasty for Fuchs' dystrophy with cataract: complications and clinical results with the new triple procedure. *Ophthalmology* 2009;116:631-639.
16. Terry MA. Pre-cut tissue for Descemet stripping automated endothelial keratoplasty: complications are from technique, not tissue [editorial]. *Cornea* 2008;6:627-629.
17. Chen ES, Terry MA, Shamie N, Hoar KL, Friend DJ. Pre-cut tissue in Descemet's stripping automated endothelial keratoplasty: donor characteristics and early post-operative complications. *Ophthalmology* 2008;115:497-502.
18. Terry MA, Shamie N, Chen ES, Phillips PM, Hoar KL, Friend DJ. Pre-cut tissue for Descemet's stripping endothelial keratoplasty: vision, astigmatism, and endothelial survival. *Ophthalmology* 2009;116:248-256.
19. Chen ES, Terry MA, Shamie N, Hoar KL, Phillips PM, Friend DJ. Endothelial keratoplasty: vision, endothelial survival, and complications in a comparative case series of fellows vs attending surgeons. *Am J Ophthalmol* 2009;148:26-
20. Chen ES, Terry MA, Shamie N, Phillips PM, Friend DJ, McLeod SD. Descemet-stripping automated endothelial keratoplasty: insertion using a novel 40/60 underfold technique for preservation of donor endothelium. *Cornea* 2008;27:941-943.
21. Price MO, Price FW Jr. Endothelial cell loss after Descemet stripping with endothelial keratoplasty influencing factors and 2-year trend. *Ophthalmology* 2008;115:857-865.
22. Suh LH, Yoo SH, Deobhakta A, et al. Complications of Descemet stripping with automated endothelial keratoplasty: survey of 118 eyes at one institute. *Ophthalmology* 2008;115:1517-1524.
23. Price FW Jr, Price MO. Descemet's stripping with endothelial keratoplasty in 200 eyes: early challenges and techniques to enhance donor adherence. *J Cataract Refract Surg* 2006;32:411-418.
24. Price MO, Baig KM, Brubaker JW, Price FW Jr. Randomized, prospective comparison of pre-cut vs surgeon-dissected grafts for Descemet stripping automated endothelial keratoplasty. *Am J Ophthalmol* 2008;146:36-41.
25. O'Brien PD, Lake DB, Saw VP, Rostron CK, Dart JK, Allan BD. Endothelial keratoplasty: case selection in the learning curve. *Cornea* 2008;27:1114-1118.
26. Terry MA, Saad HA, Shamie N, et al. Endothelial keratoplasty: the influence of insertion techniques and incision size on donor endothelial survival. *Cornea* 2009;28:24-31.
27. Price FW, Price MO. Does endothelial cell survival differ between DSEK and standard PK? [editorial] *Ophthalmology* 2009;116:367-368.
28. Ham L, Dapena I, van Luijk C, van der Wees J, Melles GR. Descemet membrane endothelial keratoplasty (DMEK) for Fuchs endothelial dystrophy: review of the first 50 consecutive cases. *Eye* 2009 Jan 30 [Epub ahead of print].

PEER DISCUSSION

DR. STEPHEN D. MCLEOD: Dr. Terry has contributed greatly to the evolving techniques of lamellar endothelial surgery through fastidious examination and rigorous examination of his surgical methods and outcomes. The use of precut tissue for Descemet stripping automated endothelial keratoplasty (DSAEK) reduces in-room operating time and the risk of gross damage to the tissue during graft preparation that could preclude completion of the case.

In this study, Dr. Terry attempts to address the question of whether these advantages are offset by a higher rate of early graft dislocation or later endothelial cell loss measured at 6, 12 and 24 months. Of note, Dr. Terry asks in his introduction if these risks are affected by surgeon donor preparation as opposed to technician preparation, or by the time interval between cutting and transplantation, but his study design does not allow us to examine those questions specifically.

The relative merits of precut versus surgeon prepared graft tissue have been addressed previously by Price and colleagues[1] who demonstrated in a prospective, randomized trial of 40 procedures performed by a single surgeon similar detachment rates, visual and refractive outcomes and endothelial cell loss at 6 months and 1 year. However, a distinguishing feature of Dr. Terry's retrospective study of 225 procedures is that he restricts the indication for surgery to Fuchs endothelial dystrophy, thus standardizing as best possible the ocular environment.

Dr. Terry's results confirm the finding that endothelial cell loss is similar between the two tissue preparation techniques. However, we must acknowledge that the study is not large enough to detect a difference in dislocation rates. Dr. Terry's previously published data suggests that his own dislocation rate for precut tissue is in the order of 1%[2]. If this is assumed to be as much as double the rate seen with surgeon prepared tissue, assuming a standard alpha error level of 5% and a beta error of 50%, a sample size of over 1600 in each group would be required to likely identify a difference.

This issue aside, Dr. Terry has again provided us with useful information that convincingly supports the case that time-sparing precut tissue does not adversely affect long term endothelial cell survival after DSAEK.

ACKNOWLEDGMENTS

Funding/Support: None

Financial Disclosures: None

REFERENCES

1. Price MO, Baig KM, Brubaker JW, Price FW. Randomized, prospective comparison of precut vs surgeon-dissected grafts for Descemet Stripping Automated Endothelial Keratoplasty. *Am J Ophthalmol* 2008;146:36-41.
2. Chen ES, Terry MA, Shamie N, Hoar KL, Friend DJ. Precut tissue in Descemet's stripping automated endothelial keratoplasty. Donor characteristics and early postoperative complications. *Ophthalmology* 2008;115:497-502.

RICHARD K. FORSTER: I have no conflict of interest, but I do have some major concerns. I do not do DSAEK, because I feel that by the time it is perfected I probably will not be operating any more. So, I have decided to become an observer in regard to this procedure. My questions are twofold; first, I would like to know what your indications for surgery are with respect to corneal thickness over the day's time and visual acuity. The reason I ask the question is because I have observed surgeons in South Florida who, for example, might previously have done ten corneal transplants a year who are now doing fifty or sixty DSAEKs a year. I do not know where these patients are coming from, and whether they just have cornea guttata or whether they have true visually impairing Fuchs dystrophy. The second question relates to the reliability of the endothelial cell counts. I frequently look at the counts from our eye bank done with endothelial microscopy and I do not believe the cell density. What is the reliability of the cell counts preoperatively in your donor tissue and what is the statistical reliability of your cell counts postoperatively?

DR. EDUARDO C. ALFONSO: I have no conflict of interest. Was there a difference in the dislocation rate when you studied the time from cutting by the technician to time of surgery? Secondly, was there a difference whether you left the cap or did not leave the cap on the donor tissue? This issue becomes an important eye banking concern in terms of being able to use the cap for other surgical procedures. Lastly has the Eye Bank Association of America developed any requirements for technician certification?

DR. VERINDER S. NIRANKARI: No conflicts. Mark, this is just a wonderful paper with your series. I have a couple of questions. You read that dislocation still happens and is a primary concern among many DSAEK surgeons. I am sure you have read the article from the Wilmer Eye Institute talking about using BSS+ and Optisol and then using that tissue. Have you had any experience with that solution? Secondly there is always a question of endothelial cell loss especially during the folding technique. Are you planning to switch either to another technique or perhaps use one of more recently described procedures with some of the cartridges that fold and unfold corneal tissue? Do you think that might be a key in reducing endothelial cell loss?

DR. MARK A. TERRY: Well, first of all thank you very much for all those excellent questions. Dr. McLeod brought up the Price study that was a randomized study of pre-cut versus surgeon cut tissue. They found no difference between the two groups, but they had a 10% rate of dislocation in each group, which was much higher than what Dr. Price has reported in his larger studies. There were problems with that paper in that there were only 20 eyes in each group. It was not a very large series, so I have some problems with that particular study.

The primary question raised by Dr. McCleod about my study related to the sample size in each group of only a few hundred eyes and the dislocation rate comparison of these groups. Obviously when you have a dislocation rate of only 1% it is very hard to do a comparison study with ample statistical power, unless you have 1600 eyes. I would like at the outset of my remarks to apologize for having such a low dislocation rate. The questions by Dr. Forster are excellent. I have great concern about this procedure being promoted throughout the United States by surgeons who have very little experience as corneal surgeons. They may have not completed a fellowship and may not understand the fragile nature of these endothelial cells. Your perspective about whether the indications for surgery have been lowered is quite good. I should say the indications for surgery have changed and the paradigm has changed for endothelial keratoplasty compared to penetrating keratoplasty. I used to wait until the patient was almost 20/200 before I recommended corneal transplantation or if their thickness was at 700microns. The problem with that approach is that we were trying to use a terrible procedure of penetrating keratoplasty to cure a preoperative terrible situation. Now we have a wonderful procedure that allows us to give patients great vision within just a couple of weeks. We have lowered the bar in terms of what we will accept for preoperative disability. I do not believe that everyone with guttata must have an endothelial keratoplasty. I believe that patients who are having morning blurring and may have 20/20 at 3:00 in the afternoon, but whose vision is 20/200 for five hours in the morning are the patients should have endothelial keratoplasty. I do not have a thickness measurement that I go by, because it is so variable. As you know, patients with Fuchs dystrophy can have pachymetric readings of 580 microns and central bullae. The reliability of the cell counts was another excellent point raised by Dr. Forster. Specular microscopy is almost worthless for the individual patient, because there is such technique variation from one moment to the next moment. For one patient you cannot really say the endothelium has changed unless you follow that one patient for months or years; however, it is very valuable for determining change in a large series of patients. The variation in individual measurements is filtered out when you have large groups of eyes. With hundreds of eyes we can then show the trends in cell loss that occur with DSAEK. Finally, I completely agree with Dr Forster that you cannot trust a specular microscopy without comparing those numbers with a good slit lamp analysis.

Finally, Dr. Alfonso asked if the dislocation rate is related to the storage. We published a paper based on the findings in a large number of patients that demonstrated no relationship between dislocation rate and tissue stored for one or five days. Even eleven days of storage was not associated with an increase in the rate dislocation in the individual cases that I have done overseas. All of these low complications may be related to our specific technique rather than any donor characteristic. The cap was left on for the entire storage

time. With our technique of pre-cut tissue the cap has been left on and in place. Several investigators have shown that the tissue will swell if you do not put the cap back on before you ship it to the surgeon. There is no certification currently for eye bank technicians to pre-cut tissue. This is a failing of the Eye Bank Association of America that must be remedied. Finally, the complication of dislocations was described in a paper by my friend Walter Stark and his group. They reported a horrible dislocation rate with their first 80 DSAEK procedures and a lower rate and in their last 25 eyes when the tissue was washed with BSS. I believe that their experience improved throughout their consecutive series and that this is what enabled them to lower their dislocation rate, rather than the decision to wash or not wash the tissue. Finally regarding the question of using an injector versus folding the tissue, our current technique with forceps insertion that you saw on the video was used in our first 900 cases. We now are performing a prospective, randomized controlled masked study on injectors versus forceps insertion of the tissue. I will let you know next year what our results are.