Review of Posterior Lamellar Keratoplasty Techniques

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Abstract

Many corneal surgeons have adopted posterior lamellar keratoplasty (PLK) as a substitute for penetrating keratoplasty in eyes with endothelial dysfunction. Different surgical techniques introduced by the pioneers of keratoplasty have led to advances in PLK over the last decade. Although many patients have experienced restoration of near-normal vision and histological structure of the cornea with modern PLK techniques, there remains a long way to go toward a perfect standard of care for the treatment of endothelial decompensation. Here, we review PLK techniques and provide a comprehensive overview of the trends and advances in these procedures.

Keywords: Keratoplasty; Posterior lamellar keratoplasty

Introduction

Before the advent of endothelial keratoplasty in corneal surgery, penetrating keratoplasty (PK) had been the standard of care for endothelial decompensation for many years. Since 2005, there has been a rapid shift from PK to endothelial keratoplasty [1] The advantages of endothelial keratoplasty that have prompted this shift include: 1) minimal changes in the corneal surface, induced astigmatism, and rapid visual recovery [2-6]; 2) smooth and uneventful postoperative course in patients with ocular surface disorders; 3) preservation of the corneal sensation and an intact corneal nerve plexus; 4) prevention of potential complications of open sky surgery; 5) use of larger donor disks containing more endothelial cells compared with donor buttons in PK; and 6) tectonically stronger cornea.

During PK, the endothelium remains untouched, lying gently over a protective smooth viscoelastic layer, throughout the procedure until the surgeon sutures the tissues of the corneal surface and stroma. In various forms of endothelial keratoplasty surgery, the donor tissue is prepared, inserted, and attached to the recipient’s tissue. Logically, this could induce more endothelial cell loss than with PK in experienced hands [7-9]. Endothelial cell loss is one of the most important concerns in endothelial keratoplasty [10-20]. Endothelial keratoplasty has undergone a metamorphosis with recent modifications and continues to reduce the endothelial cell loss compared with PK [21]. However, extreme gentleness must be a cornerstone of endothelial keratoplasty procedures when the bare endothelial layer is exposed.

Historical Overview

In 1954, Tillett [22] described the first posterior lamellar keratoplasty, but the results were not good enough to persuade other corneal surgeons to adopt this surgical intervention. In 1984, Barraquer [23] reported on a technique for posterior lamellar grafting. Ko et al. [24] reported the sutured opposition of a posterior lamellar graft in rabbits. Several corneal surgeons investigated the replacement of the posterior lamellar disk with donor tissue after creating a corneal flap, as in Lasik surgery, and then securing the disk and flap with sutures [25-29].

In 1998, Melles et al. [30] made a leap forward in the evolution of modern endothelial keratoplasty by performing a posterior lamellar keratoplasty (PLK) in human cadaver eyes and in cat and monkey models. They made a stromal pocket at about one-half of the corneal thickness and excised a 6-mm diameter posterior corneal stromal disk from the central posterior lamella using a flat trephine and scissors. They created a 6-mm donor disk by punching the donor tissue after making a similar stromal pocket and introduced the donor disk into the lamellar pocket in the recipient cornea. They used air tamponade for donor/recipient adhesion. The photograph in their report showing a clear monkey cornea 1 month after receiving human donor tissue was an indication of the revolution taking place in corneal surgery, providing much better visual results.

In 1999, Melles et al. [31] performed the first human PLK with air tamponade. Terry and Ousley used new instruments and an artificial chamber for performing PLK and named the procedure deep lamellar endothelial keratoplasty (DLEK); they reported the results of their case series and introduced small-incision DLEK in 2004 [32-35]. In 2002, Melles et al. [36,37] described a modification of their previous technique: the donor disk was folded in half and the incision for introducing the donor disk into the anterior chamber was reduced to 5 mm in width. In 2004, Melles et al. [38] introduced the descemetorhexis technique, in which they removed Descemet’s membrane (DM) and the endothelium from the posterior surface of the recipient cornea in a circular fashion and used the bare posterior surface of the corneal stroma as the donor recipient interface. They did not perform any dissection through the recipient cornea. Price and Price [39,40] popularized the technique, and the procedure was referred to as Descemet’s stripping with endothelial keratoplasty (DSEK). In 2006, Gorovoy [41] replaced the manual dissection of donor tissues with automated dissection using a microkeratome, referring to this procedure as Descemet’s stripping with automated endothelial keratoplasty (DSAFEK). DLEK was replaced by DSEK and DSAFEK, as they were simpler and gave better results.

In 2003, Seitz et al. [42] used a femtosecond laser for lamellar dissection through the corneal stromal tissues in vitro, paving the way for non-mechanical endothelial keratoplasty. Mehta et al. [43] realized that a double-pass femtosecond application resulted in easier tissue separation and smoother cut surfaces. In 2007, Chen et al. [44] performed the first femtosecond-assisted DSEK in an 82-year-old man with pseudophakic bullous keratopathy.

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After reporting the transplantation of DM carrying viable endothelium in cadaver eyes in 2002, Melles et al. in 2006 reported the first Descemet’s membrane endothelial keratoplasty (DMEK), which restored near-normal anatomic layers in the recipient cornea [45,57]. McCauley et al. [46] reported a hybrid technique in which DM was transplanted with a peripheral rim of corneal stroma to provide the visual results of DMEK and stability of DSAEK. Most recently, in 2011, Dapena et al. [47] reported the “no touch” technique for performing DMEK, accompanied by some maneuvers to make the procedure more practical.

Evolution of Techniques

Donor tissue preparation

In 1998, Melles et al. reported the donor tissue preparation for posterior lamellar keratoplasty. Using a custom-made spatula (Medical Workshop, De Meern, Netherlands), they made a stromal pocket across the donor cornea and punched out the corneoscleral button, with the endothelial side up [30]. Many corneal surgeons still manually prepare the donor disk for DSEK, with good results [48]. The procedure has the advantage of producing a uniformly very thin donor disk, 40 to 70 µm thick, [49] and keeping the control of all surgical steps in the surgeon’s hands. In addition, it is less expensive than automated tissue preparation. Conversely, it bears the risk for posterior lamellar perforation and lengthens the procedure.

Many corneal surgeons use a microkeratome to dissect the donor cornea and obtain the donor disk because it results in a smoother surface and faster visual rehabilitation [6,41]. It also carries little risk for donor disk perforation and is faster than manual dissection [50,51]. However, if the cutting depth is not selected precisely, a buttonhole may appear in the donor tissue [52]. For automated dissection of the donor cornea, a corneoscleral button is mounted and secured in an artificial chamber, which is filled with Optisol-GS to produce a pressure of about 80 mm Hg [53]. The epithelium should be removed. When the central pachymetry measurement is ≤570 µm, the cutting depth is set at 300 µm; otherwise, the cutting depth is set at 350 µm. A full-path dissection is performed, and the dissected tissue is punched with the endothelial side up. This usually results in a posterior donor disk, 150–200 µm thick.

The procedure may be performed in advance by an eye bank technician, and the tissue is sent to the surgical facility as pre-cut tissue. When an experienced technician prepares the presectioned tissue using an automated microkeratome, there is no difference between pre-cut and surgeon-cut donor tissues with regard to endothelial cell loss 1 year postoperatively or clinical outcomes [9,50,54,59]. Centering the donor tissue in the corneal punch is extremely important for obtaining good results, and it has a tolerance of no more than 0.25 mm of decentralization [59]. Decentration of the donor tissue in the punch results in non-uniform thickness of the rim over the circumference of the donor disk and may be associated with graft dislocation [51]. Marking the donor cap rim with Trypan blue allows centration over the microkeratome cut borders rather than the geometrical center, thereby reducing donor disk problems even if the microkeratome cut were to be slightly decentralized [60,51]. Sikder et al. [53] showed that a double pass of the microkeratome, making the first pass at a thicker cutting depth and the second at a thinner cutting depth, resulted in ultra-thin donor disks.

Using a femtosecond (FS) laser to precisely cut tissues has applications for donor preparation in PLK [44,61,62]. Cheng et al. reported a single case of FS laser-assisted DSEK and showed the feasibility of using a FS laser for preparing a donor disk [63]. Although FS laser application through the anterior stromal layers results in a smooth surface, [64–67] experience indicates that laser application through the deeper layers of the corneal stromal tissues produces rougher surfaces [9,68,69]. The laser may cause concentric ridges that adversely affect the optical quality of the surface [61]. The quality of the surface cut with a 15-kHz FS laser was comparable to that of a manually dissected surface [62]. Jones et al. [70] showed that donor tissue preparation using a 30-kHz FS laser at energy up to 7.4 microjoules gave a rougher surface compared with a microkeratome-cut surface. The pattern of laser application appears to affect the smoothness of the cut surface, as a raster pattern of laser application creates a smoother surface than a spiral pattern [73]. Comparing the cuts made through the anterior stromal layers with a microkeratome and a 60-kHz IntraLase FS shows that the FS laser produced smoother surfaces [71]. Mehta et al. [43] found that a double pass of the donor tissue with a FEM TEC 20/10 40-kHz laser resulted in smoother surfaces, as evaluated by light and scanning electron microscopy, reduced the rim tags, and improved the removal of the donor disk. In addition, Mehta et al. [72] showed that a FEM TEC 40-kHz laser was accurate for deep stromal laser application in corneas up to 690 µm thick. The donor disks made with a microkeratome and FS laser are thin at the center and thicker at the periphery, which may contribute to the hyperopic shift observed in the postoperative refraction [8,73]. The hyperopic shift is greater in FS laser-assisted DSEK [74]. The reported difference in thickness between the central and peripheral portions of the donor disk is up to 53.9% at 6 months postoperatively. The thickness of the donor disk is not necessarily uneven in manually dissected buttons in DSEK.

Melles et al. were the first to harvest isolated DM and endothelium as donor tissues for DMEK, in both laboratory and clinical settings [37,75]. Other in vitro studies have confirmed that viable endothelium and DM can be harvested as donor tissue for DMEK [76], Zhu et al. [77] harvested a rectangular DM sheet from a donor button while avoiding an underwater environment, in order to prevent the scarring of the DM that occurs in an aqueous environment. Studeny et al. [78] introduced DMEK with a stromal rim (DMEK-S) and separated the DM from the stromal layers by injecting air to create a Big bubble at the DM/stroma interface. They removed almost 80% of the stromal tissue with a crescent knife and bored a 6-mm area of DM over the central cornea. The resultant donor tissue with bare DM at the center and a stromal rim at the periphery was used for PLK to obtain the visual benefits of DMEK and ease of tissue handling of DSEK. McCauley et al. [46] performed a similar procedure, but used a microkeratome to remove the stromal tissue. They concluded that the resulting procedure, Descemet’s membrane automated endothelial keratoplasty (DMAEK), has the potential to give 20/20 vision while avoiding the difficulties of DMEK. Kymionis et al. [79] applied DMAEK by using an epikeratome to harvest the DM from a rabbit corneoscleral button positioned with the endothelial side up in an artificial chamber. The endothelium and DM were preserved in seven of the 10 rabbit eyes.

The idea of using human cultured endothelial cells (HCECs) as donor tissue for endothelial keratoplasty dates back 30 years [80,81]. To obtain clinically acceptable results with cultured HCECs, several steps are necessary.

1) Endothelial cells should be isolated without contamination by adjacent fibroblasts in corneal stromal tissue, as fibroblasts can easily overgrow the slowly proliferating HCECs in culture.

2) Endothelial cells must exit G1 arrest and progress through the cell cycle, remaining in a normal physiological state. Arrest in G1 phase results from strong contact inhibition by the DM and the
The maintenance of recipient adhesion [20]. When viscoelastic material is used, it is crucial to remove all of
the anterior chamber. The maintainer should be oriented so as not to
be introduced too deeply into the anterior chamber and so that the
fluid of fluid is not directed toward the center of the anterior chamber
[21]. When viscoelastic material is used, it is crucial to remove all of
it, because retained viscoelastic material interferes with the donor/recipient adhesion [20].

Removing all of the DM within the recipient bed is of paramount importance. Retained DM fragments are a major cause of failure in
DSEK surgery [100]. Retained DM islands are reported to remain in 50% of cases [47]. Terry et al. [101] introduced a modified DSEK
procedure, using a Terry scraper (Bausch & Lomb, St. Louis, MO) to
roughen 1–1.5 mm of the circumference of the stromal bed near the
descemetorhexis borders, while the central part of the bed remained
untouched. This reduced the dislocation rate in their study.

Insertion techniques

Several techniques have been introduced to either push the donor
disk into the anterior chamber or pull it through. Terry et al. [35] showed that a 60:40 overfold donor lenticule, rather than the 50:50
folded lenticule described by Melles et al. [36], facilitated unfolding of the donor disk in the anterior chamber. Chen et al. [108] used a 40:60
underfold donor lenticule to reduce endothelial cell loss by avoiding contact between the endothelium and the punch rims; the lenticule
easily turned into a 60:40 folded lenticule when the surgeon’s hand was
pronated. In early DSAEK/DSEK surgery, considerable endothelial cell
damage occurred when McPherson forceps (Sklar, West Chester, PA)
were used to push the folded donor disk into the anterior chamber,
because the forceps touch along the length of the blade. Goosney forceps
(model 19090; Moria SA, Antony, France) and Charlie forceps (Bausch & Lomb), which make contact only at one point at the end of the blade,
are thought to cause less trauma to the donor endothelium.

Balachandran et al. [49] described the needle insertion technique. After making a 5-mm scleral tunnel at 12 o’clock and bending a 30G
needle at its distal third to create a curve, they folded the donor disk into 50:50 taco-shaped lenticule and inserted it with the needle, moving the disk over a glide through the scleral tunnel wound and into the anterior chamber. By moving the needle inferiorly toward 6 o’clock while simultaneously moving the glide superiorly, they converted the lenticule into a 60:40 or 70:30 lenticule, which was easier to unfold.

Mehta et al. [103] introduced the glide insertion technique. They used a sheet glide (BD Visitec) trimmed to a width of 4.5 mm and a
viscoelastic material to protect the endothelium after positioning it over the glide. The glide was introduced into the anterior chamber over
the iris surface. Kawai capsulorhexis forceps (model AE-4388; ASICO) were used to pull the donor disk from a contralateral corneal opening,
over the glide surface, through a 5-mm scleral tunnel, and into the anterior chamber.

In 2008, Busin et al. [99] described a pull-through technique using a
specialized glide called the Busin glide (Moria SA). They placed the donor disk with the endothelial side up and dragged it into the
funnel-shaped part of the glide, using microincision forceps. The glide was inverted and kept at the entrance of a 3.2-mm clear corneal incision. Then the disk was pulled by the microincision forceps from a contralateral corneal opening, through the 3.2-mm corneal incision, and into the anterior chamber.

Khor et al. [21] used an EndoGlide (Angiotech, Reading, PA,
USA/Network Medical Products, North Yorkshire, UK) to perform a pull-through donor disk insertion. The glide is a transparent oval
plastic chamber with a flat anterior part to prevent iris prolapse, while simultaneously moving the glide superiorly, they converted the
lenticule into a 60:40 or 70:30 lenticule, which was easier to unfold.

Melles et al. [75] described the introduction of isolated DM and
endothelium into the anterior chamber using a custom-made injector
(Hippocratesch, Rotterdam, Netherlands) to draw up a delicate roll of
DM, which had been stained with 0.06% Trypan blue solution, and
transfer it into the anterior chamber [37,45]. Alternatively, a Pasteur
glass pipette [47] or an intraocular lens inserter [104] can be used for
donor insertion. Dapena et al. [49] presented a no-touch technique
for DMEK surgery and emphasized that a soft eye without excessive
vitreous pressure is essential for performing DMEK. After the rolled
DM is inserted, it should be unrolled. As the endothelial layer is located on the outer surface of the roll, a small air bubble may facilitate indirect manipulation of the DM roll in the anterior chamber (Ham maneuver). In addition, tapping the corneal surface with a cannula overlying the graft (Van Dijk taps) can help to unroll the DM. The graft is unrolled when the endothelium faces the iris surface, and this can be checked using the Moutsouris sign. When the disk is unrolled with the endothelium facing the iris, an air bubble will assist in positioning the disk into the host bed.

To promote donor/recipient adhesion, the donor disk is tamponaded with air for various periods, while the patient lies in the supine position. The time required for donor/recipient adhesion in DMEK is longer than that required in DSAEK/DSEK. Initially, Melles et al. [75] used 30 minutes in DMEK, but later proposed that at least 45–60 minutes be used [47].

Discussion

Penetrating keratoplasty has long been the standard of care for treating eyes suffering from endothelial decompensation. Some factors make the procedure far from ideal in terms of visual rehabilitation. These include prolonged refractive instability, high irregular astigmatism, and a mean residual regular astigmatism of 4.5 D [105,106]. These hinder functional success in 10–20% of cases, [107] and there can be dramatic shifts in the refractive status and topography of the cornea after suture removal [105]. Regarding visual rehabilitation, there has been continuous progress over the past 12 years, from DLEK to DSEK to DSAEK to DMEK.

Many corneal surgeons worldwide perform DSAEK/DSEK, which provides a compromise between the quality of visual results and the rate of complications, ease of execution, handling of tissues, and repeatability. DSAEK/DSEK is currently the most widely used procedure for treating eyes with endothelial decompensation and healthy overlying corneal tissues [108].

Compared with PK, we get better visual results with various types of PLK surgery at the cost of close contact with or manipulation of the endothelium or adjacent tissues, which may result in significant endothelial cell loss. Endothelial cell loss is the major cause of postoperative donor disk detachment [100] and the major determinant of long-term clarity of the cornea. Hence, endothelial cell loss is a major concern when evaluating different PLK techniques (Table 1). Endothelial cell loss can occur during the preparation of donor tissue, the insertion of the donor disk into the recipient anterior chamber, or the manipulation of donor tissues within the anterior chamber before donor/host adhesion.

Mehta et al. [109] compared two donor tissue insertion techniques: the push-in technique using end-contacting Goosney forceps and the pull-through glide insertion technique. They assessed endothelial cell damage using both vital dye staining and scanning electron microscopy. The maximum endothelial cell damage occurred along the blades of the inserting forceps and along the fine linear streaks where the cornea was folded for the push-in technique. The mean cell damage in the glide insertion group was 9.24% (range, 3.9–16.8%), far less than the 38% (range, 22.2–52.4%) mean cell damage in the push-in group.

Although some other studies comparing the push-in and pull-through techniques have not confirmed these results, [110] it seems logical that reducing the amount of material passing through the entrance wound by eliminating the use of forceps blades and transporting the donor disk into the anterior chamber by a pull-through technique would reduce the compression force induced by the wound lips on the donor tissue and probably result in less endothelial cell loss. Using a larger incision (5 vs. 3.2 mm) with the push-in technique has been documented to reduced endothelial cell loss [111].

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**Table 1:** Endothelial cell loss following keratoplasty.

<table>
<thead>
<tr>
<th>Author, year of study</th>
<th>Surgical technique</th>
<th>Number of eyes</th>
<th>Follow-up (months)</th>
<th>Mean endothelial cell loss (%)</th>
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<td>40</td>
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<td>31</td>
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<td>24</td>
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<tr>
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<td>7</td>
<td>6</td>
<td>22</td>
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</table>

Abbreviations: DMAEK: Descemet’s Membrane Automatic Endothelial Keratoplasty; DMEK: Descemet’s Membrane Endothelial Keratoplasty; DSAEK: Descemet’s Stripping Automatic Endothelial Keratoplasty; DSEK: Descemet’s Stripping Endothelial Keratoplasty; DLEK: Deep Lamellar Endothelial Keratoplasty; PK: Penetrating Keratoplasty
The compression force of the wound lips on the donor lenticule and the resultant endothelial cell loss should be proportional to the volume of material passing through the wound and inversely proportional to the size of the entrance wound.

In an attempt to facilitate tissue insertion and reduce donor tissue damage, Busin et al. introduced the Busin glide. Although the rigid walls of the glide protect the donor tissue from adverse compression force, they do not continue to protect the disk as it passes through the wound because the glide itself does not enter the anterior chamber.

The recently introduced EndoGlide enters the recipient anterior chamber to deliver the donor disk, thereby protecting the disk all the way from the preparation base to the anterior chamber. EndoGlide resulted in a mean endothelial cell losses of 9.6% (95% CI, 3.3–15.8%), 13.1% (95% CI, 8.4–17.8%), and 15.6% (95% CI, 7.0–24.2%) at 3, 6, and 12 months postoperatively, respectively [21]. The mean endothelial cell loss may be further reduced if the inner lumen of the glide were to be larger and the wound were to be longer than 4.5 mm.

Although DMEK gives better visual results than other endothelial keratoplasty techniques and restores near-normal anatomy of the recipient cornea, it is not recommended for eyes with a hazy cornea that interferes with proper visualization of the DM roll in the anterior chamber, eyes with a filtering device, eyes with a shallow anterior chamber, or aphakic eyes with a fixed and dilated pupil as the DM roll may be lost in the posterior chamber. With DMEK, the reported endothelial cell loss is 25% in the early postoperative phase and 28% after 6 months [112]. Insertion of the DM roll into the recipient anterior chamber seems to cause the least trauma to the donor endothelium. In addition, donor tissue preparation for DMEK is not as damaging to endothelial cells; the mean percentage of the endothelial surface area damaged during donor tissue preparation was 3.4% in one study [113] and was similar in other studies [76,77]. The remaining endothelial cell loss in DMEK may be associated with excessive manipulation of the donor tissue in the anterior chamber when unrolling the tissue and properly placing it or may be related to the longer time required for an air-filled anterior chamber compared with the DSAEK/DSEK procedure. No study has examined the effect that filling the anterior chamber with air has on endothelial cell density after PLK.

Studen et al. [78] introduced the DMEK-S technique to gain the visual results of DMEK and the stability of DSAEK/DSEK as a push-in procedure. DMAEK has been introduced to achieve the same objectives, while using a microkeratome for donor tissue preparation and the Busin glide as a pull-through procedure. Perhaps better results would be achieved by using the donor disk as prepared in DMAEK, but inserting it using an EndoGlide.

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