Introduction

In the last 10 years, Descemet membrane endothelial keratoplasty (DMEK) has become an increasingly popular first line treatment for patients with corneal endothelial disorders and corneal decompensation.1 Most commonly, DMEK is ideal for patients with Fuchs endothelial dystrophy (FED), and pseudophakic and aphakic bullous keratopathy (PBK and ABK). In treating these disorders, many corneal surgeons prefer DMEK over Descemet stripping endothelial keratoplasty (DSEK) and Descemet stripping automated endothelial keratoplasty (DSAEK). Not only does DMEK create a near-perfect anatomical restoration of the cornea, but it has also been shown to provide visual acuities of up to 20/20 within the first weeks after surgery, and of having an about 10 times lower rate of graft rejection compared to DSEK/DSAEK.1-3 Although DMEK was initially perceived as a relatively difficult procedure, standardization of this technique has allowed cornea surgeons worldwide to use this surgery to the benefit of patients with corneal endothelial disorders.1 The standard surgical technique, and alternative unfolding techniques and their rationales will be discussed.

Patient selection

Selecting relatively less complex cases is recommended when learning DMEK, as it both maximizes the surgeon’s rate of success and optimizes the patient’s clinical outcomes.1 Good candidates are often pseudophakic (amblyopic) eyes with moderate FED and mild stromal edema, as this eliminates the possibility of a surgically induced cataract and allows for better visualization of the DMEK graft in the anterior chamber.1 Selecting patients with relatively normal anterior chamber anatomy facilitates effective graft manipulation and helps to prevent ocular hypotony after surgery with consequent graft detachment. Hence, it is recommended to avoid starting the learning curve with patients with large iris defects, very dark iris, glaucoma tubes, aphakia, anterior chamber intraocular lenses and/or anterior synechiae.1,4-8

Anesthesia and obtaining a soft eye

One of the most important steps in DMEK is to first obtain an appropriately soft eye, as posterior pressure is the main intraoperative complication associated with this surgery.1,6 Posterior pressure tends to collapse the anterior chamber and therefore impede DMEK graft orientation and unfolding.1,6 To facilitate preparing a soft eye for surgery, the patient is placed in an anti-Trendelenburg position before administration of retrobulbar anesthesia (4-5ml of ropivacaine 1% hydrochloride mixed with 150 IU hyaluronidase).1,6 The eye is then manually massaged for 2-3 minutes and a Honan balloon is used to provide additional oculopressure for 10-15 minutes.1,4,6 An eye speculum is then inserted and its tightness is carefully monitored throughout the procedure.1,4,6 The tension of the eye speculum may be released if signs of posterior pressure are observed.1,4 The use of an anterior chamber maintainer is not recommended since continuous infusion may overpressurize the...
anterior chamber. Overpressurization may flush the graft out of one of the ports, overhydrate the cornea and obscure visibility during surgery, or overhydrate the vitreous and induce posterior pressure.

**First surgical steps and graft preparation**

Once the main incision and side ports have been created, the anterior chamber is filled with air to provide better visualization of Descemet membrane (DM) during descemetorhexis. The recipient’s DM is scored over 360° and completely stripped from the posterior stroma.

The pre-dissected DMEK donor graft and its media are poured into a glass bowl. The media is aspirated and the graft is delicately rinsed with balanced salt solution (BSS). The DMEK graft is then stained with trypan blue for 1-2 minutes twice, to ensure that the graft will be easily visible during the procedure.

After it has been adequately stained, the graft is checked to ensure that it is in the “double roll” configuration to facilitate unfolding within the anterior chamber. If the graft is curled into a single rolls, gentle rinsing with BSS across the surface of the graft is often sufficient to open up the tissue edges enough to fall back into a double-roll.

Once a double-roll has been created, the graft is aspirated into the curved glass injector (DMEK surgical disposable set, DORC International®) and observed under the surgical microscope to ensure that the endothelium is correctly oriented. If the graft is upside down, the tip of the cannula will not appear blue, as the rolled edges are facing downward. Then flip the graft by rinsing it with BSS and check the orientation again with the Moutsouris sign. Other surgeons prefer using a trephined graft with asymmetric marks at its edge in order to track the correct orientation.

Four commonly used unfolding techniques are described below (Figures 3-6). With these, DMEK can nearly always be completed successfully. Each technique appears to yield a fairly similar outcome in terms of final visual acuity, incidence of post-operative complications, and / or endothelial cell density six months post-operatively. Therefore, the surgeon may use whichever unfolding technique is best suited for the graft or whichever he/she is most comfortable with, as it does not statistically affect the final clinical outcome.

**Technique I: Standardized “no-touch” DMEK: Unfolding a “double roll”**

This is considered a relatively easy technique to teach for surgeons learning to unfold a double-roll DMEK graft with “average” tightness. Provided its orientation is correct, the graft can be further centred and slightly unrolled by tapping on top of the cornea with the cannula. Next, an air bubble is gently
injected above the graft between the two upward facing rolls to unroll them evenly.\textsuperscript{1,6} This air bubble is then slowly enlarged until the graft is completely unrolled and flattened over the iris.\textsuperscript{1,6}

Once the graft has been completely opened, the air is withdrawn from the top of the graft. The anterior chamber is purposefully collapsed to hold the graft between the cornea and the iris, preventing it from dislocating, rolling, or turning.\textsuperscript{1,6}

Air is re-injected at the pupillary area beneath the graft to re-form the anterior chamber and push the graft up against the posterior corneal surface.\textsuperscript{1,6} With the anterior chamber completely filled with air for about 60-90 minutes graft adherence to the posterior stroma is promoted.\textsuperscript{1,6}

Finally, an air-fluid exchange is performed to reduce the air in the anterior chamber to 50\% in pseudophakic eyes and 20-30\% in phakic eyes.\textsuperscript{1,6}

Alternative techniques may be used in about 75\% of cases, either by itself in 50\% of cases or in combination with one of the below described alternative techniques.\textsuperscript{11}

An alternative technique may better facilitate DMEK graft unrolling, especially if a double-roll cannot be obtained and the graft maintains a single-roll, due to intrinsic properties of the donor tissue, such as elasticity, diameter, and donor age.\textsuperscript{12} Alternative techniques may also improve unrolling of a very “loose” or very “tight” double-roll (Figures 4-6).\textsuperscript{12} They may also sometimes further aid graft unfolding in the presence of difficult recipient anatomy, such as eyes with a shallow anterior chamber, phakic or aphakic eyes, vitrectomized eyes, and eyes with an anterior chamber intraocular lens or a glaucoma tube. These techniques, as described below, should still allow for “no-touch” unfolding, except perhaps for graft centration, which may be exceptionally performed by direct manipulation of the graft edge with a 30G bent cannula (DMEK surgical disposable set, DORC International\textsuperscript{16}).\textsuperscript{1,6}

**Technique II: “Dirisamer technique”: Using two cannulas to unfold a single DMEK-roll**

This technique is better suited for DMEK grafts which may have too much elasticity to maintain the double-roll configuration.\textsuperscript{12} These grafts therefore form very “tight” DMEK-rolls, asymmetric double-rolls, or rolls that spontaneously fall back into a single roll during injection into the anterior chamber.\textsuperscript{1,6} This technique is used in about 20\% of cases.\textsuperscript{12}

The Dirisamer technique involves gently tapping on the outer corneal surface with a cannula to open up an outer curl of a single roll or asymmetric roll, to lay it flat over the iris (Figure 4).\textsuperscript{1,6} The graft is then centered so that the edge of the opened curl is positioned in the anterior chamber angle, leaving adequate space to unfold the rest of the roll.\textsuperscript{1,6} A cannula is then used to gently compress the cornea and effectively sandwich the opened curl between the posterior cornea and the iris.\textsuperscript{1,6} With this edge stabilized, a second cannula can be used to gently tap the cornea and unfold the graft, much like “unrolling a carpet”.\textsuperscript{1,6}

When most of the graft has been unrolled, further centration and positioning can be done as in Technique I, the standardized “no-touch” technique.

**Technique III: “Dapena maneuver”: Unfolding the DMEK-roll using a small air bubble**

This technique is suited for situations where Techniques I and II have either failed to unroll a single-roll or asymmetric graft, or are more difficult to perform because of
the patient’s eye anatomy, for example in phakic eyes or in eyes with a shallow anterior chamber.11 In the case series by Liarakos et al, the Dapena maneuver was used to start unfolding the graft in about 40% of cases, while one of the previously described techniques was used to finish unrolling the graft.11

With the Dapena maneuver, a small air bubble is used as an intraocular tool to unroll the graft inside the anterior chamber (Figure 5).1,6,11 The air bubble is positioned on top of the partially unfolded graft and manipulated by tapping the corneal surface with the cannula.1,6,11 When the graft is adequately unrolled, a larger air bubble is used to flatten it against the iris, as in the standardized “no-touch” technique.1,6

**Technique IV: “Single sliding cannula maneuver” to unfold a loose DMEK graft**

This technique is best for DMEK grafts that are too loose and tend to unroll themselves after injection into the anterior chamber.1,6 Loose rolls, a result of intrinsic donor tissue properties, occur in about 15% of cases.12

With this technique, a single cannula is used to gently and repetitively tap the outer corneal surface where the loose or partially unfolded DMEK graft is near the edge of the anterior chamber (Figure 6).11 While tapping, the cannula is slid across the corneal surface towards the periphery, parallel to the DMEK graft.11 This unfolds the rest of the loose roll, and can also be used in combination with other techniques to completely unfold partially rolled grafts.1,6

**Auxiliary techniques**

Three other auxiliary techniques have been described for handling specific situations.

**Flushing: Turning the graft over**

This technique is used after the graft has been injected into the recipient anterior chamber if it is upside down. The orientation of the graft should be checked before unfolding, and is upside down if the rolls are facing downward (negative Moutsouris sign).1,6 To correct this, BSS is gently flushed through one of the side ports to turn the graft around. Orientation should be re-checked with the Moutsouris sign,1,6 once the graft has been turned over.

**Manual centration**

In most cases, the DMEK graft is centred in the anterior chamber by gently tapping on the corneal surface with a cannula. If centration cannot be achieved through this indirect maneuver, it can be centered by inserting a 30G bent cannula (DMEK surgical disposable set, DORC International®) to gently pull the graft at the periphery,


REFERENCES


into the desired position. This technique is not ideal because direct contact with the graft, even though from the Descemet membrane side, may damage the endothelial cells and decrease their final density.

In order to reduce direct manipulation of the graft and subsequent endothelial cell damage, slightly decentralized grafts that cover the central cornea may also be acceptable. Clinical observation has shown that the cornea overlying the gap between the peripheral rim of the recipient Descemet membrane and the decentralized DMEK graft may still clear because this denuded stroma is repopulated by migrating donor and / or recipient endothelial cells. Further, slight decentration has not shown to significantly change final visual outcomes.

**Bubble bumping: Unfolding peripheral inward folds**

After the DMEK graft has been unfolded with a large bubble, small peripheral inward folds of endothelium facing the host stroma may persist. The elasticity of the donor tissue’s small inward folds may cause it to spring away from the recipient stroma, thereby causing the graft to detach in that area. It is therefore important to correct these folds before the complete air fill. Gentle taps applied to the outer cornea overlying the folds while an air bubble is under the graft can create an aqueous flow that will flatten the folds. This technique is known as “bubble-bumping”.

**Learning curve**

Clinical studies by Dapena et al indicate that the outcomes after DMEK with respect to best corrected visual acuity and endothelial cell density relate more to whether a graft is attached and functional than to the skill and expertise of the surgeon. That is, similar clinical results may be obtained by new surgeons with proper DMEK training and adequate practice or supervision. However, obtaining a functional graft correlates with the DMEK surgery learning curve. The number of graft detachments tends to decline with more DMEK experience, and elimination of potential causes of graft detachment, such as lingering inward folds. The preparatory points and surgical techniques discussed can greatly improve DMEK surgery and therefore reduce intra-operative and post-operative complications.