Standardized “No-Touch” Technique for Descemet Membrane Endothelial Keratoplasty

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We describe a standardized technique for “no-touch” isolated Descemet membrane transplant, ie, Descemet membrane endothelial keratoplasty (DMEK). All essential steps, including patient preparation and descemetorhexis as well as DMEK graft implantation, orientation, unrolling, centering, appositioning, and fixation, are described in detail. In the management of Fuchs endothelial dystrophy, the technique may provide a best-corrected visual acuity of 20/25 or better (≥0.8) in three-quarters of cases and an endothelial cell density of about 1800 to 2000 cells/mm² at 6 months after surgery. No-touch DMEK may therefore be a safe and effective procedure for the treatment of corneal endothelial disorders, making endothelial keratoplasty accessible to most corneal surgeons without requiring major investments while providing an unprecedented visual rehabilitation rate and outcome.


METHODS

OBTAINING A SOFT EYE

In the analysis of the first series of 150 DMEK surgeries, the presence of intraoperative posterior (vitreous) pressure was found to be the main cause of complicated tissue handling during surgery. In DMEK, maintaining the anterior chamber pressure by infusion of balanced salt solution (BSS) may be avoided because an overpressure in the anterior chamber bears the risk of flushing the graft out, even through a side port. In the presence of posterior (vitreous) pressure, a shallow anterior...
The anterior chamber is completely filled with air. Under air, the recipient Descemet membrane endothelial keratoplasty (DMEK) graft in a vial with organ culture medium. After stripping off the Descemet membrane from a donor corneoscleral rim at the eye bank, the tissue spontaneously forms a DMEK roll. After 1 to 2 weeks of organ culture, during which the endothelial cell density and sterility are checked, the graft is sent off for transplant in a DMEK procedure.

To achieve a soft eye, 4 precautions or actions should be considered: the surgical bed should be positioned in an anti-Trendelenburg position; after retrobulbar injection (4-5 mL of 10-mg/mL ropivacaine hydrochloride mixed with 150-IE hyaluronidase), a manual ocular massage should be performed for 2 to 3 minutes, followed by oculopressure with a Honan balloon for another 10 to 15 minutes; and during surgery, the tightness of the eyelid speculum should be carefully monitored, and it should be released if the anterior chamber is shallow or if any signs of vitreous pressure are observed.

INCISIONS AND DESCEMETORHEXIS

At the 12-o’clock surgical position, a 30% scleral-depth limbal incision, 3.0 mm wide, should be made and extended by lamellar dissection into the clear cornea with a slit knife to create a self-sealing 3.0-mm clear cornea tunnel incision. Three side ports can be created at the 10:30, 1:30, and 7:30 (right eye) or 4:30 (left eye) clock positions (green arrows). The donor DMEK graft should be presoaked in an eye bank to enable endothelial cell density measurements and sterility testing before releasing the tissue for surgery. At Amnitrans Eyebank Rotterdam, Rotterdam, the Netherlands, a DMEK roll is routinely stripped off from a donor sclerocorneal rim (with a minimal cell count of 2300 cells/mm² and no age restrictions) and stored for 1 or 2 weeks in a glass vial with modified minimum essential medium at 31°C, until the date of transplant (Figure 2). At surgery, the content of the glass vial is poured into a glass bowl, and with a glass pipette (catalog No. 612-2297; Omnilabo, Breda, the Netherlands), the culture medium is carefully drained from the bowl, avoiding any contact and/or damage of the membrane (Figure 3).

In the bowl, the DMEK roll is thoroughly rinsed (2-3 times) with BSS (Alcon Nederland BV, Gorinchem, the Netherlands) until all macroscopically visible preservation medium residues attached to the tissue are removed. The DMEK roll is then stained with trypan blue, 0.06% (catalog No. VBL.105 USA, VisionBlue; DORC International), for about 30 seconds, rinsed with BSS, and again stained with trypan blue to obtain an intense blue tissue to ensure visibility of the graft in the recipient anterior chamber throughout the surgery. The DMEK roll can be rinsed again with BSS to remove all excess dye. New surgeons starting out with DMEK may want to apply a direct flow on top of the tissue with BSS to open up the roll and to create a double roll, like the plastic tubes of an electrical cord, to further facilitate unfolding of the tissue after implantation in the recipient anterior chamber (Figure 3). If the blue staining of the membrane fades away during the surgery, the graft can be restained by a few drops of trypan blue, 0.06%, injected in the anterior chamber, followed by rinsing out the excess dye.

IMPLANTATION OF THE DMEK GRAFT

After staining, the DMEK roll is sucked into a custom-made glass injector or a conventional Pasteur glass pipette, and under the surgical microscope, the injector is turned so that the double roll is facing upward, ie, with the hinge down (Figure 4). On the DMEK roll, unlike a taco-shaped graft in DSEK/DSAEK, the endothelial cells are located on the outer surface. Because of this, it is best to use...
validated glass injectors instead of plastic intraocular lens–inserting devices, since glass surfaces are much smoother than those of plastic and glass injectors can be manufactured without sharp molding edges.

Using the glass injector, the DMEK roll is then inserted into the anterior chamber through the main incision at 12 o’clock (Figure 4). During insertion, the incision size should allow a sufficient leak of BSS so that the recipient anterior chamber is not overpressurized.

**ORIENTING THE DMEK GRAFT**

Once implanted, the DMEK roll should be rotated toward the horizontal meridian to better fit inside the anterior chamber. The graft can be easily manipulated by gentle strokes of a cannula over the outer corneal surface or the sclera overlaying the iris root. This maneuver can be facilitated by injecting a small air bubble in the anterior chamber and using the bubble to indirectly rotate or move the graft (Ham maneuver) (Figure 5).

The DMEK roll may then be opened up, ie, slightly unrolled by tapping the outer corneal surface directly overlying the graft (van Dijk taps). Thereafter, the orientation of the graft in the anterior chamber may be checked by positioning the tip of a 30-gauge cannula on top of the membrane and underneath one of the peripheral curls: if the graft is correctly oriented (endothelium facing toward the iris), the tip of the cannula should be embraced by one of the rolls, becoming slightly blue as the curl overlays the cannula (Moutsouris sign) (Figure 6). If the graft is oriented upside down (endothelium facing the cornea), the tip of the cannula will not turn blue, since it cannot find an upward curl because the graft will be curling toward the iris, ie, away from the cannula. If oriented upside down, the graft may be rolled over by gently irrigating it within the anterior chamber. If the graft is turned over, its orientation may be confirmed using the Moutsouris sign. Obtaining a correct orientation of the graft is an essential step in the procedure: if the endothelium is positioned upward (facing the stroma) instead of downward (facing the iris), the DMEK graft may be prone to detachment in the early postoperative phase.

Special care should be taken while manipulating the DMEK graft using irrigation because the thin graft is easily flushed out of the eye when the anterior chamber is overpressurized. All manipulation should preferably be performed through one of the side ports, and if the main incision is to be used, the eye should first be softened by draining the anterior chamber through one of the side ports. Alternatively, the main incision may be partially closed with a suture.

**UNFOLDING THE DMEK GRAFT**

Once the DMEK graft is correctly oriented with the edges facing upward, a small air bubble may be injected in between the double roll(s) or on top of the membrane inside a curl (Figure 5). If the graft is oriented upward, the air bubble will be caught in between the rolls, and it may be manipulated to further unfold the graft by rolling the air on top of the membrane, using a cannula on the outer corneal surface (Dapena maneuver). When further unfolded, the air bubble may be enlarged until the central part of the DMEK graft is flattened over the iris. Throughout the unfolding process, direct contact between the graft and the cannula should be carefully avoided.

**CENTERING THE DMEK GRAFT**

Once unfolded, additional BSS should be injected into the anterior chamber to make the air bubble and the underlying DMEK graft float, ie, avoid a downward force by the air bubble that pushes the graft against the iris; alternatively, the air bubble may be reduced. The mobile graft should then be centered inside the anterior chamber by gentle strokes with the cannula over the outer corneal surface (Figure 5). Slightly decentered grafts that cover the central cornea are acceptable, because clinical observation shows that a gap between the recipient Descemet membrane peripheral rim and the decentered DMEK graft is commonly repopulated by migrating donor and/or recipient endothelial cells and decentering does not seem to re-
late to the final visual outcome. Excessive manipulation to center the graft may be avoided to minimize donor endothelial cell damage.

**APPPOSITIONING THE DMEK GRAFT**

After centering, the air bubble on top of the DMEK graft should be enlarged to fully flatten the transplant over the iris. After approximately 10 seconds, the air should be aspirated from the anterior chamber, while holding the tip of the cannula at the center of the air bubble. Without exiting the anterior chamber, the cannula should then be slowly moved toward the edge of the transplant, positioned underneath the transplant, and again carefully moved toward the pupillary area, while slightly digging onto the iris tissue to minimize donor endothelial cell damage. At the pupillary border, a small air bubble should be injected underneath the DMEK graft to lift the transplant upward toward the recipient cornea. Then the air bubble should be slowly enlarged, while carefully observing the edges of the transplant. Not infrequently, peripheral inward folds may be present, ie, an inward curl with the endothelium facing the recipient stroma. These folds may be flattened out with a “bubble-bumping maneuver,” ie, gentle taps of the cannula on the outer corneal surface overlying the fold, to create a flow of aqueous solution by which the remnants of the fold disappear (Figure 5 and Figure 7). Once the DMEK graft is completely unfolded, the anterior chamber should be completely filled with air to position the transplant onto the recipient posterior stroma.

**FIXATING THE DMEK GRAFT**

To avoid postoperative graft detachment, fill the anterior chamber completely with air for at least 45 to 60 minutes, at approximately 20 mm Hg. Thereafter, a partial air-BSS exchange should be performed to leave the eye pressurized with a 30% to 50% air fill in the anterior chamber. After surgery, the patient should remain in a supine position for 24 hours to further secure the position of the DMEK graft against the recipient posterior stroma.

In phakic eyes, the air bubble should be reduced to 20% to 30% at the end of the surgery to avoid air-induced displacement of the iris diaphragm after surgery. If during surgery the air tends to move behind the iris, remove all air from the anterior chamber at the end of the procedure, since these eyes may be prone to capture the air bubble behind the iris following surgery.

**COMMENT**

To the best of our knowledge, our report is the first to describe a standardized no-touch technique for DMEK that may enable corneal surgeons to achieve the 2 most important goals in corneal transplant: a near complete visual recovery while minimizing donor endothelial cell damage. With the technique described, 95% of cases may currently reach a best-corrected visual acuity of 20/40 or better (≥0.5), and 75% may reach 20/25 or better (≥0.8) within 6 months after surgery.1,3,10,15 Since a best-corrected visual acuity of 20/20 (1.0) at 1 week after DMEK is not uncommon, the procedure may have the potential to provide instant visual recovery, as is routinely observed after phacoemulsification surgery.3 As with other endothelial keratoplasty techniques, DMEK may be associated with a drop in donor endothelial cell density in the early postoperative phase. If performed as a no-touch technique as described herein, endothelial cell damage to the isolated DMEK graft may be minimized so that an endothelial cell density of about 1800 to 2000 cells/mm² at 6 months after DMEK may be obtained, ie, a 20% to 25% decrease relative to the preoperative endothelial cell density.16

These outcomes after DMEK may compare favorably with those after DSEK/DSAEK, which may be the most widely performed endothelial keratoplasty technique today. After DSEK/DSAEK, the best-corrected visual acuity may be on average 20/40 (0.5) at 6 months, with only a few cases reaching 20/25 or better (≥0.8).17-21 A major concern in
DSEK/DSAEK is donor endothelial cell damage, up to 30% to 50% at 6 months, although the endothelial cell density may be better preserved with various injectors that are currently being developed. Apart from faster visual rehabilitation and near-normal visual recovery, DMEK may have several other advantages. Because the DMEK graft can be stripped off a corneoscleral rim, DMEK does not require a microkeratome or femtosecond laser to prepare the donor tissue so the procedure may be accessible to most corneal surgeons in any clinical setting. Descemet membrane endothelial keratoplasty may also increase overall donor tissue availability, because a single donor cornea can potentially be used for 2 lamellar keratoplasty procedures, and DMEK grafts may be harvested from corneas not eligible for penetrating keratoplasty or DSEK/DSAEK.

Like DSEK/DSAEK, DMEK is also a relatively safe procedure, since it is performed using a closed system during surgery, and most of the long-term complications that characterize penetrating keratoplasty (high astigmatism, suture-related complications, wound dehiscence) are rare after endothelial keratoplasty. As in DSEK/DSAEK, however, the main complication after DMEK is early graft detachment. Using the technique currently described, graft detachments may occur in 2% to 5% of cases and may be managed with a rebubbling procedure or a secondary DSEK/DSAEK. To lower the risk of (partial) graft detachments, we observed that recipient Descemet membrane remnants and/or peripheral inward folds of the DMEK graft should be avoided as well as the use of plastic vials and viscoelastic materials and that it may be critical to keep the anterior chamber completely filled with air for at least 45 to 60 minutes at the end of the procedure. The risk of graft detachment may be further reduced by careful patient selection: DMEK may be relatively contraindicated in all eyes in which the anterior chamber cannot be pressurized with an air fill at termination of the surgery, for example, in aphakic or vitrectomized eyes and in eyes with large iridecto-
cies, a glaucoma tube, and/or a relatively shallow anterior chamber.

If both cataract extraction and DMEK surgery are required, it may be best to first perform phacoemulsification and then DMEK as a secondary operation for 2 reasons. First, the use of a viscoelastic should be avoided in any endothelial keratoplasty procedure, since it may relate to a higher risk of postoperative graft detachment.30 Second, after cataract extraction, 10% to 30% of patients were satisfied with the visual improvement achieved so DMEK could be postponed. If the crystalline lens is clear, the pupil may be constricted with pilocarpine, 2%, prior to commencing DMEK to avoid iatrogenic cataract formation due to air or surgical trauma.31

In summary, no-touch DMEK is a feasible surgical technique with the potential to give the fastest and most complete visual recovery in the management of corneal endothelial disorders today. In past years, improvements in surgical technique and tissue handling enabled our institute to develop a standardized technique that is, after proper training, accessible to most corneal surgeons at minimal costs. The procedure described was designed in such a way that each step is defined and reproducible, in particular the airbubble manipulations, so that it can easily be taught to novice surgeons. With DSEK/DSAEK and penetrating keratoplasty still available as valuable back-up procedures,29 we anticipate that DMEK will become a preferred treatment method for corneal endothelial disorders.

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