Descemet Membrane Endothelial Keratoplasty

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Definition

Descemet's membrane endothelial keratoplasty (DMEK) is a partial thickness cornea transplant where the host Descemet membrane (DM) and endothelium are replaced by donor DM and endothelium. This is different than Descemet's stripping automated endothelial keratoplasty (DSAEK) where donor DM, endothelium, and posterior stroma replace host DM and endothelium. DMEK and DSAEK are both endothelial keratoplasty procedures, in contrast to a full thickness penetrating keratoplasty (PK).

History

Full thickness cornea transplantation, also known as penetrating keratoplasty (PK), was first performed in 1905 by Dr. Eduard Zirm.[1] Dr. Gerrit Melles described a posterior lamellar keratoplasty (PLK) years later in 1998, where only a select portion of the cornea was transplanted.[2] PLK was originally performed by creating a deep stromal pocket originating at the limbus with a 9 millimeter (mm) incision and then manually dissecting out posterior stroma, DM, and endothelium using a specialized trephine or scissors. A donor button consisting of the same cornea layers was then inserted through the pocket and held in place by an air bubble instead of sutures. Dr. Melles later revised the technique by folding the graft, which enabled the incision size to decrease to 5 mm.[3] However, PLK was not adopted by most surgeons because of the extreme complexity of the technique.[4] Dr. Mark Terry subsequently adopted the technique in 2001, adding modifications including the use of viscoelastic to stabilize the anterior chamber, and renamed the procedure deep lamellar endothelial keratoplasty (DLEK).[5] However, DLEK was technically challenging and created a vision-limiting lamellar interface.

Dr. Melles then described a procedure where the DM and endothelium were stripped from the host cornea (descemetorhexis) and replaced with a donor button consisting of posterior stroma, DM, and endothelium. This surgery was much easier technically and eliminated the need for stromal dissection, creating a smoother graft interface.[6] Dr. Francis Price was the first to publish clinical results of the technique, which he named Descemet's stripping endothelial keratoplasty (DSEK).[7] Dr. Mark Gorovoy reported the use of a microkeratome for donor dissection in 2006 and coined the term Descemet stripping automated endothelial keratoplasty (DSAEK).[8] DSAEK results in fast recovery of vision, minimal complications and stable visual outcomes. However, DSAEK may still limit the best-corrected vision due to the donor lamellar interface.

In 2006, Dr. Melles developed another technique that he named Descemet's membrane endothelial keratoplasty (DMEK).[9] DMEK involves only donor DM and endothelium being transplanted, in contrast to posterior stroma, DM, and endothelium used in DSAEK. A modification of DMEK was described in 2009 where a rim of stroma was left at the periphery of the donor tissue. This was named Descemet's membrane automated endothelial keratoplasty (DMAEK).[10] Another technique was described in 2010, called Descemet's membrane endothelial keratoplasty with a stromal rim (DMEK-S).[11] The difference between DMEK-S and DMAEK is that DMEK-S donor tissue is prepared manually while DMAEK utilizes a microkeratome or femtosecond laser for the initial posterior lamellar dissection.

To avoid redundancy in this article DSAEK will refer to all DSEK/DSAEK procedures unless a distinction between the two is needed. Also, DMEK will refer to all DMEK/DMAEK/DMEK-S procedures unless otherwise specified.

Epidemiology

The term endothelial keratoplasty (EK) encompasses PLK, DLEK, DSEK, DSAEK, DMEK, and DMAEK. EK replaced penetrating keratoplasty in 2012 as the most commonly performed keratoplasty in the United States. 25,965 EK procedures were reported in 2014, an increase from 1,398 in 2005 and 19,159 in 2010.[12]

The vast majority of EK procedures in 2014 in the U.S. were DSAEK, with 23,100 cases performed. This was a 1.6% decrease from 2013. In contrast, DMEK cases were fewer but are increasing at a rapid rate with 2,865 DMEK cases performed in 2014 compared to 1,522 in 2013, representing an 88.2% increase. There was a 283% increase in DMEK cases in the United States from 2012-2014.[12] In 2023 DMEK became the most common keratoplasty procedure in the United States with 17,116 cases, followed by DSAEK (16,207 cases) and PK (14,486 cases). [13]

Endothelial cell disorders remain the most common indication for keratoplasty in the U.S., comprising 40.2% of cases. Fuchs' dystrophy was the most common indication for keratoplasty in the United States in 2014 (15,013, 21.5%) with post-cataract surgery edema being second (8,529, 12.2%). Keratoconus (6,981, 10.1%) and repeat transplants (6,811, 9.8%) were the next most common indications for keratoplasty.[12]

Indications

EK procedures are not suitable for patients with healthy corneal endothelium, such as patients with stromal scarring or keratoconus. These patients still require a PK.

Good candidates for DMEK

- Fuchs' endothelial dystrophy
- Posterior polymorphous membrane dystrophy
- Congenital hereditary endothelial dystrophy
- Bullous Keratopathy
- Iridocorneal endothelial (ICE) syndrome
- Failed endothelial keratoplasty[14] [15]

Not suitable or highly complex scenarios for DMEK

- Stromal scarring
- Keratoconus
- Inability to lie flat
- Hypotony
- Aphakia[4]
- Aniridia or large iris defects[4]
- Anterior chamber intraocular lens
- Previous glaucoma surgery[4][16]
  - Risk of tissue loss through tubes, trabeculectomies, or peripheral iridectomies
  - Postoperative gas bubble loss with resulting graft detachment can occur
- Endothelial failure after penetrating keratoplasty
  - Questionable candidate. Limited success in 4 patients was reported in a small case series with a 75% re-bubble rate and 25% primary failure rate.[17]

Eye Bank Protocol For Preparing Donor Tissue for DMEK[18]

The following steps were adapted from the Eversight Eyebank protocol[18] for DMEK tissue preparation:

1. The corneal tissue is removed from the viewing chamber in a sterile environment by gently grabbing the scleral rim.
2. The tissue is placed with cornea epithelial side down on the vacuum block ensuring centration.
3. The seating ring is lowered on to the vacuum block using the guide posts followed by slowly releasing the piston of the suction syringe. The seating ring is then removed and set aside.
4. A partial trephination to score through the Descemet's membrane is performed.
5. The vacuum block is tilted and a sterile swab spear is placed at the limbus to remove excess medium.
6. Trypan blue stain is placed at the limbus to stain the edge of the scored Descemet's membrane for 60-90 seconds.
7. A surgical spear is used to remove excess stain from the limbal area of the cornea, taking care not to touch the endothelium.
8. Balanced Salt Solution (BSS) is used to rinse the cornea of staining solution, and sterile swab spears to remove excess BSS.
9. A partial dissection of Descemet's membrane is performed beginning where the tubing connects to the vacuum block. Using open forceps, one tip is placed at the edge of the score mark and Descemet's membrane and endothelium are gently separated away from the stroma. Descemet's membrane and endothelium are separated not more than 1 mm from the scored edge with dissection 360 degrees around.
10. If the trephine did not penetrate completely through Descemet's membrane, the beveled edge of a prepared 30 G needle is used to completely score through the Descemet's membrane where necessary, followed by a second application of staining as needed.
11. Forceps are used to remove any endothelial tags that overlap the score mark.
12. The vacuum block is rotated so that the location of any micro tears is at 6 o'clock. This will become the hinge of the flap.
13. Using the forceps, Descemet's membrane is grasped at 12 o'clock and gently separated from the stroma by peeling towards the hinge. The hinge is created by stopping the separation 2 mm from the score mark. NOTE: Peripheral edges of flap will begin to scroll during separation.
14. The flap is gently laid back in place on the stroma. BSS and swab spears are used to unscroll the endothelium and return it to its original position.
15. Residual fluid is removed from between Descemet's membrane and stroma with sterile swab spears so the flap stays in position.
16. A skin marker is used to draw an arrowhead on the scleral rim pointing to the center of the hinge, remove any excess ink using a sterile swab spear.
17. Vacuum is released by depressing the piston of the syringe connected to the vacuum block. While vacuum is disengaged, use forceps to remove cornea from the vacuum block.

Note: The Descemet side of the graft receives a dry ink stamp of an "S" mark in the peripheral portion of the donor tissue after prestripping the tissue. This prestripped, premarked donor tissue is shipped to the surgeon and can be used to verify tissue orientation during trephination, before insertion, after unscrolling the graft in the anterior chamber, and critically before the tissue is lifted into position with the gas bubble. Eye banks with properly trained staff can safely provide prestripped tissue for DMEK.[19][20]

Surgical Steps

The following surgical steps were adapted from the DMEK wet laboratory curriculum at the University of Michigan[21], available at: https://www.mededportal.org/publication/10101. A laser peripheral iridotomy is performed prior to surgery to minimize the risk of pupillary block with intracameral gas. Alternatively, the peripheral iridotomy may be constructed intraoperatively using an anterior vitrector, or using a 25 gauge needle.

A. Preparing recipient eye

1. Although sometimes performed after retrobulbar injection. DMEK is often performed under topical anesthesia.

2. Using 1 mm diamond blade, create 2-3 paracentesis sites
3. Fill the chamber with Healon
4. Use 8.0-9.0 mm trephine to mark the central surface of the cornea
5. Use the marking pen to create multiple spots along trephination mark
6. Insert reverse Sinskey hook via paracentesis and score Descemet's membrane along 8.0-9.0 mm marking
7. Refill the anterior chamber with Healon to pressurize the eye
8. A keratome is used to make a temporal incision at the corneal limbus
9. Insert reverse Sinskey hook through paracentesis or main wound to continue stripping of Descemet's membrane
10. Remove host Descemet's membrane through main wound
11. Utilize the phacoemulsification irrigation/aspiration device to remove all the Healon from the anterior chamber
12. Observe the size of the pupil. Ensure the pupil in as small as possible
13. Stroke the iris surface or use miochol or miostat in order to constrict larger pupils
14. The IOP is left normal or slightly soft by using BSS injections

B. Preparing, injecting and positioning donor endothelium-Descemet's membrane

1. Using tying forceps, remove prepared DMEK tissue from viewing chamber and use swab spears to remove excess fluid from scleral rim. Use caution to ensure graft does not displace from stroma. If graft displaces, use BSS and swab spears to encourage replacement
2. Place corneoscleral rim in empty shallow container
3. Stain with VisionBlue by applying enough dye to cover the surface of the endothelium for 60 seconds
4. Remove stain and gently rinse with BSS
5. Ensure that the endothelium-Descemet's membrane is lying flat on the posterior stroma
6. If tissue is not laying flat, refloat with BSS and use spear sponges to draw the tissue toward the edges. Be careful to avoid touching the endothelium
7. Mount and center tissue on vacuum block endothelial side up
8. Apply suction by depressing syringe attached to vacuum block to secure tissue in place
9. Obtain and slowly lower trephine punch onto vacuum block until trephine is resting on endothelium
10. Gently apply pressure and tapping to cut donor Descemet's membrane and minimal stroma 360^{o} around the edge of the graft. Do not perform complete trephination
11. Optional: If S stamp is not used, obtain 1.0mm trephine and punch three holes along peripheral edge of graft in a manner that will allow distinguishing between the endothelial and epithelial views. If possible, position these marks at locations of larger tags or tears
12. Use tying forceps to remove peripheral Descemet membrane and place in shallow container filled with BSS (For practice loading and unloading modified Jones tube). Be careful not to remove peripheral tissue too quickly as some of the graft may not have been cut. If areas are still attached, use diamond knife to hand cut or repeat trephine
13. Apply BSS on top of graft to submerge endothelium
14. Use tying forceps to gently lift the edge of the graft 180^{o} from the marked hinge
15. Slowly peel graft back toward hinge and lift out of BSS
16. While holding tissue with forceps, fill corneoscleral button with VisionBlue
17. Lower graft into stain and apply further stain on top to completely submerge tissue
18. Allow staining for 3 minutes
19. During this time, construct the insertion device

    a. Obtain 14 French gastric tubing and cut 1.5-2.0cm section with drape scissors
    b. Soak the inside with BSS
    c. Connect one end of tubing into Luer lock of 3cc syringe
    d. Attach the other end of tubing to the proximal tip of modified Jones tube
    e. Draw BSS into syringe via Jones tube and withdraw to ensure tight junctions
    f. Retain enough BSS to fill Jones tube
    g. Test the injection device by drawing peripheral segments of the graft set aside earlier. Practice loading and unloading into BSS to appreciate the amount of pressure required in doing so. Avoid aspirating air during this process

20. Return attention to donor tissue submerged in VisionBlue
21. Use spear sponges to remove VisionBlue. Use caution to prevent touching tissue
22. Gently apply BSS onto corneoscleral rim to dilute VisionBlue and remove with spear sponges
23. Repeat until blue graft is floating in almost clear solution
24. Use tying forceps to carefully transfer corneoscleral rim to shallow chamber filled with BSS and float graft off of corneoscleral button and into the shallow dish
25. Use forceps to remove corneoscleral rim
26. Obtain assembled injecting device
27. Submerge tip of Jones tube into BSS containing donor graft and situate bevel next to the end of the EDM
28. Gently aspirate tissue into Jones tube keeping in mind the amount of pressure needed as tested prior
29. Check orientation of EDM by observing the direction of curling edges. Edges should be curling upward
30. Insert tip of modified Jones tube into main wound of recipient while maintaining correct orientation of graft. Tip of Jones tube should end on top of pupil
31. Again, check orientation of graft ensuring that scrolls are facing upward. Rotate injector as necessary
32. Slowly depress syringe plunger to inject graft into anterior chamber while removing injector even more slowly. Inject extra bursts of BSS to help orient the graft perpendicular to main wound and prevent efflux. Be careful that the graft does not eject from wound. Prevent this by allowing fluid to drain from main wound or paracentesis or use a cannula to close the main wound while withdrawing injector.
33. Use 10-0 nylon to place one interrupted suture closing the main wound
34. Again, check orientation of graft ensuring that the scrolls are facing upward while the graft is floating in the anterior chamber
35. To manipulate the graft in the anterior chamber, utilize bursts of BSS if necessary to flip graft into correct orientation, center the EDM, or open a tightly scrolled Descemet roll
36. Use the cannula to perform short swift taps to the external cornea to help center the graft and open the scroll
37. Manipulating the graft is facilitated by obtaining a shallow anterior chamber. This can be done by using the index finger on the non-dominant hand and applying pressure about 5mm from the limbus
38. After centering and fully unrolling the graft, introduce tip of cannula attached to 20% SF6 into the anterior chamber, posterior to the graft taking care never to touch the endothelium

39. Once the tip is above the pupil, slowly inject gas to allow apposition of the graft to the posterior stroma allowing the edges to unfold and the center to touch stroma
40. Fill the anterior chamber with gas
41. Observe the entire margin of the graft evaluating for any folds and detachments
42. Manipulation of the bubble, or bubble bumping, can help reduce folds and detachments
43. Once all the edges are checked, perform sweep of entire surface of cornea with a barraquer spatula

Terry et al. described a new technique in 2015 that utilizes eye bank prestripped donor tissue, a modified Straiko/Jones glass tube injector, a modified Yoeruek tap technique for unscrolling the tissue, and SF6 gas.[19] SF6 gives prolonged bubble support and has been shown to reduce rebubble rates.[22] See included references for other technique descriptions.[10][23][24][25][26][27][28]

Postoperative Management[29]

After the procedure, the patient should lie supine as much as possible with periodic breaks for meals or using the restroom. The amount of time spent supine should gradually decrease over the course of the first week.

One sample medication regimen: Prednisolone acetate 1% should be used every two hours while awake for the first week, 4 times daily over the next 3 months, then slowly tapered and stopped at year 1. A recent study showed that loteprednol etabonate 0.5% gel was as effective as prednisolone acetate 1% solution in preventing immunologic graft rejection episodes after DMEK and was significantly less likely to cause IOP elevation.[30] Antibiotic drops should be used for 1 week after surgery.

Patients should initially be seen on postoperative (PO) day 1, week 1, week 2, month 1, month 3, month 6 and month 12. Some advocate an OCT before surgery and on PO day 1, PO week 1, and PO month 1 to look at the stroma and edge position of the graft. The graft should be attached and the stroma should be less edematous than after DSAEK. A significantly edematous stroma may indicate the graft is not functioning well or is upside down.

Complications

- Graft detachment: rates are variable and depend on surgeon experience
  - A series of 135 cases published by Dapena et al. reported a rebubble rate of 20% in the first 45 cases that decreased to 4.4% in the last 35 cases.[31]
  - Another series by Dirisamer et al. of 200 cases, after an initial learning curve of 25 cases, showed decreasing detachments with increased surgeon experience. Overall, 18 of 200 (9%) patients had a graft detachment that required a secondary surgical intervention by rebubble or regraft. 13 of these occurred within the first 100 cases and only 5 during the second 100 cases, confirming this complication decreases with surgeon experience.[25]
  - A series of 361 patients by Price et al. demonstrated a rebubble rate of 14-15% and an iatrogenic primary graft failure rate of 1.5-2.8%.[32]
- Damage to tissue during preparation or surgery
- Upside down grafts
- Epithelial defect or erosion (3.0%)[33]
- Raised intraocular pressure (IOP) in as high as 12% of patients, with ~ 2.8% developing secondary glaucoma[33]
- Descemet graft folds (1.9%)[33]
- <1% risk of anterior synechiae, hypotony, pupillary block, subepithelial haze, and interface pigment deposits.[33]
- Cystoid macular edema (CME): one study reported a high rate of CME of 12.5% in eyes with DMEK alone and 13.3% of eyes with DMEK and cataract extraction.[34]

[35]

Graft Rejection

Graft rejection rates ranged from 1.4-5% with a mean of 3.7% in a large multicenter series.[33] Allograft rejection in DMEK seems to have a slower onset and immune response than DSAEK or PK and can present different clinically.[36] Another series demonstrated a 0.7% rejection rate after DMEK compared with historical control groups of DSAEK (9%) and PK (17%).[35][37]

Outcomes

- Visual acuity at 3 months: 63% with vision ≥ 20/25 and 26% ≥ 20/20.[10]
- Visual acuity at 6 months: 79–94% with BCVA ≥ 20/40 and 22–47% ≥ 20/20.[25][38]
- Multiple studies have reported that DMEK causes a mild hyperopic shift of < +0.50 D after 6–12 months' follow-up.[10][35][39] DSEK has been reported to have a hyperopic shift of around +1.00, due to the shape of the donor tissue.[39]
- Postoperative refraction stabilizes at 3 months with no significant spherical equivalent change between 3 and 6 months postoperatively.[40]
- Endothelial cell loss estimates following DMEK vary widely, from 32-40% at 3 months to 36-40% at 6 months.[10][25][35][41] [42] [43] [44] At 1 year, studies have reported EC loss of around 19–36% at 1 year.[4][25][32][45][46] One study reported a median 5-year EC loss of 39% in DMEK (28 eyes), which is better than previous reports of DSEK (53%) and PKP (70%) performed for similar indications.[47]

Advantages of DMEK over DSAEK

DMEK has been shown to have superior visual outcomes when compared to DSAEK. In multiple studies where patients had DSAEK in one eye and DMEK in the fellow eye, significantly better visual acuity and preference were reported in the DMEK eye.[41][48] [49][50] Guerra[48] et al. reported a best corrected visual acuity in a DMEK group at 1 year of 20/24 compared to 20/32 in a DSAEK group. 85% reported a better quality of vision in the DMEK eye. Endothelial cell loss at 1 year was 31% in DMEK eyes and 34% in DSAEK eyes.[42][48]

However, some studies suggest that DSAEK visual outcomes can be improved by ultra-thin tissue.[51][52] Though recovery is slower with ultra-thin DSAEK versus DMEK, final visual outcomes at 1 year are comparable. If the ultra-thin DSAEK technique continues to improve, the ease and reliability of it may decrease the utilization of DMEK.[35][52]

DMEK also has a lower immunologic rejection rate and has the advantage of using a smaller incision (2.8 mm) than DSAEK (5 mm).[16]

Advantages of DSAEK over DMEK

Donor preparation and transplant surgery are technically easier with DSAEK. DSAEK is a more versatile procedure than DMEK, and is preferred in some complex cases although there is a lack of literature comparing the two procedures in this setting.[16] Although eye banks now can prestrip tissue for DMEK, some surgeons perform the entire stripping in the operating room, which carries the risk of destroying tissue at time of surgery.[19] There are higher rates of rebubbling and primary graft failure in DMEK compared to DSEK.[10][24][25][42][43][45][53]

Future Directions

DMEK is still a relatively new procedure and surgeons continue to develop many new techniques and strategies. The use of real-time intraoperative OCT[54] and femtosecond laser[55] with DMEK have continued to be developed. Eye banks will likely continue to play an important role in DMEK surgery, and their involvement with pre-stripping DMEK tissue decreases tissue wasting by the surgeon during preparation.[56] Enhancing endothelial cell number

and viability should remain an important research focus.[57] Descemet membrane endothelial transfer[58], gene therapy, or Rho-associated kinase inhibitors[59] are particularly exciting areas of research in this area. The utilization of cultured endothelial cell injections may also have a significant impact on the future of endothelial keratoplasty.[60]

Additional Resources

1. DMEK case report and detailed article from the University of Iowa[22], available at: http://webeye.ophth.uiowa.edu/eyeforum/cases/182-DMEK.htm
2. DMEK wet laboratory curriculum from the University of Michigan[21], available at: https://www.mededportal.org/publication/10101
3. DMEK tissue preparation video[18], available at: http://www.jove.com/video/51919/corneal-donor-tissue-preparation-for-descemet-s-membrane-endothelial
4. ASCRS 2015 DMEK course video[61]: https://www.youtube.com/watch?v=-QKhUMYRVCA
5. DMEK surgery video[62]: https://www.youtube.com/watch?v=AXXNkkBlSYo
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