**Title**: Free-floating DMEK in the host anterior chamber: surgical management

**Authors**: Nardine Menassa1, Luca Pagano1, Kunal Gadhvi1, Giulia Coco1, Stephen B Kaye1,2, Hannah J Levis2, Vito Romano1,2

**Affiliations:**

1St. Paul's Eye Unit, Royal Liverpool University Hospital, Liverpool, UK

2Department of Eye and Vision Science, Institute of Ageing and Chronic Disease, University of Liverpool, Liverpool, UK

**Correspondence:**

Vito Romano, MD

Department of Corneal and External Eye Diseases,

St Paul’s Eye Unit, Royal Liverpool University Hospital,

Liverpool, United Kingdom

Email: vito.romano@gmail.com

Tel: 0151 706 3997

**Disclosure**

None of the authors have any potential conflict of interest

**Abstract**

**Purpose:** To describe a method to visualize and manage a completely detached DMEK tissue scroll in the anterior chamber.

**Methods:** A 56-year-old male patient with pseudophakic bullous keratopathy, who underwent uncomplicated DMEK surgery, had a complete graft detachment diagnosed at one week follow up. The graft was re-attached using a new technique: the free-floating graft was stained in the anterior chamber with trypan blue, immediately followed by air injection to separate the host stroma from the dye. The stained DMEK graft was opened by gentle tapping and attached to the host stroma by air tamponade.

**Result:** This technique allowed sufficient staining of the DMEK tissue to further evaluate and correct the graft orientation inside the anterior chamber without compromising the stroma. The DMEK graft was attached one week after the re-attachment procedure. The cornea cleared confirming the functionality of the endothelial cells.

**Conclusion:** The technique described may be useful in cases of complete detachment of DMEK tissue and poor visualisation of the DMEK tissue orientation. Staining with trypan blue under a “protective” air bubble can provide sufficient visualisation to ensure the unfolding of DMEK tissue and reduce the risk of host stromal staining.

**Key words**

DMEK; surgical management; complication; graft detachment; Trypan blue staining

**Introduction**

Descemet’s Membrane Endothelial Keratoplasty (DMEK) is becoming one of the commonest types of corneal transplantation for endothelial dysfunction due to its fast visual rehabilitation and low risk of immunogenic rejection,1,2 however, it still poses numerous challenges such as the technically demanding graft preparation technique,3 length of the learning curve4,5 and most noticeably, early postoperative complications.1 Partial or complete graft detachment are more common in DMEK surgery compared to DSAEK (Descemet Stripping Automated Endothelial Keratoplasty). In DMEK surgery partial graft detachment has been noted in up to 62-63 % of cases,6,7,8 most of which are managed conservatively, the others (with more than 33% of graft area detached) undergo re-bubbling at the slit lamp or in the operating theatre, with a good rate of success.9 Instead, the rate of complete graft detachment after DMEK, when the graft has entirely peeled away from the posterior corneal surface and is free-floating in the anterior chamber, ranges from between 2.5%-17.5%.10,11 This is a challenging situation due to persistent corneal oedema, and therefore, graft repositioning manoeuvres are usually hampered due to poor visualisation of the graft. Intraoperative anterior segment optical coherence tomography (AS-OCT) or handheld slit beam illumination could be useful in cases of corneal opacities, however, they are not always available and not always helpful.12,13 Usually in these cases a re-DMEK or DSAEK is performed with a good clinical outcome. 14,15 Here we describe the surgical management of a free floating DMEK in the anterior chamber that allows rescue of the detached graft and prevents excessive staining of the stroma with Vision Blue.

**Materials and Methods**

A 56-year-old male patient with pseudophakic bullous keratopathy underwent an uncomplicated 8.5 mm DMEK graft and presented at one week follow up with corneal oedema due to complete graft detachment (Figure 1A, 2A). The patient was taken back to the operating theatre and a local anaesthesia (peribulbar block) was performed. Leaving the sutures in place, the oedematous epithelium was removed and another paracentesis was made with a MVR- Lance 20 gauge on the horizontal meridian (Figure 2B). Using a right cannula, trypan blue (Vision Blue® 0.06%, DORC, Zuidland, the Netherlands) was directly injected into the anterior chamber (Figure 2C) and was seen to cover the entire anterior chamber (Figure 2D). Air was then injected immediately into the anterior chamber following Vision Blue (Figure 2E) to protect the host stroma from staining by allowing an air bubble to rest adjacent to the bare stroma (Figure 2F). A small volume of aqueous was released from the anterior chamber in order to increase the bubble size and decrease the amount of free Vision Blue. After a staining period of 2 minutes, the residual Vision Blue was washed away using balanced salt solution. This allowed sufficient staining of the DMEK tissue to be visualized and correct the orientation of the DMEK graft during the unfolding procedure (Figure 2G). Once the graft was in the correct position, it was gently tapped and opened with Descemet’s membrane side facing the stroma (Figure 2H). The DMEK graft was attached to the host stroma using an air tamponade (Figure 2I) (Supp. Video 1) followed by topical cycloplegia and instillation of cyclopentolate 1% and phenylephrine 2.5% drops. The patient was postured supine for 48 hours to ensure the graft attached well to the host stroma in the anterior chamber. To highlight the consequences of 2 minutes of trypan blue staining on the bare stroma we performed a descemetorhexis and then stained the bare stroma of an ex vivo cornea. We imaged the cornea using a backlit dissection microscope and also a conventional camera with no back lighting.

**Results**

The rescued DMEK graft was attached on the first post-operative day with 50% residual air bubble still visible. At a post-operative visit one week later, no further complications were noted, the cornea was clear, and the graft attached, the central corneal thickness was 541 microns (Figure 1B).

The staining of the bare stroma with trypan blue for 2 minutes in the ex vivo experiment, especially with no back lighting (as would be seen in the patient under a surgical microscope in the operating theatre), highlighted the difficulties of visualization of the anterior chamber (Figure 3).

**Discussion**

Management of a completely detached DMEK tissue is challenging especially as the affected eyes present with epithelial and stromal oedema and poor visualisation. In a previous case series, it was observed that completely detached and upside-down DMEKs had to be replaced by DSAEKs.14,15. With the increase in popularity of DMEK surgery and growing surgical expertise in the procedure, replacing a DMEK with a new DMEK should now be considered as an alternative approach16. However, due to the limited availability of the donor corneas, it is not always feasible and so rescue of the original graft would be ideal. Mariacher et al. flipped an upside-down DMEK graft four weeks after the original procedure obtaining a favourable outcome.17 One option when using the same DMEK tissue in cases of a free floating DMEK grafts in the anterior chamber would be to remove the DMEK tissue from the chamber, re-stain it outside, reload it in the glass injector and reinject it. However, the loading and injection steps have been associated with endothelial cell loss18 so this method may not be ideal. Re-using a free floating DMEK by visualizing and orienting the graft in the anterior chamber may provide a safe and cost-effective solution. This technique has been described by Dragnea et al.19 in three patients where they inject Vision Blue into the anterior chamber to visualize the graft before reorientation, however, they do not use an air bubble to prevent stromal staining.

Trypan blue 0.06% is an effective and safe tool to enhance graft visualisation,20 however, it has high affinity to the stroma. Hence, tissue staining in the anterior chamber risks host stromal staining which can complicate surgical manoeuvres by obscuring the intraoperative view of the anterior chamber and the DMEK tissue.21 Furthermore, inadvertent stromal trypan blue staining seems to persist for months or longer and may be permanent in human tissue22. Jhanji et al. presented a case in which trypan blue was accidentally injected intra-stromally in an attempt to stain the anterior lens capsule and it was still present in the final day of follow up23. Farooq et al. described 4 cases of persistent staining in patients with lattice corneal dystrophy still present after 2 years of follow up.24.

Marking of the DMEK tissue using various letter marks 25 or cuts, even if visible after a long time,26 does not help to rescue a free floating DMEK. This is because the graft is still transparent as, on average, trypan blue dye only lasts 110 minutes 20 so any initial staining will not be present, increasing the difficulty of the unfolding manoeuvre. The marks (cuts or letter) are useful only to recognize the graft orientation, but only once the graft has been dyed. Hence our described technique reduces the risk of stromal staining and allows a more controlled manipulation of the DMEK tissue without the need to replace or re-stain outside of the eye that may lead to additional endothelial cell loss.

**References**

1. Stuart AJ, Romano V, Virgili G, Shortt AJ. Descemet's membrane endothelial keratoplasty (DMEK) versus Descemet's stripping automated endothelial keratoplasty (DSAEK) for corneal endothelial failure. Cochrane Database Syst Rev 2018;6:CD012097.
2. Parekh M, Salvalaio G, Ruzza A, Camposampiero D, Griffoni C, Zampini A, Ponzin D, Ferrari S. Posterior lamellar graft preparation: a prospective review from an eye bank on current and future aspects. J Ophthalmol 2013;2013:769860.
3. Parekh M, Borroni D, Ruzza A, Levis HJ, Ferrari S, Ponzin D, Romano V. [A comparative study on different Descemet membrane endothelial keratoplasty graft preparation techniques.](https://www.ncbi.nlm.nih.gov/pubmed/29520992) *Acta Ophthalmol* 2018;96:e718-e726
4. [Parekh M](https://www.ncbi.nlm.nih.gov/pubmed/?term=Parekh%20M%5BAuthor%5D&cauthor=true&cauthor_uid=29498968), [Ruzza A](https://www.ncbi.nlm.nih.gov/pubmed/?term=Ruzza%20A%5BAuthor%5D&cauthor=true&cauthor_uid=29498968), [Romano V](https://www.ncbi.nlm.nih.gov/pubmed/?term=Romano%20V%5BAuthor%5D&cauthor=true&cauthor_uid=29498968), [Favaro E](https://www.ncbi.nlm.nih.gov/pubmed/?term=Favaro%20E%5BAuthor%5D&cauthor=true&cauthor_uid=29498968), [Baruzzo M](https://www.ncbi.nlm.nih.gov/pubmed/?term=Baruzzo%20M%5BAuthor%5D&cauthor=true&cauthor_uid=29498968), [Salvalaio G](https://www.ncbi.nlm.nih.gov/pubmed/?term=Salvalaio%20G%5BAuthor%5D&cauthor=true&cauthor_uid=29498968), [Grassetto A](https://www.ncbi.nlm.nih.gov/pubmed/?term=Grassetto%20A%5BAuthor%5D&cauthor=true&cauthor_uid=29498968), [Ferrari S](https://www.ncbi.nlm.nih.gov/pubmed/?term=Ferrari%20S%5BAuthor%5D&cauthor=true&cauthor_uid=29498968), [Ponzin D](https://www.ncbi.nlm.nih.gov/pubmed/?term=Ponzin%20D%5BAuthor%5D&cauthor=true&cauthor_uid=29498968). Descemet Membrane Endothelial Keratoplasty Learning Curve for Graft Preparation in an Eye Bank Using 645 Donor Corneas. *Cornea* 2018;37:767-771.
5. Parekh M, Baruzzo M, Favaro E, Borroni D, Ferrari S, Ponzin D, Ruzza A. [Standardizing Descemet Membrane Endothelial Keratoplasty Graft Preparation Method in the Eye Bank-Experience of 527 Descemet Membrane Endothelial Keratoplasty Tissues.](https://www.ncbi.nlm.nih.gov/pubmed/28968293) *Cornea* 2017;36:1458-1466.
6. Guerra FP, Anshu A, Price MO, et al. Descemet’s membrane endothelial keratoplasty: prospective study of 1-year visual outcomes, graft survival, and endothelial cell loss. Ophthalmology. 2011;118:2368e73
7. Guerra FP, Anshu A, Price MO, et al. Endothelial keratoplasty: fellow eyes comparison of Descemet stripping automated endothelial keratoplasty and Descemet membrane endothelial keratoplasty. Cornea. 2011;30:1382e6
8. Price MO, Giebel AW, Fairchild KM, et al. Descemet’s membrane endothelial keratoplasty: prospective multicentre study of visual and refractive outcomes and endothelial survival. Ophthalmology. 2009;116:2361e8
9. Vasquez-Perez A, Allan B, Fernandez-Vega Cueto L, Aiello F. Paracentesis as valve re-bubbling technique for Descemet's membrane endothelial keratoplasty (DMEK) graft detachment. Int Ophthalmol. 2020 Jan 25. doi: 10.1007/s10792-020-01295-7.
10. Parekh M, Leon P, Ruzza A, Borroni D, Ferrari S, Ponzin D, Romano V. Graft detachment and rebubbling rate in Descemet membrane endothelial keratoplasty. *Surv Ophthalmol* 2018;63:245-250.
11. Dapena I, Moutsouris K, Ham L, Melles GR. Graft detachment rate. *Ophthalmology* 2010;117:847–847.e1.
12. [Burkhart ZN](https://www.ncbi.nlm.nih.gov/pubmed/?term=Burkhart%20ZN%5BAuthor%5D&cauthor=true&cauthor_uid=23407317), [Feng MT](https://www.ncbi.nlm.nih.gov/pubmed/?term=Feng%20MT%5BAuthor%5D&cauthor=true&cauthor_uid=23407317), [Price MO](https://www.ncbi.nlm.nih.gov/pubmed/?term=Price%20MO%5BAuthor%5D&cauthor=true&cauthor_uid=23407317), [Price FW](https://www.ncbi.nlm.nih.gov/pubmed/?term=Price%20FW%5BAuthor%5D&cauthor=true&cauthor_uid=23407317). Handheld slit beam techniques to facilitate DMEK and DALK. *Cornea* 2013;32:722-4.

Cost B, Goshe JM, Srivastava S, Ehlers JP. Intraoperative optical coherence tomography-assisted descemet membrane endothelial keratoplasty in the DISCOVER study. Am J Ophthalmol. 2015 Sep;160:430-7

Dirisamer M, van Dijk K, Dapena I, Ham L, Oganes O, Frank LE, Melles GR. [Prevention and management of graft detachment in descemet membrane endothelial keratoplasty.](https://www.ncbi.nlm.nih.gov/pubmed/22084160) *Arch Ophthalmol* 2012;130:280-91.

Dapena, I., Ham, L., van Luijk, C., van der Wees, J., & Melles, G. R. J. Back-up procedure for graft failure in Descemet membrane endothelial keratoplasty (DMEK). *British Journal of Ophthalmology* 2009;94:241–244.

1. Baydoun L, van Dijk K, Dapena I, et al. Repeat Descemet membrane endothelial keratoplasty after complicated primary Descemet membrane endothelial keratoplasty. *Ophthalmology* 2015;122:8–16.
2. Mariacher S, Mariacher M, Boden KT, Szurman P, Januschowski K. Favourable outcome after late reorientation of an upside-down Descemet Membrane Endothelial Keratoplasty (DMEK) graft: a case report. *BMC Ophthalmol* 2019;19:163.
3. [Droutsas K](https://www.ncbi.nlm.nih.gov/pubmed/?term=Droutsas%20K%5BAuthor%5D&cauthor=true&cauthor_uid=29148524), [Lazaridis A](https://www.ncbi.nlm.nih.gov/pubmed/?term=Lazaridis%20A%5BAuthor%5D&cauthor=true&cauthor_uid=29148524), [Kymionis GD](https://www.ncbi.nlm.nih.gov/pubmed/?term=Kymionis%20GD%5BAuthor%5D&cauthor=true&cauthor_uid=29148524), [Chatzistefanou K](https://www.ncbi.nlm.nih.gov/pubmed/?term=Chatzistefanou%20K%5BAuthor%5D&cauthor=true&cauthor_uid=29148524), [Moschos MM](https://www.ncbi.nlm.nih.gov/pubmed/?term=Moschos%20MM%5BAuthor%5D&cauthor=true&cauthor_uid=29148524), [Koutsandrea C](https://www.ncbi.nlm.nih.gov/pubmed/?term=Koutsandrea%20C%5BAuthor%5D&cauthor=true&cauthor_uid=29148524), [Sekundo W](https://www.ncbi.nlm.nih.gov/pubmed/?term=Sekundo%20W%5BAuthor%5D&cauthor=true&cauthor_uid=29148524) Comparison of endothelial cell loss and complications following DMEK with the use of three different graft injectors. *Eye (Lond)* 2018;32:19-25.
4. Dragnea DC, Nobacht S, Gericke A, Parker J, Oellerich S, Ham L, Melles GRJ.

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Keratoplasty Grafts. Cornea. 2019 Feb;38:162-165.

1. Majmudar PA, Johnson L. Enhancing DMEK success by identifying opti- mal levels of trypan blue dye application to donor corneal tissue. Cornea 2017;36:217–21.
2. [Fernández López E](https://www.ncbi.nlm.nih.gov/pubmed/?term=Fern%C3%A1ndez%20L%C3%B3pez%20E%5BAuthor%5D&cauthor=true&cauthor_uid=27055219), [Baydoun L](https://www.ncbi.nlm.nih.gov/pubmed/?term=Baydoun%20L%5BAuthor%5D&cauthor=true&cauthor_uid=27055219), [Gerber-Hollbach N](https://www.ncbi.nlm.nih.gov/pubmed/?term=Gerber-Hollbach%20N%5BAuthor%5D&cauthor=true&cauthor_uid=27055219), [Dapena I](https://www.ncbi.nlm.nih.gov/pubmed/?term=Dapena%20I%5BAuthor%5D&cauthor=true&cauthor_uid=27055219), [Liarakos VS](https://www.ncbi.nlm.nih.gov/pubmed/?term=Liarakos%20VS%5BAuthor%5D&cauthor=true&cauthor_uid=27055219), [Ham L](https://www.ncbi.nlm.nih.gov/pubmed/?term=Ham%20L%5BAuthor%5D&cauthor=true&cauthor_uid=27055219), [Melles GR](https://www.ncbi.nlm.nih.gov/pubmed/?term=Melles%20GR%5BAuthor%5D&cauthor=true&cauthor_uid=27055219). Rebubbling Techniques for Graft Detachment After Descemet Membrane Endothelial Keratoplasty. *Cornea* 2016;35:759-64.
3. Marcon A, Périllat N, Garcin T, et al. Transplantation Blues: Inadvertent Staining of Amyloid Deposits With Trypan Blue. *Cornea* 2018;37:824–828.
4. Jhanji V, Agarwal T, Titiyal JS. Inadvertent corneal stromal staining by trypan blue during cataract surgery. *J Cataract Refract Surg* 2008;34:161–162.

Farooq AV, Tu EY, D'jalilian AR, Traish AS, Hou JH. Persistent staining of lattice lines after intraoperative trypan blue use in patients with lattice corneal dystrophy. *Cornea* 2014;33:1235–1237.

1. Veldman PB, Dye PK, Holiman JD, et al. Stamping an S on DMEK donor tissue to prevent upside-down grafts: laboratory validation and detailed preparation technique description. *Cornea* 2015;34:1175–8.

Romano V, Parekh M, Ruzza A, Willoughby CE, Ferrari S, Ponzin D, Kaye SB, Levis HJ. Comparison of preservation and transportation protocols for preloaded Descemet membrane endothelial keratoplasty. *Br J Ophthalmol* 2018;102:549-555.

**Figure legends**

**Figure 1:** Anterior segment –optical coherence tomography A) at 1-week follow-up to observe the primary DMEK scroll that was completely detached (magnified view of free floating section in inset). B) at 1 week follow up after second procedure.

**Figure 2:** A)Corneal oedema as observed on the patient after 1 week. B) First incision to advance the cannula in the anterior chamber. C) Injection of Vision Blue in the anterior chamber and D) covering the entire anterior chamber. E) Injection of air immediately into the anterior chamber to avoid host corneal staining F) while protecting the host stroma from staining. G) washing off the Vision Blue to visualize and correct the orientation of the DMEK graft during unfolding procedure. H) Gently opening while correcting the orientation of the DMEK graft facing the stroma. I) Attaching the DMEK graft to the host stroma using air tamponade.

**Figure 3**. Ex vivo cornea stained with trypan blue for 2 minutes imaged with A) conventional camera and no back lighting as would be in a patient. B) on a dissection microscope to highlight the level of the staining to the stroma.

**Supplementary video legend**

**Supplementary video 1:** The video shows surgical management of a completely detached DMEK graft in the anterior chamber.