

Pre-Descemets endothelial keratoplasty: the PDEK clamp for successful PDEK

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Abstract

Purpose To design and produce a clamp that enables good handling of donor sclera-corneal disks, allows air to be injected in the corneal stroma and consistently provides pre-Descemets endothelial keratoplasty (PDEK) tissue by creation of a type-1 big bubble (BB) avoiding a type-2BB by shutting the fenestrations in the periphery of the pre-Descemets layer and preventing escape of air.

Patients and methods A clamp with spring loaded handles attached to two rings of 9 mm diameter and 1 mm width with a side port for insertion of a needle for air injection was designed and produced. The clamp was tested in 20 human donor sclera-corneal disks and refined over three prototypes. The final design was used for PDEK in 8 patients.

Results The clamp was able to prevent any escape of air or the formation of a type-2BB. By preventing air leak, it provided better control over the volume of air injected allowing for consistent formation of a type-1BB, which could be expanded to its full diameter by advancing the tip of the needle into the bubble cavity. Centration of tissue in the clamp was important. The clamp was used successfully to obtain PDEK tissue from 8 donor sclera-corneal disks for transplant in three eyes with pseudophakic bullous keratopathy and five eyes with pseudophakia and Fuchs' endothelial dystrophy.

Conclusion The PDEK clamp is a simple and useful instrument that will give surgeons the confidence of consistently obtaining PDEK tissue with ease and without the risk of separating the Descemets membrane in a type-2BB.

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Introduction

Lamellar corneal grafts have not only revolutionized corneal transplantation surgery but have also provided insights into posterior corneal anatomy.^{1–5} In most specialist centers, deep anterior lamellar keratoplasty (DALK) has replaced penetrating keratoplasty (PK) for indications related to corneal stromal pathology; and endothelial keratoplasty (EK) has become the procedure of choice for all indications related to corneal endothelial dysfunction. For EK, Descemets membrane EK (DMEK) is considered to be a major improvement over Descemets stripping EK but has certain limitations.^{1–4} It is technically challenging both surgically and in donor tissue preparation. Younger corneas with associated high endothelial cell counts cannot usually be used due to the increased risk of tissue loss related to the firm adhesion of DM.^{6–8} Tight DM scrolls are difficult to unroll resulting to excessive endothelial cell loss during intraoperative handling.⁹

Pre-Descemets EK (PDEK) is the latest innovation in EK. The concept was introduced by Dua *et al*⁵ and the first case series was reported in 2014.¹⁰ It involves the intrastromal injection of air in a donor sclera-corneal disk to create a type-1 big bubble (BB).⁵ The wall of the BB, comprised of the pre-Descemets layer (Dua's layer (PDL)),⁵ DM and endothelium is trephined or excised with scissors and used as the donor material for EK. Prior to this report,⁵ others had used pneumodissection to produce DMEK tissue.¹¹ Inadvertently some had produced PDEK tissue but were unaware of this fact and had performed and reported the procedure as DMEK,¹¹ as the knowledge of the difference between PDEK and DMEK tissue did not exist. A reference to the prevailing misunderstanding at the time has been made in the original publication on PDEK.¹⁰ PDEK tissue scrolls less than DMEK tissue,¹² is easier to handle and unroll in the anterior chamber¹⁰ and can be harvested from very young donors.⁸ However, there are two

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limitations, the maximum diameter possible is between 7.5 and 8.5 mm and at times intrastromal injection or air can result in a type-2BB⁵ (separation of DM without PDL), enforcing conversion to DMEK for which the surgeon may not have the desirable experience.

We have demonstrated that during pneumodissection a type-2BB results from the escape of air through clusters of holes in the periphery of the PDL, along the circumference of the corneal periphery.^{13,14} These holes allow air to pass through the PDL which is otherwise impermeable to air. Air injected in the corneal stroma, anterior to the PDL accesses the plane between PDL and DM, lifting the DM off to produce a type-2BB.^{13,14} Based on this knowledge we designed a clamp to ensure that the chances of getting a type-2BB are markedly reduced if not entirely eliminated.

Materials and methods

Based on the observation that a type-2BB almost always starts at the periphery of the sclera-corneal disk and commencement of the BB correlates with the location of tiny perforations in PDL at the periphery, we hypothesized that by occluding the holes during air injection the probability of a type-2BB forming could be

markedly reduced or eliminated. The aim was to design a clamp that shuts out the peripheral holes and prevents formation of a type-2BB; provides a firm grip on the donor sclera-corneal disk and easy access for insertion of the needle to inject air. We designed a PDEK clamp and partnered with e. Janach (Via Borgo Vico 35 22100 Como—Italy) to manufacture and develop a prototype.

PDEK clamp design

The PDEK clamp (Figure 1a) is made of steel and has a spring handle with two complementary rings (internal diameter of 9 mm) and a central locking screw for maintaining the clamp in a closed position. The rings are 1-mm wide with the opposing surfaces sand-blasted for a better grip (Figure 1b). At 45° from the attachment of the handle to the lower ring, which is thicker than the upper ring, is a side port of 0.7 mm × 1.7 mm (Figure 1c) with a corresponding small notch in the upper ring to give the port a dimension of about 0.9 mm in the closed position. The site of the port is marked by an etching on the upper ring (Figure 1c). In the fully open position the rings are 10 mm apart.

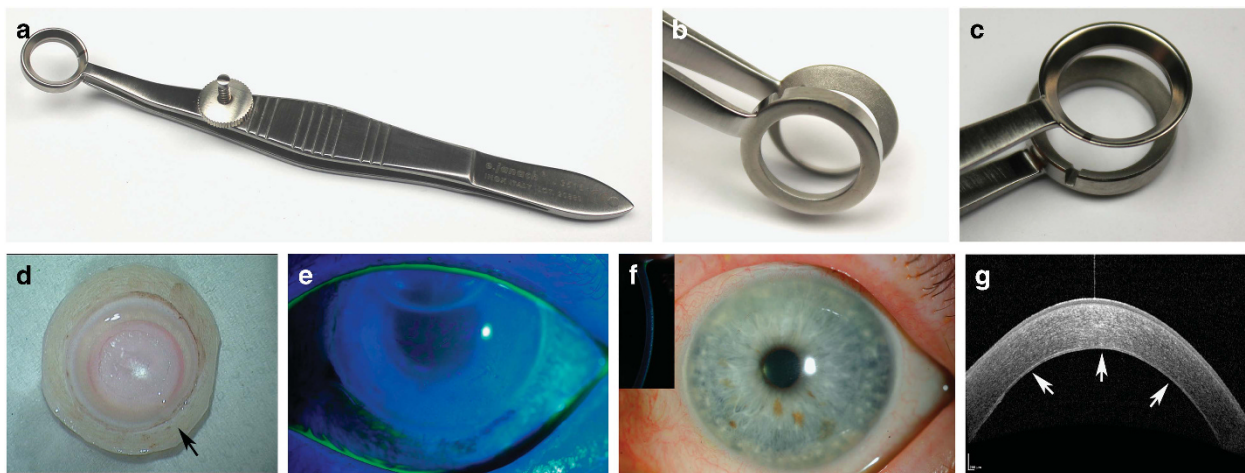


Figure 1 (a) The PDEK clamp with two rings of an internal diameter of 9 mm, in the closed position. When a sclera-corneal disk is placed between the rings and the clamp closed, the rings compress the peripheral holes and prevent escape of injected air in to the plane anterior to the DM. (b) The opposing surfaces of the ring are sand blasted to make the surface rough for a better grip. This is clearly seen on the under surface of the upper ring. (c) Illustrates the side port in the lower ring next to the handle. Its position is marked by an etching on the upper ring as the port cannot be directly visualized when the tissue is clamped between the rings. (d) A sclera-corneal disk that was clamped in the PDEK clamp to obtain a type-1BB. The central white area with a type-1BB represents the aerated corneal stroma. The surrounding clear circumferential zone is the part that was compressed in the PDEK clamp. No air entered this zone. The arrow marks the point of entry of the needle used for injecting air through the side port of the PDEK clamp. (e) Slit lamp diffuse image with cobalt blue filter of a cornea stained with fluorescein dye to illustrate the post-operative day-1 image of an eye treated with PDEK for bullous keratopathy. The bullae are visible in the central cornea and a partially absorbed air bubble injected during the procedure to tamponade the PDEK tissue is seen in the upper part of the anterior chamber. (f) The same cornea as in E, one month post-PDEK. The cornea is very clear and the edge of the PDEK graft is clearly visible in the superior temporal quadrant. The interface of the PDEK graft and host corneal stroma cannot be seen on a slit beam image (inset). (g) Optical coherence tomography image of the same eye at 1 month post-PDEK. A double contour line is seen at the posterior surface of the cornea (arrows) representing the PDEK tissue.

PDEK clamp use and validation

With the clamp fully open, the sclera-corneal disk, endothelial side up, is placed on the lower ring and centered. The transparency of the cornea allows visualization of the ring underneath and helps with centering. The clamp is then closed and the screw tightened. Under an operating microscope, the disk is held on a black plate (provided with the clamp) for better contrast and a 30-gauge needle, bent at 135°, attached to a 5 ml syringe filled with air, is inserted through the side port, starting in the scleral rim and advanced to the center of the cornea in mid-stroma. The clamped disk obscures visualization of the port but the etching on the upper ring indicates the point for insertion of the needle. Air is firmly but slowly injected into the stroma. When the stroma is fully aerated it becomes white and tiny bubbles form in the center under the PDL. These coalesce to form a type-1BB (Figure 1d). Once the BB has formed, the needle can be tilted and directed into the cavity of the bubble to expand it further by injection of more air (Supplementary video clip 1). The air is then aspirated to collapse the bubble and the clamp opened and the disk removed. Alternatively, with the bubble inflated, the clamp can be opened and the tissue withdrawn (Figure 1d).

The PDEK clamp was tested in 20 human eye bank donor eyes provided by the National Health Service Blood and Transplant Eye Banks and duly consented for research and development. Details of the donor eyes are given in Table 1. The use of air injection for lamellar corneal separation was approved by Nottingham research ethics committee-1 (06-Q2403-46).

Retrieval of PDEK tissue

PDEK tissue was retrieved in two ways as previously described.¹⁰ When air is aspirated to collapse the type-1BB, a circular disk of PDEK tissue can be punched out using a trephine of appropriate diameter. Alternatively, when the sclera-corneal disk is removed from the clamp with an inflated type-1BB, the wall of the bubble is incised with a sharp knife at the attachment to the stroma, the tissue is stained by injecting VisionBlue (Dutch ophthalmic, USA) in to the bubble, and the PDEK tissue is

separated by cutting along the circumference of the BB (Supplementary video clip 2).

Results

The dimensions of the clamp were optimized over three versions. In the first version the diameter of the rings was set at 10 mm, and the width of the rings was 0.5 mm. This did not completely occlude all the peripheral holes and a type-2BB was formed in 2 of the 5 disks tested with this version. This version was not used to harvest PDEK tissue for human transplantation. In the second version, the inner diameter was reduced to 9 mm and the width of the rings increased to 1 mm. With this, no leakage of air was seen and the desired type-1BB formed in 13 of 13 sclera-corneal disks where the rings were accurately centered. However, in 2 samples a type-2BB formed. In both these instances the tissue was decentered in the clamp. This version confirmed that the desired objective of occluding the peripheral fenestrations was achieved and no escape of air occurred. However the side port was considered to be narrow as it restricted manipulation of the needle in the corneal stroma. This version too was not used to harvest PDEK tissue for human transplantation. In the third and final version, the dimension and trajectory of the side port were revised to allow insertion of the needle in the horizontal plane even though the slope of the rings is directed downwards (Figure 1c) and the size enlarged to 0.7 × 1.7 mm to allow easy manipulation of the needle compared to the previous version where it was smaller and the trajectory was directed slightly downwards. The width of the fully open clamp allowed removal of the sclera-corneal disk with an inflated type-1BB without any contact of the endothelial surface with the upper ring.

Only the final version presented here (Figure 1) was used to perform PDEK in 3 eyes with pseudophakic bullous keratopathy and 5 eyes with pseudophakia and Fuchs' endothelial dystrophy. PDEK tissue was successfully obtained in all cases using the PDEK clamp and PDEK completed (Figure 1e–g).

Discussion

Air injection in the corneal stroma of patients was described initially by Anwar and Teichmann¹⁵ in the DALK procedure. However, the procedure was described as a 'Descemet's baring technique',^{15,16} which was later proved not to be the case and a distinct pre-Descemet's layer, offering a cleavage plane during pneumodissection, was reported in a couple of international meetings.^{5,14} Others reported 'residual stroma' on the anterior surface of the DM in both *in vivo* and *ex vivo* procedures.^{17,18} A detailed description and characterization of the PDL and types of BB was published in 2013.⁵ Although the concept

Table 1 Donor details of Sclera-corneal disks used in the study

Sex		Age (years)		Time in storage (weeks)		Cause of death		
Male	Female	55–60	61–83	4–6	6–9	Cardiac	Stroke	Other
8	12	4	16	7	13	5	7	8

Other: sepsis, pneumonia and malignancy. Central corneal thickness ranged from 650 to 730 μ.

was initially challenged¹⁹ a number of publications have contributed to the further characterization of the PDL and its attributes. It is a very tough layer with a high bursting pressure such that phacoemulsification can be performed under this layer in the DALK-triple procedure.²⁰ It is unique such that if ablated by excimer laser phototherapeutic keratectomy air injection in the stroma does not result in the formation of a type-1BB,²¹ it is continuous at the periphery with the collagen core of the trabecular meshwork,²² has a higher concentration of elastin than the rest of the corneal stroma,²³ and has a paucity or an absence of keratocytes.^{5,24} A recent high-resolution optical coherence tomography study has demonstrated the layer *in vivo* in humans.²⁴

Clinically there is no doubt that it forms an important part of the surgical anatomy of the cornea. Its 'rough' looking anterior surface enables intraoperative differentiation of a type-1 from a type-2BB.²⁵ It offers a distinct surgical plane that can be exploited to complete successful DALK when a BB does not form^{14,26} and also determines spread of infections.²⁷ Spontaneous separation of the PDL from the deep stroma is seen in acute hydrops and following cataract surgery.^{28,29} Besides the DALK-triple procedure,²⁰ knowledge of PDL has been exploited in the management of acute hydrops in keratoconus²⁹ and in the PDEK operation.¹⁰

In PDEK tissue, PDL splints the DM and limits the scrolling of the tissue and also facilitates handling and centration of the tissue both inside and outside the eye. Endothelial cell counts in PDEK tissue have been shown to be similar to that in DMEK tissue obtained by pneumodissection³⁰ and one study has shown that both PDEK and DMEK tissue can be stored in organ culture for a week without affecting endothelial cell counts.³¹ Thus far in PDEK the predictability of consistently obtaining a type-1BB is limited because injected air escapes from natural fenestrations located on either side of the trabecular meshwork beyond the termination of the DM. Therefore, in order to obtain a critical intra-tissue pressure to produce a type-1BB the surgeon has to adjust the pressure on the plunger of the air filled syringe to compensate for the loss of air. If too much force is applied the bubble can form rapidly and burst. If too little force is applied a small type-1BB can form giving a PDEK tissue of variable diameter. Further, as hypothesized, when the fenestrations are central to the termination of the DM, a type-2BB can form. The PDEK clamp overcomes all the above limitations. The clamp completely shuts off the peripheral holes and all the air injected is retained in the corneal stroma and with no loss due to leakage. The intrastromal pressure can therefore be increased in a controlled manner until a BB has formed. The fenestrations in PDL anterior to the DM are also closed by the clamp and thus a type-2BB does not form.

To ensure that the above advantages of the clamp are achieved proper centration of the tissue is important. The clamp also permits robust handling of the tissue without an assistant. Once a type-1BB has formed the needle can be maneuvered to advance the tip in the cavity of the bubble and more air can be injected to expand the diameter of the bubble by 0.5–1 mm thus enabling a larger diameter of PDEK tissue.

Sclera-corneal disks used for testing and developing the clamp were stored and supplied by NHSBT in tissue culture medium without dextran. These were comparatively thicker than the disks used for human transplantation, which were in medium containing dextran to deturgescence them. Apart from the extra care required during insertion of the needle to avoid perforation, there was no difference in the ability to obtain the desired type-1BB with the clamp, in the sclera-corneal disks stored with and without dextran. The PDEK clamp should prove to be a simple useful instrument that will give surgeons the confidence of consistently obtaining PDEK tissue without risk of creating a type-2BB.

Summary

What was known before

- Pre-Descemet's endothelial keratoplasty (PDEK) is a viable option for endothelial keratoplasty.
- PDEK tissue is obtained by intracorneal injection of air.
- Escape of air from peripheral fenestrations makes retrieval of PDEK tissue unpredictable and inconsistent.
- If the Descemet's membrane is separated by air (type-2 big bubble (BB)) Descemet's membrane EK has to be performed.

What this study adds

- The new surgical instrument, the PDEK clamp, shuts out the peripheral fenestrations and prevents air loss.
- It prevents formation of a type-2BB.
- It allows for good handling of the donor tissue and controlled injection of air so that the largest possible size of PDEK tissue can be consistently obtained.

Conflict of interest

HSD is the inventor of the PDEK clamp, which is manufactured by e. janach, Italy. The instrument is not patented and no money has been paid by the manufacturer to the inventor.

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Supplementary Information accompanies this paper on EYE website (<http://www.nature.com/eye>)