A New Graft Insertion Device for Descemet Stripping Automated Endothelial Keratoplasty.

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ABSTRACT

Purpose: Corneal endothelial dysfunction is a major indicator for corneal graft surgery worldwide, and whilst surgical intervention via a range of posterior lamellar surgeries has proven to be hugely beneficial, challenges remain. This is especially so where the anterior chamber is relatively shallow, as is often the case in the Asian population, though not exclusively so. Here, we introduce a new insertion device to deliver endothelial graft tissue for Descemet stripping automated endothelial keratoplasty (DSAEK).

Methods: A new surgical tool was designed and manufactured so as to enable a one-step insertion of corneal graft tissue into the anterior chamber based on a pressure-flow concept, rather than the a pull-through one. This was tested *ex vivo* to assess endothelial cell damage, then performed in 12 first-in-man surgeries.

Results: Pre-cut DSAEK lenticules implanted in donor corneas *ex vivo* via the new technique showed less endothelial cell damage occurs compared to a pull-through technique. Grafts were successful in all patients receiving the new surgery, with no cases of primary graft failure.

Conclusion: The newly developed DSAEK inserter is a simple and useful tool for endothelial graft delivery, lessening intraoperative mechanical stress on the graft tissue

INTRODUCTION

Although Descemet's membrane endothelial keratoplasty (DMEK)[1] has been supplanting Descemet stripping automated keratoplasty (DSAEK) in recent years, leading to faster visual rehabilitation and better visual outcome, graft detachments, failures and difficulties manipulating the delicate tissue are associated risks, which may in part account for the situation that established DSAEK surgery is often preferred to DMEK. In DSAEK, however, folding and grasping the donor tissue with forceps or pull-through technique using glides to enable graft insertion through a small incision can represent a challenge,[2-4] and this is particularly so in Asian eyes, which tend to have shallower anterior chambers. One significant complication with DSAEK is endothelial cell loss, especially in the early postoperative period.[5-7] Consequently, there is a growing demand for a surgical graft delivery system for DSAEK that allows for easy manipulation of graft tissue, whilst also minimizing mechanical stress on the graft and helping prevent anterior chamber collapse during surgery. Partially in response to this need, techniques such as the Sheets glide insertion method and the Tan Endoglide were specifically developed for Asian eyes, and their utility has been reported.[8,9]

In cataract surgery, the shift away from intraocular lens (IOL) insertion using forceps to graft insertion using injectors has undoubtedly contributed to improved

outcomes. In DSAEK, the superiority of graft insertion devices over forceps has not been demonstrated unequivocally,[10-12] nevertheless, the use of insertion devices has become increasingly popular in recent years. Essentially, DSAEK insertion devices can be categorized into three groups based on their mechanism of action; the folding technique (i.e. taco-folding), pull-through designs (glides) and push-in designs (injectors).[13] By applying the fundamental concept of an IOL injector to the DSAEK insertion device, we have developed a new surgical tool in which the donor graft is introduced into anterior chamber along with a steady flow of balanced salt solution (BSS). Here, we describe the device's design, mode of action, and use in 12 first-in-man surgeries.

METHODS

Device Design and Surgical Technique

The new DSAEK graft inserter consists of the main body of the device, which is made of polypropylene, with a hydrophilically coated and flexible polyethylene platform at its front end on which the pre-cut graft lenticule is placed just prior to surgery, endothelial cells facing upwards. A movable polypropylene cartridge is fitted to the main body, along with a valved conduit made of silicone rubber. A 2.5ml syringe, to be filled with BSS prior to surgery, is continuous with the main body of the

inserter. Overall, the device measures 8.5 mm in width, is 63 mm long, and weighs 1.85 g. The major and minor axes of the lumen of the new inserter's nozzle are 3.57 mm and 2.02 mm, respectively. It is intended for single use (Figure 1).

To operate, the syringe is first filled with BSS after which the plunger is partially depressed to lubricate the surface of the hydrophilic platform with BSS. The DSAEK graft is then carefully placed onto the platform (Figure 2A), endothelial cells facing upwards, using forceps. Importantly, the surface of the graft insertion platform remains lubricated owing to the hydrophilic nature of the platform's coating, which is a key design feature to prevent the graft from adhering to the platform. After the graft coated with viscoelastic gel is in place on the platform, the flexible platform and graft are partially rolled up and drawn within the main body of the inserter by steadily moving the cartridge forward (Figure 2B).This is achieved via another important design feature, i.e. a valved conduit located on the inner tube of the movable cartridge. Thus, when the cartridge is moved forward over the platform holding the graft, a negative pressure is generated which keeps the graft in position as the flexible platform is partially rolled up and enclosed in the inner cylinder of main body of the device. This closed system for fluid flow has an additional benefit in that it prevents anterior chamber collapse when delivering the corneal graft into the recipient's eye. Prior to inserting the graft into the recipient's eye the insertion device

is rotated 180 degrees around its axis, so that the corneal endothelial cells on the inner aspect of the partially rolled-up lenticel face away from the posterior corneal surface once injected into the anterior chamber. During graft insertion through a pre-made, 4.6 mm incision in the peripheral cornea, the leading edge of the cartridge tip of the inserter enters the anterior chamber, but is not projected deeply into the chamber. The graft can then be delivered into anterior chamber, along with BSS, by gently depressing the syringe's plunger (Figure 2C). The graft moves readily into the anterior chamber because water molecules retained on the hydrophilic polymers of the platform on which it sits work as carrier to allow the graft to slip smoothly across and off the platform once the flow of BSS is started.

Ex Vivo **Testing**

A single donor cornea, obtained from the SightLife Eye Bank (Seattle, WA, USA) was used as an *ex vivo* proxy to represent the recipient tissue. This was secured on an artificial anterior chamber (K20-2125 Barron Artificial Anterior Chamber, Katena, Denville, NJ, USA). A 20 gauge chamber maintainer (#19092, Moria) was used to maintain the tissue's shape, after which a 5.0 mm corneal incision was created in the corneal periphery to allow graft insertion. Ten research pre-cut corneal lenticules from the same Eye Bank were obtained, and DSAEK was carried out in 10 test

surgeries; five using the new DSAEK insertion system and five using a 5.0 mm Busin spatula (#19098, Moria, Doylestown, PA) and the pull-through technique. The mean thickness of pre-cut donor grafts used for the pull-through Busin glide surgery was 113 ± 11 μm (average ± SD, range; 96-124 μm); for the inserter test-surgeries it was 126 ± 22 μm (range; 98-149 μm). Donor lenticules were 8 mm in diameter. After each procedure the graft tissue was removed from the anterior chamber and stained with 0.25% alizarin Red S and 4 % trypan blue for 90 s to assess the general level of endothelial cell damage[14] using Image J in accordance with method of Saad and associates.[15]

Clinical Applicability

Twelve patients underwent DSAEK with the new insertion device between July 2016 and Jan 2017, after which intra- and early postoperative outcomes were examined. Underlying diseases were cytomegalovirus endotheliitis (3 eyes), pseudophakic bullous keratopathy (2 eyes), post intraocular surgery (2 eyes), exfoliation syndrome (2 eyes), Fuchs' endothelial corneal dystrophy (2 eyes), and argon laser iridotomy-induced bullous keratopathy (1 eye) and the average observation period was 172 days ± 62 days (range, 89-265 days). In particular, we sought signs of a failure of the graft tissue to be smoothly and successfully inserted into the eye, of anterior

chamber collapse during surgery, and of graft dislocation or detachment afterwards. The work adhered to the tenets of the Declaration of Helsinki and was approved by the institutional review board of Osaka University Hospital.

All surgeries were performed by one of two surgeons (T.S., K.N.), both of whom had previously used a Busin glide to conduct DSAEK, either under local retrobulbar anestasia and facial nerve block or under general anaesthesia. Pre-cut donor corneas (target thickness, 100 μm) from SightLife Eye Bank were used in all cases. After the anterior chamber maintainer was set-up, Descemet membrane and the endothelium were stripped from the recipient's central cornea (this step was omitted in the case of non-Descemet stripping automated endothelial keratoplasty (nDSAEK)).[16] An inferior peripheral iridectomy was then created with 25-gauge vitreous cutter, and two nasal and temporal vent incisions were fashioned at the inner side of the recipient corneal marking. Following its trephination, the donor graft was placed on the flexible, hydrophilic graft insertion platform of the new inserter. After applying dispersive ophthalmic viscoelastic material (Viscoat; Alcon laboratories, Fort Worth, TX) over the entire endothelial graft, the platform and graft were rolled up and enclosed into the main body of the device by sliding the movable cartridge forward. (Figure 2 and Supplementary Information 1). As mentioned earlier, as a result of the negative pressure exerted by the inserter, the lenticule is rolled up

and engulfed into the main body of the device (while still on the flexible hydrophilic platform) without being touched with forceps or any other surgical tool. Also, we note here that after the placement of the graft on the platform (the last time it is contacted physically) it should be coated with a dispersive ophthalmic viscosurgical formulation rather than a cohesive form to lessen the risk of clumps of material being flushed into the anterior chamber when BSS flow is initiated. Once the graft had been loaded into the inserter, the nozzle was placed into anterior chamber through the 4.6 mm temporal corneoscleral tunnel and the graft delivered into the anterior chamber along with a flow of BSS by simply depressing the plunger of the syringe. The anterior chamber maintainer was turned off during graft insertion (Figure 2 and Supplementary Information 1), its use only being needed during the peripheral iridectomy using vitreous cutters and Descemetorhexis. After removal of the insertion device an air tamponade was performed to ensure good graft-host apposition. All patients held their posture facing upward on their beds for three hours following the operation.

RESULTS

Preliminary *ex vivo* test surgeries established the successful working of the procedure and the new insertion device. Figure 3 shows the post-operative corneal

staining patterns for all 10 test surgeries, five conducted using the Busin glide and five with the new inserter. No unusual staining characteristics of note were detected in the corneas following surgery with the new inserter. Average endothelial cell loss, calculated as pixels in the endothelial damage area divided by pixels in the whole area x 100%, was 10.8 ± 2.7 % in the new inserter group and 23.9 ± 2.0 % in the Busin glide group, pointing to the clinical promise of the new DSAEK inserter.

All twelve surgeries in patients using the new DSAEK inserter were successful and uneventful. Donor grafts were smoothly inserted into anterior chamber in all cases, and in no cases did an anterior chamber collapse occur. All grafts became successfully attached with no incidences of graft dislocation or detachment, postoperatively. No primary graft failures occurred in the immediate postoperative period.

DISCUSSION

Although endothelial cell loss after DSAEK is reported to be influenced by both donor and recipient factors,[17] it is widely accepted that donor tissue manipulation during surgery can directly contribute to cell loss and damage. Currently, the pull-through technique is a standard procedure for DSAEK and one of the most widely used devices is the Busin Glide. In this approach, a rolled-up donor graft is delivered into

anterior chamber and spontaneously opens, causing less endothelial cell damage compared to the taco-folding method.[18-20] However, pull-through techniques are accompanied by the risk of anterior chamber collapse during graft insertion, and this can occur too often in the eyes of Asian patients, in which the angle tends to be narrow and the anterior chamber depth shallow. In the new surgery, described here, a combination of the negative pressure, which allows the graft lenticule to become incorporated within the new surgical device without the need for mechanical manipulation, aligned to the hydrophilic nature of the flexible platform's surface, ensuring that the graft moves smoothly off the platform in the absence of any need to pull-through, means that mechanical contact with the graft tissue during the procedure introduced here is minimised, thus reducing the likelihood of graft trauma.

Commercially available surgical insertion tools for DSAEK, which are based on push-in designs include the Neusidl corneal injector (Fischer Surgical, Arnold, MO, USA) and the Endoserter (Ocular Systems, Winston‐Salem, NC, USA).[14] Both are single use devices, and several studies have reported the clinical outcomes of their use.[10,11,21] These devices have a platform which holds the donor graft tissue, as does ours. However, neither of the aforementioned designs incorporates a negative pressure system to help hold the graft on the platform, so there is a risk that the graft can become inadvertently dislodged from its proper position on the platform during

surgical manipulation. DSAEK with all injector devices requires the platform to be introduced into the anterior chamber to deliver the graft, however, the negative pressure feature of our new inserter means that, unlike with the Neusidl and Endoserter devices, we do not need to perform continuous anterior chamber irrigation. This is a significant advantage because continuous irrigation increases the intraoperative pressure within the anterior chamber, which can lead to the unwanted situation whereby the graft accidentally flows out of the anterior chamber through the incision as the insertion device is being removed. The new DSAEK device described here utilizes the flow of BSS for graft injection into the anterior chamber. Only a small volume of BSS (approximately 0.1 ml) is required, and this carries along with the unfolding graft lenticule to achieve graft insertion in a quick and simple one-step action.

A clinical trial of this approach in a larger number of the patients has been initiated to extend the results presented here. The aim is to enhance the application of DSAEK to eyes, especially those at risk of endothelial cell damage because of a shallow anterior chamber. In summary, initial first-in-man studies indicate that the new graft inserter can provide for endothelial graft delivery for DSAEK without anterior chamber collapse and can results in successful graft attachment.

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FIGURE LEGENDS

FIGURE 1.

Photographic and schematic images of the new DSAEK insertion device. **(A)** Without and (**B)** with the syringe attached. **(C)** A valved conduit made of silicone rubber located on the inner tube of the movable cartridge.

FIGURE 2.

(A) DSAEK graft is placed onto the platform. (**B)** By sliding the movable cartridge forward the flexible platform and graft are rolled-up and drawn into the inserter via the effect of negative pressure. **(C)** The graft can be easily delivered into the anterior chamber, carried along by the flow of BSS flow simply by depressing the syringe plunger.

FIGURE 3.

Corneal staining patterns after use of **(A)** the new inserter and **(B)** a Busin glide in 10 *ex vivo* test DSAEK surgeries. No unusual staining patterns are seen after a test-surgery with the new inserter, and the area of endothelial cell damage compares favorably to that which resulted from Busin glide surgery.