Title page

Title: i-PDEK: Microscope-Integrated Optical coherence Tomography Assisted Pre-Desceemet Descemet Endothelial Keratoplasty

Running title: i-PDEK

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Abstract

Four patients of pseudophakic corneal edema were subjected to pre-Descemetic endothelial keratoplasty (PDEK) under the direct guidance of microscope-integrated optical coherence tomography (i-OCT). i-OCT facilitated successful type 1 big-bubble formation during donor preparation, debridement of hypertrophic epithelium, planning and placement of surgical wounds, descemetorrhexis with removal of remnant Descemet membrane tags, and identification of correct donor orientation and interface details. It was also possible to discern the stability of intraocular lens, flat iris configuration, adequate stromal hydration and wound apposition on i-OCT. Preoperative visual acuity was counting fingers (50%), 0.78 logMAR (25%) and 1.48 logMAR (25%), while postoperative visual acuity was 0.6 logMAR (50%) and 0.3 logMAR (50%). At 6-months follow-up, all grafts were clear and well-attached, the mean central corneal thickness, graft size, graft thickness, and endothelial cell loss were 557.25±13.45µm, 7.75±0.20mm, 25.5±2.64µm, and 21.6±0.02% respectively. To conclude, i-OCT helps during various surgical steps of PDEK.
Introduction

Pre-descemet endothelial keratoplasty (PDEK) is a new entrant in the arena of endothelial keratoplasty (EK). The rationale and theory behind performing PDEK were proposed by Dua et al in 2013 and it was first clinically performed by Agarwal et al in 2014.\(^1,2\) After its initial description, the technique has been widely appreciated as an alternative to commonly performed EK procedures such as Descemet stripping EK (DSEK) and Descemet Membrane EK (DMEK). The major differentiating feature of PDEK is its manual donor preparation which essentially mandates the formation of Type-1 Big Bubble (BB) to cleave the predescemet’s corneal layer (PDL) from the overlying stroma. The result is a donor-tissue that incorporates PDL along with Descemet’s membrane-endothelial-complex (DEC). The major advantage of PDEK over DSEK is the absence of stromal tissue in the donor that could compromise visual quality from interface scarring, hypermetropia, or optical aberrations. When compared to DMEK, the inclusion of PDL in the donor tissue makes intracameral graft manipulations easier besides expanding the stringent donor selection criteria required for DMEK.

Microscope integrated optical coherence tomography (i-OCT) is a recently introduced trans-operative imaging modality known to enhance the success of both anterior and posterior lamellar corneal surgeries.\(^3\) The real-time dynamic OCT scans projected by the equipment provide high-quality images of instrument-structure interaction akin to an optical biopsy, albeit, without compromising the surgical sterility. While the equipment has been effectively utilized for managing other types of EKs, we presently describe its role in PDEK surgery.\(^3-6\)

Case description

Four eyes of four consecutive adult patients with endothelial decompensation (Table 1) were subjected to i-OCT (OPMI Lumera 700 and RESCAN 700, Carl Zeiss, Meditec, Germany) assisted PDEK under local anesthesia after being evaluated by an experienced cornea surgeon.
(NS) for baseline best-corrected visual acuity on Snellen’s chart, corneal astigmatism, refractive error, intraocular pressure (IOP), central corneal thickness, and specular microscopy. The combination of i-OCT with PDEK was approved by the Ethics committee of the institute (IECPG-588/19.12.2018, RT-14/22.04.2019). The patients were recruited according to the declaration of Helsinki, and, written informed consent was obtained from all patients. Only optical grade donor corneas with endothelial cell (EC) counts >2200 cells/mm² were utilized for the surgery.

**Surgical technique**

The donor cornea was gently placed with its endothelial side up on a Teflon block and held firmly with a McPherson forceps by the surgeon (Figure 1, Video 1, http://links.lww.com/JRS/A333). With the other hand, a 5mL air-filled syringe attached to a 30-gauge needle with its bevel up was introduced from the corneoscleral rim into the mid-periphery of the corneal stroma under the direct guidance of the i-OCT. The air was gently introduced into the stroma to form a Type 1 BB of approximately 8mm size. The bubble wall was then penetrated at its periphery with the same 30-gauge needle and 0.6% trypan blue injected inside the bubble to stain the graft. The donor PDL-DEC was then excised all around with micro-Vannas scissors. The donor tissue was covered with the tissue culture medium and loaded into a specialized glass tube (Geuder, Germany) attached to an empty 2ml syringe when ready for insertion.

The host cornea was debrided of its epithelium, an inferior paracentesis was constructed for placing anterior chamber (AC) maintainer and a 2.8mm limbal incision was fashioned with a sharp keratome (Figure 2). i-OCT assisted descemetorhexis was performed with a reverse Sinskey hook under fluid infusion and the graft was injected inside AC with minimal fluid inflow. The corneal wound was immediately sutured with a 10-0 monofilament nylon suture and the graft was unfolded using air-fluid mechanics after confirming its
orientation on i-OCT. The air tamponade was maintained for 10 minutes, residual interface fluid was massaged, and the air bubble was deflated till a flat iris configuration was imaged on i-OCT. A bandage contact lens was placed on the cornea at the end of the surgery.

Postoperatively the patients were advised supine posture for 24 hours and topical moxifloxacin and prednisolone phosphate 1% six hourly. The patients were seen 6 hours after surgery on slit-lamp, followed-up on days 1, 3, 7, and 14, and months 1, 2, 3, and 6 and a note down of BCVA, refractive error, corneal astigmatism, IOP, graft-host apposition, host corneal and donor thickness and specular microscopy were made. The preoperative EC count of the donor tissue was recorded using an eye bank specular microscope, and postoperative EC count was recorded using noncontact specular microscopy.

A successful graft preparation, a well-attached donor at the end of the surgery and at all follow-ups, lack of secondary interventions, and a decrease in host corneal thickness were considered main outcome measures.

Intraoperative observations

Donor selection

A total of 5 donors were examined. All donors were clear, with intact stroma and no Descemet membrane (DM) folds, and had a thickness of <550µm suggestive of good endothelial function. One donor had a full-thickness scar approaching the paracentral cornea and was disregarded for PDEK.

Donor preparation

In our case series, type 1 BB was formed successfully in all cases. In case 2, where the stroma became emphysematous from stromal air injection, the needle depth, and bevel orientation were well-visualized on i-OCT allowing successful type 1 BB formation. In case 3, where a mixed type 1 and type 2 bubble was formed, the layer-wise assessment of donor cornea allowed the advancement of the needle correctly into the type 1 bubble for enlarging
it. No donor tissue perforation was noted in any case. Whenever the excised edge of the donor tissue lay partially on the stroma, visualization of the correct plane of separation for further donor excision was discerned successfully using i-OCT. In case 3, micro-adhesions or microbridges between the lenticule edges and the underlying stroma could be visualized and excised successfully with the aid of i-OCT.

**Host preparation**

In case 3, the presence of epithelial thickening and hyperreflectivity could be appreciated on the i-OCT microscope. In case 2, the i-OCT aided in determining the stability of the scleral fixated intraocular lens (tilt or pseudophacodonesis). In the rest three cases, the i-OCT confirmed the presence of an intraocular lens in an intact capsular bag. In cases 2 and 4, the main wound was created temporally and in cases 1 and 3, it was created superiorly. This was to avoid ragged margins of prior surgical wounds as determined by i-OCT. A successful descemetorhexis was accomplished in all cases. Residual DM tags could be identified in case 2 and 3 and were removed effectively with the aid of i-OCT.

**Intracameral donor manipulation**

i-OCT allowed successful determination of the correct orientation of the donor (inward fold with endothelial side facing outwards) in all subjects. The modality also confirmed the complete unfurling of the donor lenticules and their central attachment in all cases. Residual interface fluid was detected in case 3 after an air tamponade of 10 minutes and was tackled by further superficial massage. Flat iris configuration, and adequate stromal hydration and wound apposition were confirmed on i-OCT at the end of the surgery in all eyes.

**Surgical outcomes**

The success rate of type 1 BB formation was 100% in i-PDEK (Figure 3). No intraoperative or postoperative complications were noted in any patient. All patients were followed-up for six months and demonstrated a clear and well-attached graft till the last follow-up. The
preoperative visual acuity was counting fingers (2/4, 25%), 0.78 logMAR (1/4, 25%) and 1.48 logMAR (1/4, 25%), while the postoperative visual acuity was 0.6 logMAR (2/4, 50%) and 0.3 logMAR (2/4, 50%). At 6-months follow-up, the mean CCT improved from 747.50±17.07µm to 557.25±13.45µm and the mean IOP changed only minimally from 18.25±1.70mmHg to 17.75±1.25mmHg. The mean graft size, graft thickness, and EC loss at 6-months follow-up were 7.75±0.20mm, 25.5±2.64µm, and 21.6±0.02% respectively.

A successful graft preparation, a well-attached donor at the end of the surgery and at all follow-ups, no need of any secondary interventions, and a decrease in host corneal thickness were seen in all patients.

Discussion

To the best of our knowledge, the role of i-OCT in PDEK is being described for the first time. The most crucial step in PDEK remains the formation of type 1 BB in the donor to cleave the PDL-DEC from the overlying stroma. The type 1 BB is clinically appreciated by its centripetal spread, distinct edge, and elevated configuration. As suggested by Agarwal et al, the closer the needle tip is to the DM, the more likely it will achieve the desired cleavage. A deeper needle may bloat the stroma hampering further direct microscopic visualization and a superficial needle may perforate the donor endothelium resulting in tissue loss. The commonly documented success rate of type 1 BB formation with a conventional ophthalmic microscope varies from 71.7% to 92.3%. However, as seen currently, it was 100% with i-PDEK with no incidence of type 2 BB or burst bubble formation, micro-ruptures, or premature emptying of the syringe. This may be because i-OCT improved the predictability of needle passage by precisely guiding its depth, location, and orientation even through an emphysematous cornea. In one case where multiple BBs were formed, direct visualization of anatomical architecture on i-OCT differentiated the type of the bubble (type 1 or 2) and successfully guided the needle movement towards type 1 BB without the need for fluid
dissection or repeated needle insertions. Additionally, a magnified comprehension of donor characteristics such as prior corneal scars allowed appropriate donor selection for PDEK.\textsuperscript{7} Subsequently, the conversion rate to DMEK, a challenging task with younger donors due to their variable biological characteristics, was reduced to zero in the current series. Besides, the tissue loss was also nullified compared to 4.3% reported by Studeny et al.\textsuperscript{7} Any residual micro-attachments of donor lenticule with the underlying stroma were also dealt with successfully with i-OCT. In comparison to PDEK Clamp and Soper technique previously described for enhancing type 1 BB formation, i-PDEK is free from risks such as additional EC loss and mechanical trauma to the donor.\textsuperscript{10, 11}

Another major advantage of i-PDEK is comprehensive imaging of graft orientation during intracameral air-fluid adjustments. Resultant EC loss and graft detachment and failure associated with the accidental reverse unfolding of the graft may, therefore, be circumvented with i-PDEK. Normally, a PDEK graft rolls inwards with endothelial side outwards and various techniques such as endoillumination-assisted PDEK, air-assisted PDEK, and S-marking of the donor have been described for assessing its correct orientation.\textsuperscript{10, 12, 13} Although all techniques are individually helpful, they have their own limitations. The use of an endoillumination is cumbersome, requires extra incisions, produces unnecessary optical reflections, carries a risk of mechanical trauma to the donor, and needs an experienced assistant to hold the tool. The air infusion pump hired for air-PDEK requires a constant titration to avoid overinflation or collapse of the eyeball and the posterior migration of the air bubble. Marking of the tissue with vital dyes may be particularly challenging in pneumatic corneas and carries a risk of DM rupture besides being endotheliotoxic in the long-run. In contrast, i-PDEK is a no-assistant no-touch technique and can be undertaken without compromising the surgical sterility or endothelial cell health. Additionally, i-OCT assisted constant visualization of the thin, transparent graft may ensure its attachment to the host
cornea thereby preventing its posterior dislocation in aphakic individuals. Besides, time required for donor attachment can also be determined with this modality thereby preventing unnecessary over-pressurization of the globe.\textsuperscript{5,6} Other added advantages of i-PDEK include visualization of interface details, flat iris configuration, and adequacy of wound hydration.\textsuperscript{4} These are required to prevent postoperative graft detachments, pupillary block glaucoma, and wound leak respectively, and are usually missed by conventional microscopic methods of PDEK.

The 100% success rate of graft attachment and subsequent corneal clearing in our series is higher than that reported with that of a conventional microscope (Huang et al reported a success rate of graft attachment and corneal clearing as 88.88\% and 77.77\% respectively).\textsuperscript{9} We believe that i-OCT contributed significantly to this by smoothening almost every intraoperative maneuver starting from donor selection and preparation to its intracameral manipulation. This is in turn expected to promote early visual rehabilitation and long-term graft survival by evading secondary procedures such as re-bubbling, re-floatation, etc., and reducing EC loss (~22\% EC loss in our series).\textsuperscript{14} Although not much employed during the postoperative phase in the present series, i-OCT assisted visualization of anterior segment structures may enable recognition and immediate correction of graft detachment/folds and interface fluid, if any, especially in children and non-compliant individuals.

Overall, the use of i-OCT during PDEK is expected to enhance its acceptance among novice corneal surgeons, more so for children and in eyes with hazy corneas. The present limitations of the equipment remain its high cost, limited availability, and the shadowing effect from overlying metallic instruments. Also, larger longer comparative studies are needed to refute or support our promising short-term results. Till then, we suggest that the centres equipped with this facility effectively employ it for all PDEK surgeries.

\textbf{Value statement}
i-OCT improves the intraoperative profile of PDEK and may decrease its learning curve by facilitating the surgeon’s judgment, technique, and knowledge. High-quality image resolution and enhanced three-dimensional depth perception with i-PDEK facilitate the successful achievement of surgical objectives thereby enhancing surgical success. The continuous video monitoring and recording feature of i-OCT can be further utilized for critical review of surgical steps later. However, a longer follow-up of a larger cohort will help establish the true potential of this modality.

**What was already known?**

1. Presdescemetic endothelial keratoplasty (PDEK) is a new entrant in the arena of endothelial keratoplasty and involves grafting of presdescemetic layer along with donor Descemet membrane and endothelial cell layer

2. A successful PDEK mandates formation of Type-1 Big Bubble to cleave the predescemetic corneal layer (PDL) from the overlying stroma.

3. The most crucial steps during PDEK remain successful donor preparation and manipulation inside the anterior chamber

**What does this manuscript add?**

1. Intraoperative optical coherence tomography (i-OCT) improves the intraoperative profile of PDEK and may decrease the learning curve of PDEK.

2. i-OCT facilitates successful type 1 big-bubble formation during donor preparation, debridement of the hypertrophic epithelium, planning and placement of surgical wounds, descemetorhhexis with the removal of remnant Descemet membrane tags, and identification of correct donor orientation and interface details.

3. It is also possible to discern the stability of intraocular lens, flat iris configuration, adequate stromal hydration, and wound apposition with i-OCT during PDEK.

**References**


**Figure legends**

Figure 1: i-OCT guided donor preparation; assessing donor characteristics before starting surgery (a); forming type 1 big bubble (b, c); injecting trypan blue 0.6% inside bubble (d); excising the tissue (e); donor scroll (f)

Figure 2: i-OCT guided PDEK; thickened and hyperreflective epithelium (a); improved corneal clarity after epithelial debridement (b); Descemet’s membrane scoring (c-d); graft loading in glass tube (e-f); correct graft orientation with inward fold (h); air injection (h); well-apposed graft with no interface fluid (i)

Figure 3: Preoperative (a-c) and postoperative (d-f) clinical and ASOCT pictures of the patient. Note improvement in corneal clarity, well-attached graft and decrease in corneal thickness

**Table legends**

Table 1: Clinical details of the patients subjected to i-PDEK

**Video legends**

Video 1: Video showing surgical steps of i-PDEK
### Table 1: Clinical details of patient in our study

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PBK- Pseudophakic bullous keratopathy; FECD- Fuch’s endothelial dystrophy; PE- Phacoemulsification; SICS- Small incision cataract surgery; PCIOl- Posterior chamber intraocular lens; SFIOL- scleral fixated intraocular lens; Va- Visual acuity; IOP- Intraocular pressure; CCT- Central corneal thickness; EC loss- Endothelial cell loss; GS- Graft size; GT- Graft thickness