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ORIGINAL PAPER

Safety analysis and results of a borosilicate glass cartridge for no-touch graft loading and injection in Descemet membrane endothelial keratoplasty

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Abstract
Purpose The aim of this study was to investigate the clinical outcome after standardized DMEK using a glass injector.
Methods A total of 254 patients undergoing DMEK surgery using a disposable DMEK borosilicate glass cartridge system were included in this retrospective study. The mean follow-up time was 13.2 months (SD ± 8.1, range 6–36 months). The used glass cartridge system has an aperture diameter of 1.6 mm and a posterior loading orifice of 4.29 mm. Scanning electron microscopy (SEM) was used for estimation of the surface relief of the glass cartridge and comparison with a standard plastic injector cartridge.
Results Mean endothelial cell count of donor grafts was 2465 cells/mm^2 (SD ± 199). After 6 weeks of DMEK endothelial cell count decreased by − 28.6% to 1759 cells/mm^2 (SD ± 435) (Wilcoxon $p = 0.001$) and remained stable at the final follow-up at 1735 cells/mm^2 (SD ± 442) (Wilcoxon $p = 0.89$). SEM showed smoother surface of the glass cartridge in comparison with a plastic cartridge.
Conclusion This study showed that this simple and effective DMEK cartridge seems to be a safe and viable device for minimized graft manipulation during DMEK surgery.

Keywords DMEK · Cartridge · DMEK injector · No-touch technique

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Introduction

Over the last decade, Descemet membrane endothelial keratoplasty (DMEK) evolved to the procedure of choice in cases of compromised endothelial cell layer [1], most notably because of advantages like rapid and better visual rehabilitation, reduced transplant rejection rates and uncomplicated postoperative management compared to penetrating keratoplasty [2–4]. Despite distinguished clinical outcome, DMEK requires excellent surgical experience with preparing and handling of the thin graft tissue to prevent endothelial cell loss or graft rejection [5]. At the initial stage of DMEK up to 50% loss of endothelial cell count caused by mechanical DM manipulation by forceps hindered the clinical success [6]. Minimizing endothelial cell loss and avoiding inadvertent tears

during tissue management by less mechanical stress are determining to secure long-term graft survival [6]. In 2012, the commercially available borosilicate glass DMEK cartridge (Geuder DMEK cartridge, Heidelberg), allowing a complete no-touch loading and injection, was introduced. The streamlined design of the cartridge and the fluid environment of the graft were developed to assure full visual control during loading and injection to minimize mechanical stress to endothelial cells. Meanwhile, other DMEK injector systems are available with variable results [1, 7, 8]. Although this Geuder DMEK glass cartridge is the most often used labelled microinjector system for DMEK, clinical results have been just once published with a small amount of patients [9]. Therefore, the aim of this study was to evaluate the clinical outcome with a larger amount of patients using this DMEK cartridge.

Methods

Subjects

In this retrospective study, we analysed the clinical outcome of patients who consecutively received a DMEK at the Eye Clinic Sulzbach between March 2012 and December 2016 using the Geuder DMEK cartridge. The surgeries were performed by three experienced surgeons. Only those eyes with a minimum follow-up period of 6 months were included. Indications for DMEK were Fuchs' endothelial dystrophy (FED) or pseudophakic bullous keratopathy. The study was performed according to the tenets of the Declaration of Helsinki and approved by the local ethical committee.

The following parameters were analysed before and 6 weeks, 3 months, 6 months and yearly after DMEK: best-corrected visual acuity (BCVA), endothelial cell density (Topcon, Tokyo, Japan), central corneal thickness (Pentacam, Oculus, Germany), slit-lamp and fundus examination. BCVA results were represented in logarithmic minimum angle of resolution (logMAR). Indications for DMEK, lens status, ocular comorbidities, difficulty of graft implantation, rebubbling frequency and graft turning intra- or postoperative were detected.

Surgical technique

DMEK surgeries were performed with a standardized technique using the DMEK surgery set (Geuder, Heidelberg, Germany). The sterile single-use DMEK cartridge set is composed of a borosilicate glass cartridge and a tube with a connector. Two sterile 5-ml syringes are required for application. DM preparation was performed using the liquid bubble technique as recently described in detail [10]. The stromal side was stained with trypan blue for better visualization.

After corneal trephination, the DM was lifted without any adherence using an olive spatula from the stromal side. After connecting the flexible silicone tube and borosilicate glass syringe to the anterior orifice of the DMEK cartridge (Geuder, Heidelberg, Germany), the DM was uploaded via the large posterior aperture of the DMEK cartridge by gentle aspiration with the syringe (Fig. 1). Once the graft was taken in the glass chamber, a second sterile fluid-filled syringe was connected to the posterior orifice of the cartridge. The tube was carefully removed from the anterior aperture of the cartridge. Injection of the DM into the anterior chamber was performed under full visual control by constant fluid injection (Fig. 2). Intracamerally, a dual irrigation set enabled a contactless fluid-controlled unfolding and positioning of

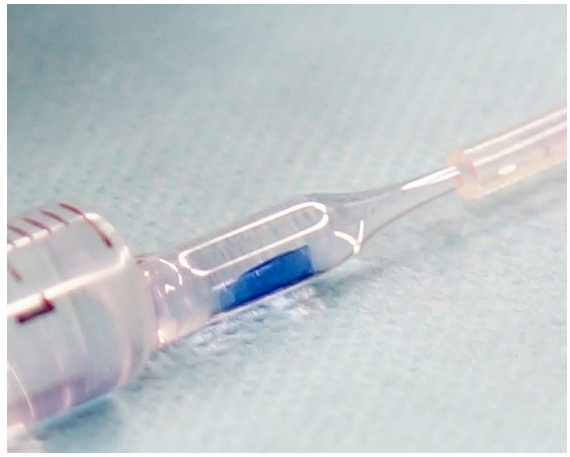

Fig. 1 Images shows a loaded DMEK cartridge connected to the syringe (left) and the aspiration tube (right). After uploading via aspiration through the large posterior orifice, the DM graft is fully visible within the glass cartridge. Once the injection syringe (left) is connected to the posterior aperture and the aspiration tube disconnected, the cartridge system is ready for implantation

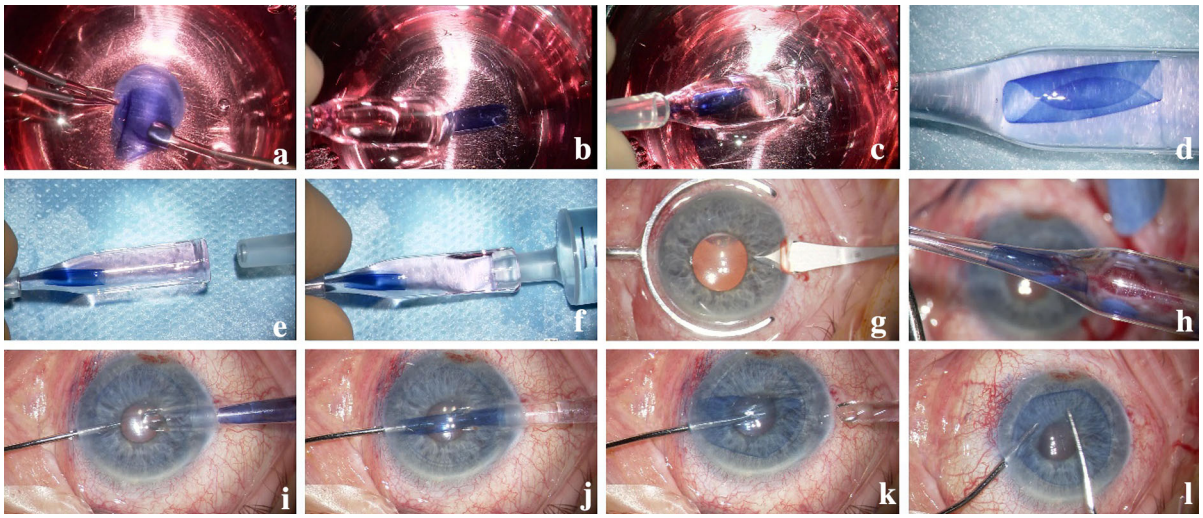

Fig. 2 After liquid bubble separation, the DM is lifted from the stromal bed without any adherence using an olive spatula (**a**). The DM is gently uploaded via the large aperture of the cartridge by aspiration through the connector tube (**b**, **c**). The rolled graft appears fully visible within the loading chamber of the cartridge allowing for visual control of the correct orientation of the DM roll (**d**). After connecting the injector syringe to the posterior orifice and disconnecting the anterior aspiration tube (**e**, **f**) the loaded cartridge is ready for implantation. This can be performed via a clear cornea tunnel incision (**g**). The DM graft is then advanced from the loading chamber to the narrow implantation canal while the correct orientation of the roll is still assured (**h**). Implantation is performed by fluid flow advancing the graft in a gentle and controlled manner into the anterior chamber (**i**). This allows the opposite instrument to fix the DM with correct orientation. This avoids an uncontrolled upside-down position of the DM and minimizes consecutive graft manipulation (**j–l**)

the DM. By gentle manipulation with fluid and air, the graft was centred endothelial-side down and attached by an air bubble to the posterior stroma.

Scanning electron microscopy (SEM)

For SEM investigation, the operating parts of plastic and glass cartridges were broken into small pieces. These samples were placed on carbon conductive tubs bonded to the aluminium specimen stubs, sputtered with gold–palladium and studied by 5 kV in a field emission scanning electron microscope Phillips FESEM XL30 (FEI, Eindhoven, Netherlands).

Statistical analysis was performed using XLSTAT 2016. $p < 0.05$ was defined as statistically significant.

Results

In total, 300 patients were reviewed, among them 254 patients fulfilled the inclusion criteria and consecutively received a DMEK using the no-touch cartridge system. DMEK was performed by three experienced surgeons using the same technique. Results were statistically not correlated among the surgeons. Patient's demographics showed a mean age of 71 years (SD ± 9.7, range 46–93 years). The mean follow-up time was 13.2 months (SD ± 8.1, range 6–36 months). Indications for DMEK were Fuchs' endothelial dystrophy (FED) in 222 eyes (87.4%) and corneal decompensation after complicated intraocular surgery in 32 eyes (12.6%). Prior DMEK, 68 patients were phakic (26.8%) and therefore underwent a triple procedure with DMEK and phacoemulsification with posterior chamber intraocular lens implantation. Limiting secondary diagnosis ($n = 87$) was glaucoma (13.8%), diabetic retinopathy (3.5%), age-related macular degeneration (5.1%) and other cases like amblyopia or pars plana vitrectomy in history (11.4%).

For separation of the DM from the donor stroma, the previously described liquid bubble technique was used [10]. After successful preparation, all DM grafts were loaded uneventfully and without the need of forceps into the posterior orifice of the DMEK cartridge via suction. We did not experience incomplete injection of the DM. Care must be taken to completely advance the DM into the loading chamber.

Herein, the correct orientation of the role with the endothelium down can be controlled. Once the injector syringe is docked to the posterior orifice and the suction syringe is disconnected from the anterior orifice, the DM is further advanced into the tip of the cartridge. Injection via a temporal clear cornea tunnel incision and unfolding of the DM within the anterior chamber were achieved in all cases. The injection system combining irrigation to maintain the anterior chamber and injection via small aperture cartridge helps to maintain orientation of the DM graft during the injection. Centration was achieved by small air bubble injection and gentle bubble movements. Intraoperative graft flipping due to primary upside-down position was necessary in 10 cases (3.9%). Adhesion to the stroma via air bubble technique was successful in all cases. High intraocular pressure was noted in 3 eyes (1.2%).

The average preoperative endothelial cell count of the donor grafts was 2465 cells/mm^2 (SD ± 199) (Topcon, Tokyo, Japan). Mean endothelial cell count decreased by 28.6% to 1759 cells/mm^2 (SD ± 435) 6 weeks after DMEK (Wilcoxon $p = 0.001$). After 6 months, endothelial cell count remained stable at 1735 cells/mm^2 (SD ± 423, − 29.6%) (Wilcoxon $p = 0.89$) (Fig. 3) resulting in a statistically significant increase in mean BCVA from preoperative 0.84 logMAR (SD ± 0.5) to 0.27 logMAR (SD ± 0.27) after 6 months (Wilcoxon $p = 0.001$). Eight patients needed a secondary DMEK (3.2%), 4 of them disclosed an upside-down orientation and were classified as early graft failure. Re-bubbling was necessary for 55 patients (21.7%) in the early postoperative period. Re-bubbling was performed after mean 9.8 days (SD ± 9.6, range 1–47 days). There was no statistically significant difference in endothelial cell count of DMEK with or without re-bubbling (Mann–Whitney-U test $p = 0.23$). Prior DMEK, the mean central corneal thickness was 670 µm (SD ± 101 µm). Compared to baseline, mean corneal thickness decreased statistically significant after 6 months to 538 µm (SD ± 55 µm) (Wilcoxon $p < 0.05$) (Fig. 4). Furthermore, corneal astigmatism did not change statistically significant from preoperative 1.7 dpt (SD ± 1.6) to 1.6 dpt (SD ± 1.7) after 6 months (Friedman-Test 0.42).

SEM images of the inner surface of the borosilicate glass cartridge showed a smoother microscopic structure of the inner lumen, while the plastic cartridge revealed a rough and hilly texture (Fig. 5) under high magnification.

Discussion

The current study evaluated the quality of the first commercially available DMEK cartridge and its clinical outcome after DMEK surgery. We could show a smooth surface of the cartridge, a rapid no-touch loading and injection of the graft, with intact cell viability and a good clinical outcome after DMEK.

Different injection systems have been described yet. Many surgeons use a standard plastic IOL injector cartridge for DMEK implantation [1, 11]. However, non-specific and off-label injector systems may have various shortcomings, including direct contact due to insertion of the graft by forceps, possible sharp edges and a rough surface of the plastic cartridge. We could

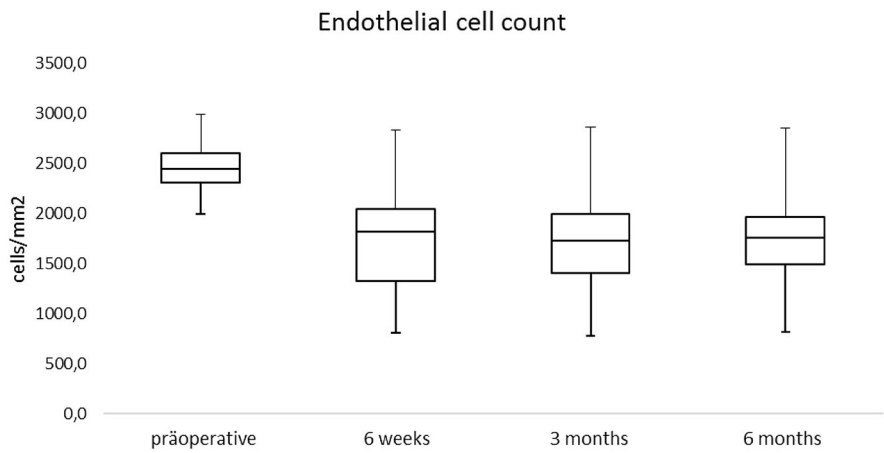

Fig. 3 Box plot of endothelial cell count preoperative, 6 weeks, 3 months and 6 months after DMEK. Note the decreased cell count after 6 weeks (Wilcoxon $p = 0.001$) and the consecutive stability during the further follow-up (Wilcoxon $p = 0.89$)

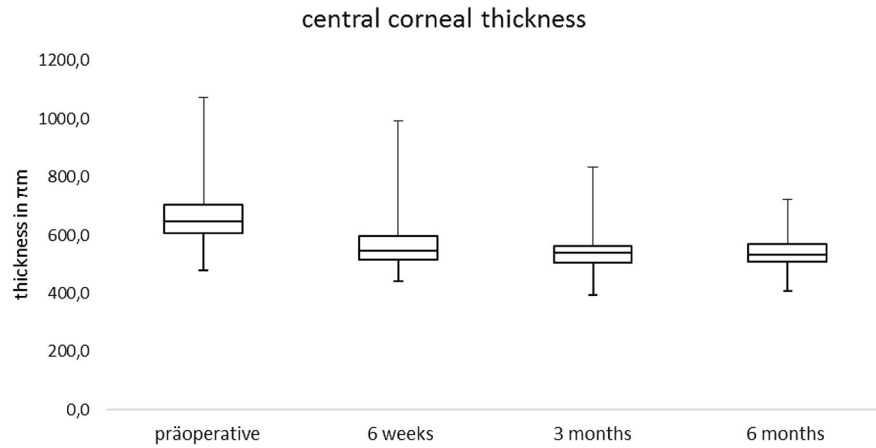

Fig. 4 Box plot of central corneal thickness preoperative, 6 weeks, 3 months and 6 months after DMEK. Mean preoperative corneal thickness decreased statistically significant during the follow-up (Wilcoxon $p < 0.05$)

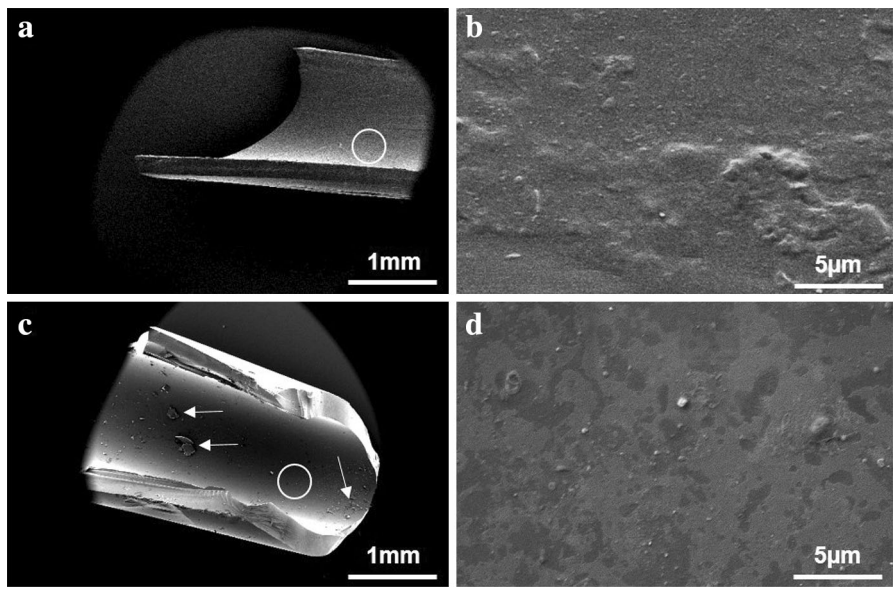

Fig. 5 SEM images of plastic (**a**, **b**) and glass (**c**, **d**) cartridges were first photographed as an overview (**a**, **c**). High magnification of the inside surface and regions marked on the overviews with circles are shown in **b**, **d**, respectively. The inside surface of the plastic cartridge looked rough and hilly (**b**), while the glass cartridge showed relative smoother surface (**d**). Some shivers were seen on the surface of glass and can be interpreted as artefacts of broken cartridge (**c**, arrows)

show by SEM imaging the superior smooth surface of the glass cartridge compared to a commonly used plastic cartridge.

Also, IOL cartridges do not allow continuous fluid flow around the graft and mostly use a plunger resulting in direct contact and pushing the graft [7]. Inadequate fluid control is also critical during graft insertion and can potentially result in incomplete insertion of the graft [7]. In contrast, the DMEK glass cartridge is a no-touch system providing a contactless loading and implantation of the graft under visual control by controlled injection into the anterior chamber. All DM grafts were loaded uneventful and without the need of forceps into the DMEK cartridge within seconds. The potential advantages are summarized in Table 1.

Manipulation and direct contact to the graft can lead to endothelial cell loss or graft failure. The early loss of endothelial cells of 28.6% after 6 weeks compared to preoperative cell count is in accordance with other research groups reporting an average endothelial cell loss by 30% within the first 6 months [3, 4, 11, 12]. It is still under discussion, if this early loss is due to a real viability loss or rather a result of different counting techniques pre- (specular microscopy) and postoperatively (endothelia microscopy). Of interest, we observed a cell loss only during the first control after six weeks, but remained completely stable during the further follow-up.

Table 1 Potential advantages of the borosilicate glass cartridge

Potential advantages of the borosilicate glass cartridge (Geuder DMEK cartridge, Heidelberg, Germany)
Non-contact loading via aspiration through the large posterior aperture
Medium-BSS exchange within the cartridge
Visual control of position and orientation of the DM role within the loading chamber
Constant fluid environment of the graft
Streamlined design of the cartridge for small incision implantation (1.6 mm)
Non-contact implantation via fluid flow
Injection of the DM into the anterior chamber under constant visual control of the DM orientation
Contactless unfolding and positioning of the DM within the anterior chamber

Busin et al. [8] described a lower endothelial cell loss of only 10% by using a contact lens-assisted pull-through technique. However, this technique provides a contact with the DM. The importance of avoiding a possible contact between endothelium and cartridge has been well demonstrated by Parekh et al. [13] shows more than 90% endothelial cell loss in uncovered areas contacting the cartridge. This is especially true for a small diameter cartridge. The tip of our DMEK cartridge has a diameter of only 1.6 mm allowing for astigmatism-free, self-sealing clear cornea incision. In our study, astigmatism did not change after DMEK. This is consistent with other studies [14–16].

Despite the small diameter of the aperture, we could exclude an implantation-associated viability loss of the delicate endothelial cell layer. This is consistent with other studies that could exclude higher endothelial cell loss in smaller injector systems of 0.5 mm to 1.4 mm [17].

Our good viability results may be due to both the streamlined design and the smooth fluid environment of the graft during implantation. Furthermore, the no-touch loading of the graft via aspiration and the smooth inner surface of the borosilicate glass cartridge may also be beneficial by avoiding any harm to the delicate endothelial cell layer during injection through the small diameter cartridge tip.

However, Droutsas et al. [9] could show in a small comparative study using three different injector systems that there was no statistical significant difference comparing endothelial cell loss 12 months after DMEK. Therefore, the authors concluded that the graft injector might be chosen according to the surgeon's preference [9].

In conclusion, we could show a smooth surface of the cartridge and viable endothelial cells after no-touch loading and injection of DM grafts using the borosilicate DMEK cartridge. This safe and viable device assures minimized graft manipulation during controlled loading and implantation during DMEK surgery.

Compliance with ethical standards

Conflict of interest Peter Szurman has a patent for the described device (EP2533724 B1; WO2012065602 A3). All other authors certify that they have no affiliations with or involvement in any organization or entity with any financial interest (such as honoraria; educational grants; participation in speakers' bureaus; membership, employment, consultancies, stock ownership, or other equity interest; and expert testimony or patent-licensing arrangements), or non-financial interest (such as personal or professional relationships, affiliations, knowledge or beliefs) in the subject matter or materials discussed in this manuscript.

Informed consent Informed consent was obtained from all individual participants included in the study.

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