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Advances in endothelial keratoplasty

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Chapter 7

Outcomes of Hemi-Descemet
Membrane Endothelial Keratoplasty for
Fuchs Endothelial Corneal Dystrophy

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ABSTRACT

Purpose: To report the mid-term outcomes of Hemi-Descemet membrane endothelial keratoplasty (Hemi-DMEK) performed for Fuchs endothelial corneal dystrophy (FECD).

Methods: In this prospective, interventional case series, we evaluated clinical outcomes of 10 eyes from 10 patients who underwent Hemi-DMEK for FECD. Main outcome measures were best-corrected visual acuity (BCVA), endothelial cell density (ECD), central pachymetry and postoperative complications.

Results: At 1 year postoperatively, 7/7 eyes (excluding 2 eyes with low visual potential) reached a BCVA of $\geq 20/40$ (≥ 0.5), 6/7 (86%) $\geq 20/25$ (≥ 0.8), 4/7 (57%) $\geq 20/20$ (≥ 1.0) and 2/7 (29%) $20/17$ (≥ 1.2). BCVA remained stable until 2 years postoperatively ($P \geq .05$) and further improved thereafter ($P < .05$). Mean ECD declined from 2740 (± 180) cells/mm² preoperatively to 850 (± 300) cells/mm² (n=9) at 1 year ($P \leq .05$) and showed an annual decrease of on average 6 to 7% thereafter ($P \geq .05$ between consecutive follow-ups). Pachymetry decreased from preoperatively 745 (± 153) μm to 533 (± 63) μm (n=9) and 527 (± 35) μm (n=8) at 1 and 3 years postoperatively, respectively. Within the first 6 postoperative months, 4/10 eyes underwent re-bubbling for visually significant graft detachment. One eye received secondary circular DMEK for persistent graft detachment 1 month postoperatively; another eye developed secondary graft failure 2.5 years postoperatively, and one eye was suspected for allograft reaction 1.5 years postoperatively.

Conclusions: Hemi-DMEK may render visual outcomes comparable to those achieved by conventional DMEK. Despite low ECD counts by 6 months, ECD levels remain fairly stable thereafter. Hence, Hemi-DMEK may become a potential alternative technique for the treatment of FECD while increasing the yield of the endothelial tissue pool.

INTRODUCTION

Descemet membrane endothelial keratoplasty (DMEK) may become the globally preferred treatment option for patients with corneal endothelial disorders.¹ Recently, we have described Hemi-Descemet membrane endothelial keratoplasty (Hemi-DMEK) as a DMEK modification that differs from conventional DMEK only in the graft shape because instead of a circular trephined DMEK graft, Hemi-DMEK utilizes an untrepined, full-diameter, semi-circular ('half-moon' shaped) graft.²⁻⁶ There is mounting evidence that in patients with Fuchs endothelial corneal dystrophy (FECD), corneal clearance may also be obtained with different graft shapes, without a completely attached graft, and sometimes by descemetorhexis alone through host endothelial cell migration.⁷⁻¹³ The advantage of Hemi-DMEK over circular DMEK is that in Hemi-DMEK two semi-circular grafts, each of the same surface area as conventional DMEK grafts, can be retrieved from one donor cornea and transplanted into two recipients, hereby potentially doubling the availability of endothelial tissue.²⁻⁶ This new DMEK-technique may be adopted, if longer-term clinical outcomes would be similar for both techniques. With this study, we therefore furnish the extended clinical results of the first cohort undergoing Hemi-DMEK worldwide, with up to 4 years of postoperative surveillance.

MATERIALS AND METHODS

A series of 10 eyes from 10 patients underwent Hemi-DMEK for FECD (Table 1). One eye received secondary circular DMEK one month postoperatively for persistent graft detachment after unsuccessful re-bubbling, hence, the clinical outcomes of nine eyes (mean patient age: 72±9 years (range 62- 86 years)), with successful Hemi-DMEK surgery are reported in this follow-up study. All patients signed an IRB-approved informed consent form for research participation and the study adhered to the tenets of the Declaration of Helsinki.

Donor tissue preparation and Hemi-DMEK surgery

Hemi-DMEK grafts were prepared as previously described.⁴ From whole donor globes obtained less than 24 hours postmortem, corneoscleral buttons were excised and stored in organ culture medium at 31°C (CorneaMax; Eurobio, Courtaboeuf, France) until the time of graft preparation; at which time the buttons were mounted endothelial side-up in a custom-made holder, bisected with a surgical knife, and Descemet membrane was stripped free from both

Table 1. Overview baseline characteristics, pre- and postoperative endothelial cell density,

Case no.	Patient				Donor		Preoperative		Surgery		ECD (cells/mm ²) [ECD decrease]	
	Age (y)	Sex	Eye	Lens status	Age (y)	Eye	ECD (cells/mm ²)	BCVA (Snellen (decimal))	CCT (μm)	Graft position	1y FU	2y FU
1	66	F	OD	Pseudo phakic	49	OD	2500	20/125 (0.15)	662	D	1010 [60%]	1000 [60%]
2	72	F	OD	Pseudo phakic	70	OD	2700	20/125 (0.15)	707	D	1340 [51%]	1230 [54%]
3	65	F	OD	Pseudo phakic	67	OS	2900	20/30 (0.7)	681	D	850 [71%]	830 [71%]
4	86	F	OD	Pseudo phakic	63	OD*	3000	20/80 (0.25)	678	H	590 [80%]	660 [78%]
5	62	F	OS	Pseudo phakic	63	OD*	3000	20/60 (0.3)	901	H	1220 [59%]	1120 [63%]
6	69	M	OS	Pseudo phakic	69	ODs	2600	20/60 (0.3)	743	H	930 [64%]	1080 [58%]
7	83	F	OS	Pseudo phakic	73	ODs	2600	20/32 (0.6)	605	D	Re-DMEK	
8	86	F	OD	Pseudo phakic	86	OS #	2700	20/125 (0.15)	1083	D	590 [78%]	570 [79%]
9	77	M	OD	Pseudo phakic	86	OS #	2700	20/50 (0.4)	643	V	720 [74%]	680 [75%]
10	69	M	OS	Phakic	55	OD	2600	20/32 (0.6)	603	H	440 [83%]	420 [84%]
Mean ±SD	72 ±9				68 ±12		2740 ±180		745 ±153		850±300 [69±11]	840±280 [69±11]

y= year(s); F= female; M= male; OD= right eye; OS= left eye; ECD= endothelial cell density; BCVA= best-corrected visual acuity; CCT= central corneal thickness; FU= follow-up; w= week(s); LTFU= Lost to follow-up; N/A= not available yet; ARMD= age-related macula degeneration; SGF=Secondary graft failure

best-corrected visual acuity and central corneal thickness.

ECD (cells/mm ²) [ECD decrease]		BCVA (Snellen (decimal))				CCT (μm)				Remarks
3y FU	4y FU	1y FU	2y FU	3y FU	4y FU	1y FU	2y FU	3y FU	4y FU	
960 [62%]	LTFU	20/22 (0.9)	20/22 (0.9)	20/22 (0.9)	LTFU	527	547	539	LTFU	
1050 [61%]	960 [65%]	20/40 (0.5)	20/50 (0.4)	20/32 (0.6)	20/40 (0.5)	535	527	528	537	Amblyopic Suspected allograft reaction (1.5y)
760 [74%]	690 [76%]	20/17 (1.2)	20/17 (1.2)	20/13 (1.5)	20/17 (1.2)	490	503	508	518	
Re-DMEK		20/60 (0.3)	20/125 (0.15)	Re-DMEK		667	706	Re-DMEK		ARMD, Re-bubbling (1w), SFG (2.5y)
1010 [66%]	N/A	20/22 (0.9)	20/20 (1.0)	20/20 (1.0)	N/A	585	595	590	N/A	
700 [73%]	N/A	20/20 (1.0)	20/22 (0.9)	20/20 (1.0)	N/A	548	565	559	N/A	Re-bubbling (3w)
				<i>Re-DMEK</i>						<i>Re-bubbling (1w), secondary DMEK (1m)</i>
550 [80%]	N/A	20/30 (0.7)	20/32 (0.6)	20/30 (0.7)	N/A	491	501	511	N/A	
700 [74%]	N/A	20/20 (1.0)	20/25 (0.8)	20/22 (0.9)	N/A	473	479	492	N/A	
430 [83%]	N/A	20/17 (1.2)	20/2 (1.0)	20/20 (1.0)	N/A	477	486	486	N/A	Re-bubbling (4w)
770 ±220 [72±8]						533	545	527		
						±63	±71	±35		

Graft orientation: H: Long graft edge oriented horizontally; D: Long graft edge oriented diagonally;
V: Long graft edge oriented vertically

* ,s, # Hemi-DMEK grafts originated from the same donor eye. *Italics* = excluded from current analysis

corneal halves using fine forceps to produce two semi-circular ('half-moon' shaped) endothelial grafts. Endothelial cell morphology and viability were evaluated before and after Descemet stripping. Hemi-DMEK grafts were then stored in organ culture medium until the time of transplantation.⁴

Hemi-DMEK surgery could be completed with minor modifications compared to conventional DMEK.^{2,14} After a circular descemetorhexis (on average 8-9 mm) was performed under air using a reversed Sinsky hook (DORC International, Zuidland, The Netherlands), the donor tissue was removed from organ culture, rinsed with balanced salt solution (BSS), stained with Trypan Blue 0.06% (VisionBlue; DORC International), and injected into the eye via a glass pipette (Melles glass inserter, DORC International). Indirect manipulations including taps on the external corneal surface and bursts of BSS were used for unfolding, after which the graft was lifted up to the posterior corneal surface by an air bubble. Subsequently, a complete air fill was maintained for 60 to 90 minutes, followed by a partial air-fluid exchange intending to leave the eye with an air bubble occupying 30% to 50% of the volume of the anterior chamber for graft support. Hemi-DMEK was performed by three experienced surgeons.

The postoperative medication regime resembled that followed after conventional DMEK, including topical steroids tapered to once daily over one year, which was, in some cases, further reduced to once every other day thereafter.¹⁴

Data collection

Routine follow-up appointments were scheduled for 1 day, 1 week, 1, 3, 6, 9 and 12 months, and every 6 months thereafter for assessing best-corrected visual acuity (BCVA), pachymetry (Pentacam HR, Oculus Optikgeräte GmbH, Wetzlar, Germany), anterior segment optical coherence tomography (Heidelberg Slit Lamp-OCT; Heidelberg Engineering GmbH, Heidelberg, Germany) and endothelial cell density (ECD), which was evaluated *in vivo* using a Topcon SP3000p non-contact autofocus specular microscope (Topcon Medical Europe BV, Capelle a/d IJssel, the Netherlands). Images of the central corneal window were analyzed and manually corrected; up to three measurements of ECD were averaged (if the central endothelium could not be visualized, paracentral images were used for analysis).

Statistics

All analyses were performed using Excel Software for Windows. BCVA outcomes were converted to logarithm of the minimum angle of resolution (LogMAR) units to enable statistical analysis. The independent paired Student t-test was applied to assess differences between consecutive follow-up time points. $P < 0.05$ was considered statistically significant.

RESULTS

Clinical outcome

All corneas with successful Hemi-DMEK cleared by 6 months, and BCVA improved in all eyes ($n=9$). At 1 year postoperatively, all eyes (excluding two with low visual potential; $n=7$) attained a BCVA of $\geq 20/40$ (≥ 0.5), 6/7 (86%) eyes $\geq 20/25$ (≥ 0.8), 4/7 (57%) eyes $\geq 20/20$ (≥ 1.0) and 2/7 (29%) eyes $\geq 20/17$ (≥ 1.2) (Table 1; Fig. 1). BCVA remained stable until 2 years postoperatively ($P \geq 0.05$) and further improved thereafter ($P < 0.05$) (Table 1; Fig. 1).

Donor ECD decreased within the first postoperative year from 2740 (± 180) cells/ mm^2 before surgery ($n=9$) to 940 (± 380) cells/ mm^2 at 6 months ($n=9$), and 850 (± 300) cells/ mm^2 at 1 year after surgery ($n=9$) ($P < 0.05$) and showed on average an annual decrease of 6 to 7% thereafter ($P \geq 0.05$ between con-

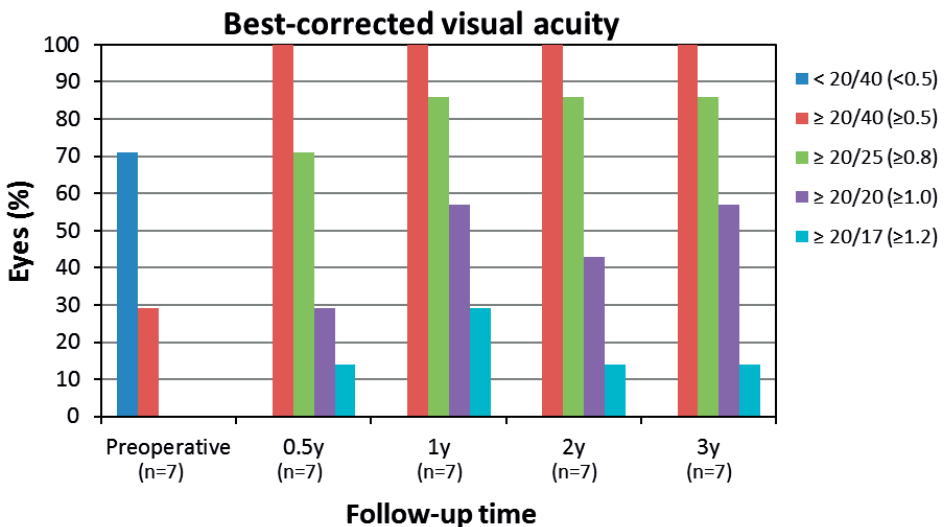


Figure 1. Bar graph displaying the best-corrected visual acuity. Best-corrected visual acuity (BCVA) is shown preoperatively and up to 3 years after Hemi-Descemet membrane endothelial keratoplasty (Hemi-DMEK).

secutive follow-ups) (Table 1; Fig. 2) with a yearly ECD decline comparable to conventional DMEK (Fig. 2).¹⁵

Mean pachymetry decreased from preoperatively 745 (± 153) μm to 533 (± 63) μm ($n=9$) and 527 (± 35) μm ($n=8$) at 1 and 3 years postoperatively, respectively.

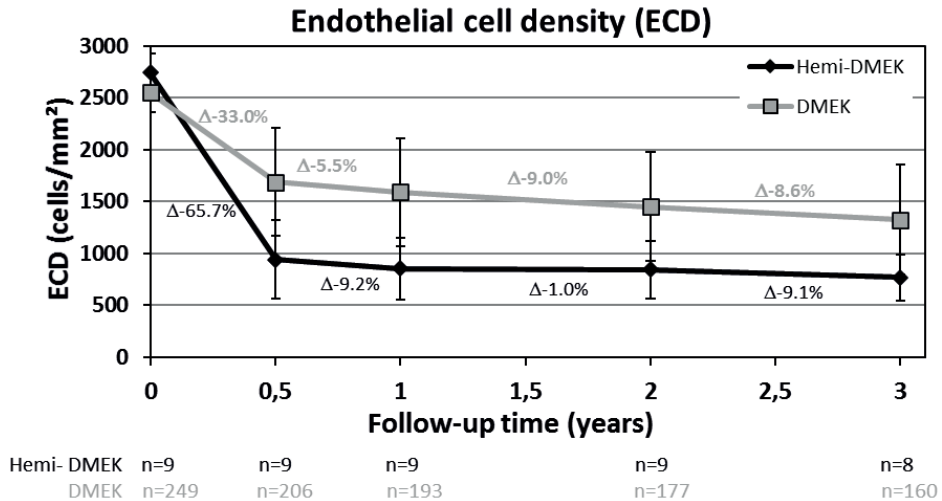


Figure 2. Graphs displaying mean endothelial cell density (ECD) before and up to 3 years after Hemi-DMEK and conventional DMEK. Percentages between follow-up time points represent the ECD decrease (Δ) between consecutive time points. Data for ECD decrease after conventional DMEK are taken from Ref. 15.

Complications

In the early postoperative period, 4 eyes (Cases 4, 6, 7 and 10) had visually significant graft detachment that required re-bubbling. In one of these eyes (Case 7) the detachment persisted and the eye therefore underwent secondary circular DMEK one month postoperatively; however also the circular graft showed poor graft attachment. Another re-bubbled eye (Case 4) developed secondary graft failure 2.5 years after Hemi-DMEK and was successfully re-operated with conventional circular DMEK. Except for a strongly adherent Hemi-DMEK graft, re-intervention was uneventful. Beyond 6 months postoperatively, one eye (Case 2) was suspected to have developed an allograft reaction at the 1.5 year-follow-up, which was successfully reversed by an intensified regimen of topical steroid therapy.

DISCUSSION

Theoretically, Hemi-DMEK represents an attractive surgical option because, if also successful in the longer term, it may potentially increase the amount of available corneal donor tissue. Previously, we reported our 6-month results for this first worldwide cohort of eyes undergoing Hemi-DMEK and the 3-year outcomes of the first three operated cases;^{5,6} in this study, we describe the clinical course of 3 to 4 years of follow-up for this cohort.

As expected, BCVA after Hemi-DMEK may resemble that of conventional DMEK. The early and quick initial visual recovery was followed by a further improvement at the end of the follow-up period.^{5,15,16} Still, entire corneal clearance after Hemi-DMEK may be a bit slower than after conventional DMEK due to the bare areas resulting from the mismatch of the circular descemetorhexis and the semi-circular Hemi-DMEK graft; however, all corneas with successful Hemi-DMEK were clear 6 months postoperatively (Fig. 3).^{15,16}

In contrast to conventional DMEK, our study and previously published reports show that the initial sharp decline in ECD within the first 6 months is considerably higher after Hemi-DMEK (34% versus 65%).^{2,6,15} This may be explained by different patterns of endothelial cell redistribution and migration after Hemi-DMEK compared with conventional DMEK, because of larger stromal bare areas. In addition, ECD measurements at different graft areas (centrally for conventional DMEK, and more peripheral or at the graft edge for Hemi-DMEK) may produce this difference in the ECD decrease.^{2,3,6} Interestingly, contrary to our previously published report on the clinical outcomes of the very first 3 Hemi-DMEK eyes, in this 'larger' cohort a yearly ECD decrease of 6 to 7% could be observed, which would be similar for both DMEK-techniques.^{6,15,17} Hence, the ECD decrease after this early drop may be caused by similar mechanisms in both DMEK-techniques.

As with conventional DMEK, after Hemi-DMEK, the main early complication was graft detachment, for which re-bubbling was required in 4/10 (40%) eyes. A possible explanation for the higher detachment rate after Hemi-DMEK than after conventional DMEK might be a 'learning curve' effect of this modified technique. The difference in graft shape may be another reason, since the Hemi-DMEK graft has one shorter axis, an edge detachment in the central graft area may more often affect the visual axis prompting faster re-bubbling.¹⁶ Interestingly, the eye that received conventional DMEK one month postopera-

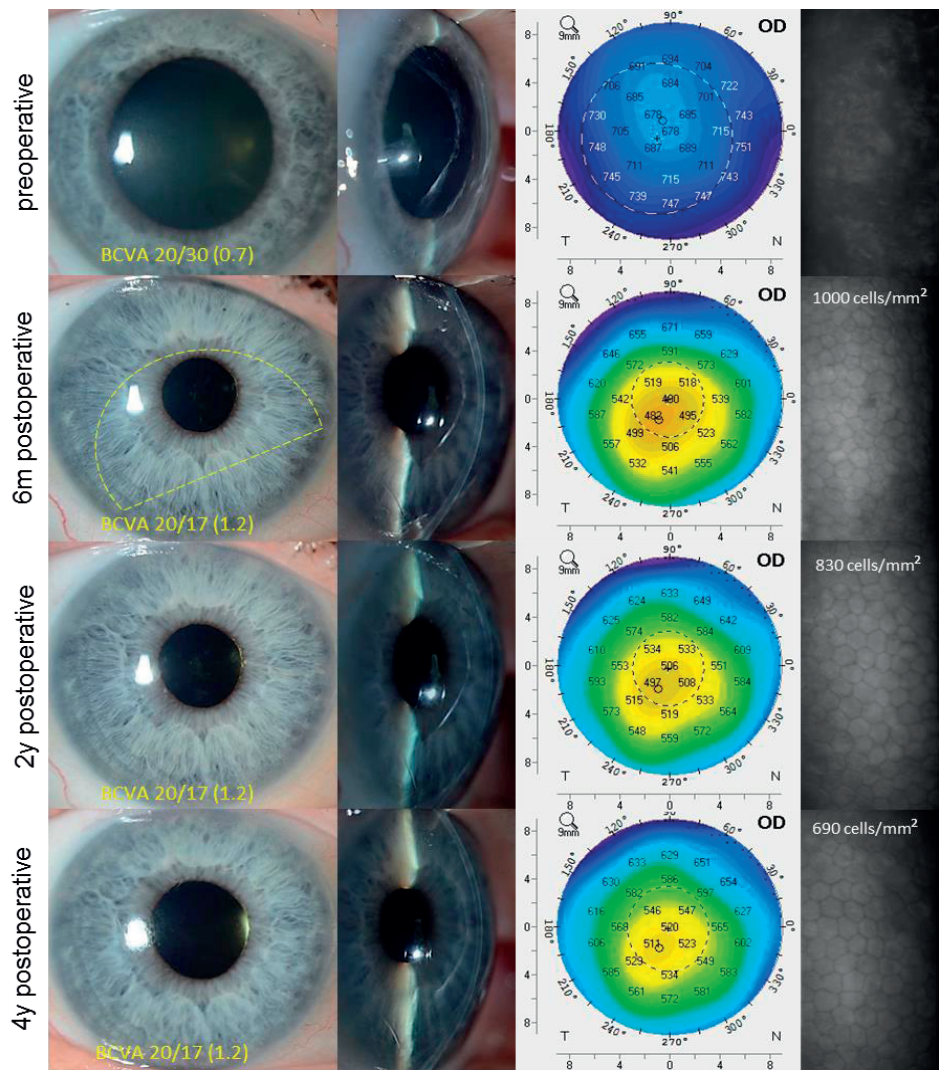


Figure 3. Slit-lamp, pachymetry and specular microscopy images before and after Hemi-Desemet membrane endothelial keratoplasty. Images are shown preoperatively (top row), at 6 months (second row), at 2 years (third row) and at 4 years (bottom row) after Hemi-DMEK (Case 3). The intermittent yellow line outlines the position of the Hemi-DMEK graft. Note continuous corneal clearance at 6 months, 2 years and 4 years as shown in slit-lamp images (left 2 columns).

tively after failed re-bubbling, also showed poor attachment of the circular DMEK graft, which suggests that there may also be recipient-related factors influencing graft attachment. One of the other re-bubbled eyes developed secondary graft failure 2.5 years after Hemi-DMEK. In the longer term, one eye

was suspected of having a mild allograft reaction. All other grafts remained clear, and no further complications were observed throughout the study period.

Theoretically, Hemi-DMEK allows to utilize two endothelial transplants originating from the same donor cornea. In this study, this approach was successful in 2 pairs (Cases 4/5 and Cases 8/9, Table 1). However, for a wider-spread clinical application of multiple endothelial grafts from the same donor cornea, eye banks may need to decide about the feasibility of allocating multiple grafts from one donor cornea and about more critical logistics because multiple grafts from one donor cornea with poor endothelial cell viability (although ECD may be high) may result in graft-related complications (i.e. graft detachment or failure) in multiple recipients.

Overall, although our case series was limited in size, the outcome after Hemi-DMEK may be encouraging since the procedure may allow for clinical outcomes similar to conventional DMEK and the procedure may potentially increase the yield of endothelial tissue from the same donor pool. Furthermore, in more complex eyes with anterior synechiae, glaucoma tubes and/or anterior segment dysgenesis, Hemi-DMEK may be considered over conventional DMEK as it may be easier to position and accommodate the graft in recipient eyes with asymmetrical anterior chamber dimensions. Hemi-DMEK may therefore become an alternative to conventional DMEK.

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