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Impact of Topographic Hot Spots on the Refractive Outcomes of Combined DMEK and Cataract Surgery

Ziv Rotfogel, MD, PhD,[1,2,3] Marco Pellegrini, MD,[1,4,5] Elena Franco, MD,[1,4,5] Giorgio Zauli, MD, PhD,[4,6] Angeli Christy Yu, MD[1,4,5] Massimo Busin, MD.[1,4,5]

[1.] Ospedali Privati Forlì "Villa Igea", Department of Ophthalmology, Forlì, Italy;

[2.] Ophthalmology Research Laboratory, Kaplan Medical Center, Rehovot, Israel;

[3.] Faculty of Medicine, Hadassah Medical School, The Hebrew University, Jerusalem, Israel;

[4.] University of Ferrara, Department of Translational Medicine, Ferrara, Italy;

[5.] Istituto Internazionale per la Ricerca e Formazione in Oftalmologia (IRFO), Forlì, Italy;

[6.] Research Department, King Khaled Eye Specialist Hospital, Riyadh, Saudi Arabia

Running head: Impact of Hot Spots on the Refractive Results of Triple DMEK

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Correspondence and reprint requests to:

Massimo Busin, MD

Dept. of Ophthalmology, Ospedali Privati Forlì “Villa Igea”, 47122 Forlì, ITALY

Tel.+39 3472449343, FAX: +39 0543419566

Email: mbusin@yahoo.com

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ABSTRACT

Purpose: To compare the refractive results of combined Descemet membrane endothelial keratoplasty (DMEK) and cataract surgery in eyes with Fuchs endothelial corneal dystrophy (FECD) with and without topographic hot spots.

Setting: “Villa Igea” Hospital, Forlì, Italy.

Design: Interventional case series.

Methods: In this single-center study, 57 eyes of 52 patients with FECD undergoing combined DMEK, cataract surgery and monofocal intraocular lens (IOL) implantation were included. Patients were classified based on the presence or absence of topographic hot spots on the preoperative axial power map. Prediction error (PE) was calculated as the postoperative manifest spherical equivalent (SE) refraction minus the SE predicted refraction.

Results: Six months after surgery, mean PE was +0.79 ± 1.12 D. In eyes with hot spots, mean K, K flat and K steep significantly decreased after surgery (all $P < 0.05$), while no significant changes were observed in eyes without hot spots (all $P > 0.05$). Eyes with hot spots showed a significantly more hyperopic PE than eyes without hot spots (+1.13 ± 1.23 vs +0.40 ± 0.86 D; $P = 0.013$)

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Conclusion: Combined DMEK and cataract surgery can result in a hyperopic refractive surprise. The presence of topographic hot spots before surgery is associated with a higher hyperopic shift.

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INTRODUCTION

When performing combined Descemet membrane endothelial keratoplasty (DMEK) and cataract surgery, expectations of both surgeons and patients have shifted from restoring corneal clarity to achieving high-level uncorrected visual acuity.[1] The major obstacle encountered in this attempt is the postoperative hyperopic shift frequently reported after DMEK.[2,3] To compensate for this hyperopic shift, most corneal surgeons implant an intraocular lens (IOL) with a dioptric power intended to yield a myopic result between -0.75 to -1.0 D.[4] However, the accuracy of this adjustment is limited by the difficulty in predicting the refractive change induced by DMEK surgery.[2]

Eyes with Fuchs endothelial corneal dystrophy (FECD) can present with focal steepening of the anterior cornea appearing as a topographic “hot spot”.[5-7] Previous studies have demonstrated that topographic hot spots usually resolve following endothelial keratoplasty.[5] Therefore, in eyes with hot spots undergoing triple DMEK, postoperative changes in anterior keratometry readings could theoretically introduce a major error in IOL power calculation. To date, the effect of the presence of hot spots on the refractive outcomes of triple DMEK has not been evaluated. In this study, we compared the postoperative refractive results of triple DMEK in eyes with and without a topographic hot spot.

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METHODS

In this retrospective study, all consecutive FECD patients who underwent combined DMEK, cataract extraction and IOL implantation (triple DMEK) between January 2017 and March 2022 at a single tertiary care referral centre (Ospedali Privati Forlì "Villa Igea", Forlì, Italy) were reviewed. Patients with follow-up of at least three months and Snellen correct distance visual acuity (CDVA) > 20/40 at 1 month after surgery were included. Exclusion criteria were previous ocular surgery, presence of other ocular comorbidities, intraoperative or postoperative complications (except for rebubbling). The study was approved by the Institutional Review Board of Ospedali Privati Forlì "Villa Igea" and adhered to the tenets of the Declaration of Helsinki.

Preoperatively, all patients underwent a complete ophthalmologic examination including slit-lamp examination, best spectacle-corrected visual acuity, manifest refraction, applanation tonometry and fundoscopy. Additionally, all patients underwent anterior segment optical coherence tomography (AS-OCT) (Tomey, Tokyo, Japan) and optical biometry (Lenstar LS 900®, Haag-Streit AG, Switzerland) within 7 days from surgery. At least two scans were acquired, and the best one was selected based on centration of the corneal topography and accuracy of the automated corneal segmentation. Patients were classified, by a masked observer, based on the presence or absence of topographic hot spots on the preoperative AS-OCT axial power map. Hot spots were defined as an isolated area within the central 4 mm of the anterior curvature with a refractive power higher than 1.5D compared to the corresponding area 180 degrees away on the same meridian (Figure 1A). To evaluate the possible effect of posterior corneal changes, patients were also divided in two groups: those with a prolate (negative Q value) or oblate (positive Q value) posterior cornea. Preoperative posterior Q Values were automatically calculated by

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the AS-OCT device (CASIA) using a 9 mm radius, as previously described.[8] The predicted spherical equivalent (SE) refraction was calculated using the SRK/T formula with keratometry readings and axial length measured by optical biometry. The postoperative manifest SE refraction was measured at 6 months after surgery. Prediction error (PE) was calculated as the postoperative manifest SE refraction minus the SE predicted refraction.

Surgical technique

All triple DMEK procedures were performed according to the authors' technique,[9] and summarised briefly as follows. Anaesthesia and akinesia were obtained through peribulbar injection of 10.0-mL of 0.75% ropivacaine solution. Removal of the epithelium from the central area approximately 8 mm in diameter was preformed when epithelial edema affected visualization of the intraocular structures. A 2.8 mm scleral tunnel was prepared and extended into clear cornea. Bimanual phacoemulsification was performed using the Stellaris PC (Bausch & Lomb, Rochester, NY) and a monofocal IOL (Bausch & Lomb MX60E or Hoya iSert) was implanted within the capsular bag. An 9mm descemetorhexis was performed under air. The pre-stripped donor tissue was stained with trypan blue (Vision blue, D.O.R.C., Zuidland, The Netherlands) and punched using an 8.25-mm Barron punch (Katena Products, Inc, Denville, New Jersey, USA). The DMEK graft was then tri-folded with the endothelium inward and transferred via a sterile therapeutic soft contact lens into an intraocular lens cartridge (MDJ Company, La-Monniere-lemontel, France). After performing an inferior peripheral iridotomy, the DMEK graft was delivered bimanually under continuous, low-flow irrigation through a dedicated

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anterior chamber maintainer (Moria SA, Antony, France) placed at the 12 o'clock position. Whenever required, gentle tapping on the cornea was used to unfold the graft. Air was injected to tamponade the graft against the recipient cornea and, the side entries were sealed airtight by means of stromal hydration or 10-0 nylon single stitches.

Statistical analysis

All data were collected prospectively and recorded in the institutional database (Microsoft Excel 2013, Microsoft Corp., Washington, USA). Statistical analysis was performed using SPSS (version 27.0, IBM Corp., New York, USA). Values were expressed as mean and standard deviation for continuous variables and individual counts and percentages for categorical values. The Shapiro-Wilk's test was used to assess normality of data. And independent sample t-test was used to compare continuous variables between patients with and without topographic hot spots, and between those with a positive and negative posterior corneal Q value. A paired samples t-test was used to compare continuous variables before and after surgery. Sensitivity analyses were performed by using AS-OCT instead of optical biometry keratometry readings, and Barrett Universal II instead of SRK/T formula. The possible relationship between the presence of hot spots and the severity of FECD according to the tomography classification proposed by Sun and colleagues[10] was evaluated. A *P* value < 0.05 was considered statistically significant. A post hoc power analysis based on the difference in PE between eyes with and without hot spots showed that the study had a power of 0.72 with a *P* value of 0.05.

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Results

The study included 57 eyes of 52 patients who underwent triple DMEK for FECD. Mean age at the time of surgery was 67.1 ± 8.8 years; 33 patients (63%) were female. Six months after surgery, mean SE refraction was -0.16 ± 1.27 D (range -3.75 to +2.50) and mean PE was +0.79 ± 1.12 D (range -1.15 to +3.03). The PE was greater than ±0.5 D in 35 eyes (61.4%), and greater than ±1.0 D in 25 eyes (43.9%).

Table 1 shows the demographic data and preoperative optical biometry data of eyes with (n = 30) and without (n = 27) topographic hot spots. No significant differences in age, gender, axial length, central corneal thickness, optical biometry K mean and K steep were observed between the two groups (all *P* > 0.05). Conversely, optical biometry K flat, AS-OCT K mean, K steep and K flat were all significantly steeper in eyes with hot spot (all *P* < 0.05). Epithelial bullae were present in 7 of the eyes with hot spots and 1 of the eyes without hot spots (7 Vs 1; *P* = 0.029). Regarding the severity of FECD, no differences were found between eyes with and without hotspots in the percentage of eyes with loss of parallel isopatchs (87 vs 81%; *P* = 0.599), displacement of the thinnest point (87 vs 78%; *P* = 0.387), focal posterior depression (73 vs 59%; P = 0.268), and in the mean number of features (2.5 ± 0.8 vs 2.2 ± 1.0; *P* = 0.259).

Table 2 shows the changes in the AS-OCT corneal parameters following triple DMEK. In eyes with hot spots, mean K, K flat and K steep significantly decreased six months after surgery (all *P* < 0.05). Conversely, no significant changes were observed in eyes without hot spots (all *P* > 0.05). After surgery, mean SE refraction was +0.12 ± 1.48 D in eyes with hot spots and -0.48 ± 0.93 D in eyes without hot spots (*P* = 0.080).

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Table 3 shows that eyes with hot spots showed a significantly higher mean PE in comparison to eyes without hot spots (+1.13 ± 1.23 vs +0.40 ± 0.86 D; *P* = 0.013), indicating a tendency towards a hyperopic refractive surprise. This tendency remained significant after sensitivity analyses performed by using AS-OCT instead of optical biometry keratometry readings, and Barrett Universal II instead of SRK/T formula (Table 3). Conversely, no significant differences in the mean PE were observed between eyes with positive and negative posterior Q values (+1.07 ± 1.14 vs +0.58 ± 1.08; *P* = 0.106), nor in eyes with and without loss of parallel isopatchs (0.84 ± 1.14 vs 0.51 ± 1.06; P = 0.424), displacement of the thinnest point (0.88 ± 1.17 vs 0.33 ± 0.76; P = 0.160), focal posterior depression (0.96 ± 1.19 vs 0.44 ± 0.98; P = 0.096).

The PE was greater than ±0.5 D in 70.0% of eyes with hot spot and in 51.9% of eyes without hot spot (*P* = 0.257), and greater than ±1.0 D in 60% of eyes with hot spot and in 25.9% of eyes without hot spot (*P* = 0.020).

Discussion

Refractive surprises after triple DMEK are common.[2-4,8,11] In this study, the final refraction was within ±0.50 D of the target in only 38.6% of eyes. This result is in line with those reported by Fritz et al. (37.5% of eyes within ±0.50 D),[8] Schoenberg et al. (30.0% within ±0.50 D)[4] and Bae et al. (47.0% within ±0.50 D).[11] In agreement with previous series,[4,8,11] a tendency towards a hyperopic shift was observed, with a positive PE in more than two-thirds of the patients. The identification of risk factors for high residual refractive errors following triple DMEK would be of primary importance to improve the predictability of the postoperative refractive error.

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More than half of the FECD eyes from this series showed a topographic hot spot, namely an area of focal steepening of the anterior corneal surface. In all cases, the hot spots resolved after surgery, with a significant decrease in keratometric values. By contrast, no significant changes in anterior curvature were observed following triple DMEK in eyes without hot spots. In particular, the presence of topographic hot spots was associated with a significantly higher residual hyperopic refractive error, with a mean difference of approximately +0.70 D between eyes with and without hot spots.

The mean hyperopic shift reported after DMEK ranges from +0.03 to +0.74D.[12-16] Hence, most authors suggest to aim for a -0.75 to -1.0 D more myopic refractive target during IOL power selection for cataract surgery combined with DMEK.[4,17] However, as demonstrated in the present study, the refractive shift can be higher in patients with a preoperative hot spot. Thus, an IOL with a dioptric power of +0.50 to +0.75 D higher than that used in eyes without hot spots should be implanted to achieve the desired refraction.

Previous studies investigated other potential risk factors for a hyperopic shift after triple DMEK. In particular, Fritz. et al.[8] reported a 3-fold higher risk of hyperopic surprise in eyes with an oblate posterior corneal profile before surgery. Similarly, Cheung et al.[18] noted that eyes with a hyperopic shift after triple DMEK had a flatter and more oblate posterior cornea preoperatively. It has been suggested that the central corneal edema in FECD could induce a flattening of the posterior corneal surface, and in more advance cases, a steepening of the anterior surface appearing as a topographic hot spot.[18] Epithelial bullae could also contribute to the occurrence of hot spots. The reversal of those changes after DMEK would result in the hyperopic shift.[8,18] Anterior corneal changes have a greater impact on the final refraction

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because the difference in refractive indices between air and cornea is almost 8 times higher than between cornea and aqueous humor. Furthermore, when performing triple DMEK, IOL power calculations are based on anterior keratometry readings. Although posterior corneal changes could also affect the final refraction,[19] no difference in PE was observed between eyes with an oblate and prolate posterior profile in this series.

It should be noted that hot spots are not solely associated with FECD, but can also occur in other endothelial dysfunctions such as bullous keratopathy. A previous study by Shimizu and colleagues reported the presence of hot spots in 42.3% of eyes with pseudophakic bullous keratopathy undergoing triple DSAEK.[5] As in the present series, a larger postoperative hyperopic shift was observed in eyes with hot spots.[5]

Although the presence of topographic hot spots might theoretically affect corneal astigmatism, no changes in this parameter were observed in eyes with hot spot following triple DMEK. This unexpected finding might depend on the software algorithm used by the AS-OCT to calculate corneal astigmatism.

This study has some limitations including the retrospective design and the relatively small sample size. Since the study was not randomized, other factors such as the characteristics of the donor graft could have theoretically influenced the results. It is noteworthy that 7 of the eyes with hot spots had a myopic PE, albeit the PE was lower than -0.50 D in only 2 of them. This underlines that hot spot alone cannot account for the whole variability of refractive results observed after triple DMEK. Therefore, larger prospective studies are still required to evaluate other potential predictors of residual refractive error, as well as the possible interactions between anterior and posterior corneal changes.

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In conclusion, Combined DMEK and cataract surgery can result in a hyperopic refractive surprise. The presence of preoperative topographic hot spots is associated with a higher hyperopic shift. To minimize the residual refractive error in eyes with hot spots, surgeons should consider to implant IOLs with a dioptric power of +0.50 to +0.75 D higher than that used in eyes without hot spots.

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VALUE STATEMENT

What was known:

- A hyperopic refractive surprise is frequently observed in eyes undergoing combined DMEK and cataract surgery
- Eyes with Fuchs endothelial corneal dystrophy can present with topographic “hot spots”, which usually resolve following endothelial keratoplasty
- The effect of topographic hot spots on the refractive outcomes of triple DMEK has not been previously evaluated

What this study adds

- The presence of topographic hot spots is associated with a higher hyperopic shift after combined DMEK and cataract surgery.

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- In eyes with hot spots undergoing triple DMEK, intraocular lenses with a +0.50 to +0.75 D higher dioptric power should be implanted to minimize the residual refractive error.

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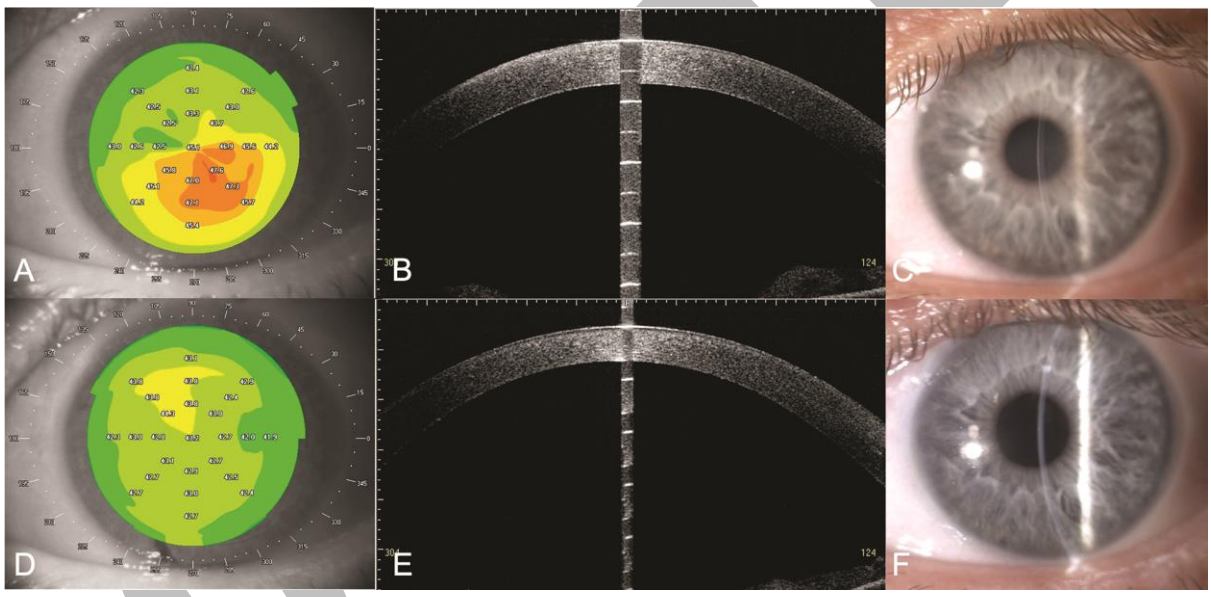
Figure 1: Axial power map, anterior segment optical coherence tomography and clinical picture of an eye with topographic hot spot before (parts A, B, and C) and after combined Descemet membrane endothelial keratoplasty and cataract surgery (Parts D, E, and F).



ACCEPTED

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