

DMEK grafts were prepared following the standardized protocol for the “no-touch” technique.²³ For DMEK surgery, a 9.0-mm epithelial mark was made to outline the area of the planned Descemet membrane (DM) excision, a main incision of 2.4 mm then performed. The anterior chamber was filled with air through the side port. After scoring the recipient endothelium with an inverted Sinsky hook, a circular portion of DM was stripped from the posterior stroma so that a 9.0-mm descemetorhexis was created. Iridectomy was performed in all cases. Using a Geuder crystal injector (Geuder AG, Heidelberg, Germany) filled with balanced saline solution, the DM rolls were inserted into the anterior chamber and then oriented endothelial side down using careful indirect manipulation of the tissue with air and balanced saline solution. An x-shaped 10/0 nylon suture was used to seal the main incision. An air bubble was used to extend the graft and then reinjected underneath to position the tissue onto the recipient posterior stroma. The anterior chamber was completely filled with air for 60 minutes, followed by air–liquid exchange to pressurize the eye. A final 60% air bubble was left in the eye overnight. Patients were placed on a regimen of 1% dexamethasone drops q.i.d, tapered down over a period of 6 months to fluorometholone b.i.d.

A complete ophthalmologic examination was performed on all patients after the DMEK procedure including best corrected distance visual acuity (CDVA), manifest and cycloplegic refractions, corneal topography (Sirius, CSO, Italy), anterior segment optical coherence tomography (Visante Zeiss-Meditec, Germany), endothelial cell density (ECD), ultrasonic pachymetry, slit-lamp microscopy, Goldmann applanation tonometry, and binocular indirect ophthalmoscopy.

The time between DMEK procedure and FemtoLASIK to correct the residual refractive error varied from 18 to 36 months. The option of LASIK with femtosecond laser surgery was agreed upon between the surgeon and the patient after full understanding the potential risks. Surgery was performed under topical anesthesia using the IntraLase femtosecond laser FS60 (Advanced Medical Optics, Inc, Santa Ana, CA) to create the flap and the VISX Star S4 (Advanced Medical Optics, Inc) excimer laser to perform corneal photoablation. Femtosecond laser flaps were programmed with the following settings: 90 μ m thickness, 8.0 to 9.0 mm diameter, 45-degree superior hinge angle to achieve equivalent corneal stromal surface exposure, 70-degree side-cut angle, laser raster patterns spot and line separation of 9 and 9 μ m, and stromal energy of 1.0 μ J with a side-cut energy of 1.8 μ J. A pocket was created with the femtosecond laser to avoid an opaque bubble layer. The excimer laser was programmed with the conventional VISX S4 algorithm to achieve emmetropia (software version 4.60). All surgeries were performed by 1 surgeon (J.F.A.). The postoperative treatment consisted of a regimen of 1% dexamethasone drops 4 times a day for 1 week and 2 times a day for the second week and then fluorometholone one time a day. The postoperative follow-up ranged between 12 and 60 months.

Manifest refraction, uncorrected distance visual acuity (UDVA), and CDVA were registered at each postoperative follow-up visit after the DMEK procedure and after the

FemtoLASIK surgery. Furthermore, the following topographic and pachymetric parameters were reviewed:

Topographic parameters (Sirius; CSO, Scandicci, Italy): keratometry, symmetry index back, symmetry index front, and 4.5- and 8.0-mm-zone root mean square value per unit area for (RMS/A) the front and back.

Pachymetric parameters (optical coherence tomography [OCT], Visante Zeiss-Meditec, Germany): thinnest corneal thickness (TCT), distance from the TCT to the apex, and central corneal thickness (CCT).

Preoperative and postoperative data were compared using the Wilcoxon nonparametric test. Statistical analysis was performed using SPSS software for Windows (version 15.0, SPSS, Inc). *P* value less than 0.05 was considered statistically significant. Data are reported as the mean \pm SD.

RESULTS

The study included 7 eyes of 6 patients with a mean age of 63.6 ± 10.4 (range 49–71) years. All surgeries (both DMEK procedures and FemtoLASIK surgeries) were uneventful, with no intraoperative or postoperative complications. No dislocation and/or detachment of the Descemet membrane graft was observed in any case. Table 1 shows patient demographics before FemtoLASIK surgery. The follow-up time after DMEK (before FemtoLASIK surgery) ranged from 18 to 36 months (Supplemental Table 1A shows topographic, pachymetric parameters, and manifest refraction, UDVA, and CDVA during the postoperative DMEK course for each case; Supplemental Digital Content 1, <http://links.lww.com/ICO/A923>). The UDVA, CDVA, and refractive error values as well as the topographic and pachymetric parameters analyzed remained stable over the postoperative DMEK follow-up period.

Table 2 shows the pre- and post-FemtoLASIK visual and refractive outcomes. The post-FemtoLASIK follow-up period ranged from 12 to 60 months. All cases experienced a significant improvement in UDVA, all of them reaching a postoperative UDVA value $\geq 20/32$. None of the eyes lost lines of CDVA, and 1 case showed a gain of lines of CDVA.

TABLE 1. Patient Demographics Before FemtoLASIK Surgery (Means \pm SD and Range)

Characteristic	Value
Eyes (n)	7
Age (yr) (range)	63.6 ± 10.4 (49 to 71)
Follow-up (mo)* (range)	22.3 ± 6.7 (18 to 36)
Spherical equivalent (range)	-0.55 ± 1.12 (+1.75 to -1.62)
Mean refractive sphere (D) (range)	$+0.57 \pm 1.59$ (+3.75 to -1.00)
Mean refractive cylinder (D) (range)	-2.25 ± 0.93 (-1.25 to -4.00)
Mean minimum K (D) (range)	41.96 ± 1.32 (40.15 to 43.65)
Mean maximum K (D) (range)	43.83 ± 1.74 (41.25 to 45.25)
Central corneal thickness (μ m)	534.6 ± 17.1 (510 to 554)
Thinnest corneal thickness (μ m)	527.4 ± 19.4 (500 to 552)
ECD (cells/mm ²)	1477 ± 288 (1102 to 1802)

*The follow-up time after DMEK (before FemtoLASIK surgery).

TABLE 2. Visual and Refractive Results Before and After FemtoLASIK Surgery (Means \pm Standard Deviation (SD) and Range)

Characteristic	Value		
Follow-up (mo) (range)	23.1 \pm 17.1 (12–60)		
	Pre-FemtoLASIK	Post-FemtoLASIK	P Value
UDVA (Snellen scale) (range)	0.34 \pm 0.13 (0.1 to 0.5)	0.71 \pm 0.12 (0.6 to 0.9)	<0.0001
CDVA (Snellen scale) (range)	0.74 \pm 0.16 (0.4 to 0.9)	0.80 \pm 0.05 (0.6 to 0.9)	0.1
Mean spherical equivalent (D) (range)	−0.55 \pm 1.12 (+1.75 to −1.62)	−0.29 \pm 0.29 (0 to −0.62)	0.2
Mean refractive sphere (D) (range)	+0.57 \pm 1.59 (+3.75 to −1.00)	−0.04 \pm 0.17 (+0.25 to −0.25)	0.09
Mean refractive cylinder (D) (range)	−2.25 \pm 0.93 (−1.25 to −4.00)	−0.50 \pm 0.43 (0 to −1.25)	0.0002

In all cases, the refractive error, UDVA, and CDVA values remained stable at their respective postoperative follow-up visits (Supplemental Table 2A shows visual and refractive outcomes during the postoperative FemtoLASIK course for each case; see Supplemental Digital Content 1, <http://links.lww.com/ICO/A923>). Furthermore, all topographic and pachymetric parameters were stable at different postoperative follow-up visits (Supplemental Table 3A shows topographic and pachymetric parameters during the postoperative FemtoLASIK course for each case; see Supplemental Digital Content 1, <http://links.lww.com/ICO/A923>).

DISCUSSION

DMEK is gaining popularity among surgeons for endothelial keratoplasty because it only involves transplanting an endothelium–Descemet membrane layer that allows a faster and better visual recovery with a significantly lower rate of complications compared with other techniques for endothelial keratoplasty.^{1–9} DMEK has provided stable visual and refractive outcomes at long-term follow-up.^{18–20} The speed and degree of visual recovery after DMEK depends on when the surgery is performed.^{24,25} Recent studies, which analyzed preoperative visual acuity²⁴ and corneal densitometry²⁵ as predictors of postoperative visual acuity, found that early DMEK surgery could have a positive impact on long-term visual acuity results. Although DMEK has been considered as a “refractive neutral procedure,” a slight hyperopic shift after DMEK is strongly documented. The mean refractive change after DMEK may be considered subtle (approximately 0.3 D of hyperopic shift¹¹); however, a larger myopic and hyperopic shift in some cases has also been reported.^{11–13} Van Dijk et al^{11,13} found that DMEK induced a refractive change larger than 1D (both myopic and hyperopic) in approximately 20%¹¹ and 35%¹³ of the eyes analyzed. When DMEK is performed in combination with cataract surgery, the IOL power calculation presents a challenge. A widely accepted approach is to select the IOL power with a refractive target of −0.50 and up to −1.00 to compensate the expected hyperopic shift induced after DMEK. However, refractive surprises in a significant number of cases after the triple-DMEK procedure have been reported (even choosing a postrefractive target of −0.50 to −1.00 D). In the study by Laaser et al,¹⁴ 30% of the eyes were outside 1.00 D of emmetropia and 12.5% were outside 2.00 D of emmetropia after the triple-DMEK procedure. Schoenberg et al¹⁵ reported a refractive error greater than

± 1.00 D in 50% of the eyes. Cheung et al,¹⁶ in turn, reported that the postoperative refraction was greater than +1.25 D of the target refractive goal in 31% of the eyes analyzed. All these outcomes are in line with the results more recently obtained by Fritz et al,¹⁷ who reported that approximately 20% of the eyes were off the planned refractive target by more than 1.00 D. At the same time, Ham et al¹⁰ found that 32% of the eyes analyzed (16/50) experienced a change in astigmatism higher than 1.00 D (ranged from 1.25 to 2.50 D) after isolated DMEK. Laaser et al¹⁴ reported, in 61 eyes which underwent the triple-DMEK procedure, an increase in the mean refractive cylinder from preoperative to 6 months postoperative.

From all these previous studies, it could be concluded that on average, the postoperative refractive error after isolated DMEK or triple-DMEK may be relatively small. Nevertheless, wide variations in the refractive shift between patients have been reported. Therefore, there will be a greater than expected proportion of patients with a residual refractive error after surgery. Although the first and main objective of DMEK is to improve corneal clarity, some residual refractive error may not be well tolerated with spectacles, could induce anisometropia, and/or achieve an unsatisfactory postoperative UDVA. Consequently, in those cases, the DMEK outcomes may be not as successful as would be expected.

To overcome this, in the current study, we present 7 eyes that underwent FemtoLASIK surgery to correct residual refractive error after a DMEK procedure. In the current study, the interval time between surgeries (DMEK procedure and FemtoLASIK) was at least 18 months. Previous studies have shown that postoperative refraction stabilization after DMEK occurred at 3 months postoperatively.^{10,11,13} However, a longer follow-up period between surgeries was established because, beyond refractive stabilization, we wanted to verify that all the topographic and pachymetric parameters remained stable before FemtoLASIK surgery. In our case series, UDVA significantly improved in all eyes, all of them reaching a postoperative UDVA value $\geq 20/32$. None of the eyes lost lines of CDVA, and case 6 showed a gain of lines of CDVA. In all eyes, the refractive error, UDVA, CDVA values and topographic and pachymetric parameters remained stable at their respective postoperative follow-up visits (ranged from 12 to 60 months). To the best of our knowledge, this is the first reported series of FemtoLASIK surgery after a DMEK surgery. A case series studied the use of LASIK and PRK in 5 patients with previous Descemet stripping

automated endothelial keratoplasty, achieving a significant improvement in UDVA without any complications.²⁶

Despite these encouraging outcomes, it is important to be cautious because corneas can be abnormally thin after DMEK,²² which could represent a risk to develop post-LASIK ectasia. Therefore, these patients must be closely monitored before planning any laser refractive procedure. In our case series, the pachymetric parameters studied (CCT, TCT, and distance from the TCT to the CCT) were within a normal range compared with healthy corneas.^{27,28} Furthermore, all these parameters remained stable over the follow-up period between surgeries. Regarding topographic parameters, in cases 1 and 6 (see Supplemental Table 1A, Supplement Digital Content 1, <http://links.lww.com/ICO/A923>), corneal shape indices after the DMEK procedure were high. It should be noted that corneal higher-order aberrations could be increased after DMEK^{29,30}; consequently, these topographic indices could be altered in comparison with normal corneas without necessarily presenting a risk or diagnosis of an ectatic disease. In both cases, over the follow-up period between DMEK and FemtoLASIK surgeries, all these corneal shape indices remained unchanged and the pachymetric parameters were maintained within a normal range and unchanged. In any case, it would also be interesting to carry out further studies to analyze the effect of Fuchs dystrophy resolution through DMEK on the corneal biomechanical properties.

In the current study, no complications occurred during FemtoLASIK surgery or over the entire follow-up time (ranged from 12 to 60 months) (including flap-related complications, graft failure, refractive instability, and corneal ectasia). If compared with a microkeratome, the use of femtosecond laser to create the flap has the advantage of creating more predictable and uniform flap thickness and stromal bed and less intraoperative epithelial injury.^{31,32} Furthermore, it has been reported that FemtoLASIK surgery does not provide significant changes in the ECD.³³ The endothelial cell count in this case series remained stable over the post-FemtoLASIK surgery follow-up. It should be noted that a rare complication secondary to LASIK is interface fluid syndrome, which is characterized by fluid collection in the flap interface. It has been reported that endothelial decompensation and steroid-induced ocular hypertension are etiological factors. Therefore, it should be considered that in case of graft failure or rejection, these patients could have a certain risk of developing interface fluid syndrome.

Although there were no complications in any case, further long-term prospective studies, including more patients, should be performed to assess possible complications and the stability of the procedure.

In conclusion, our findings suggest that the residual refractive error after DMEK can be safely and effectively treated with FemtoLASIK. Further long-term follow-up studies, including a larger number of cases, are needed to properly analyze the stability of this surgery and to confirm the safety of the procedure.

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