Optical Performance of the Cornea Six Years following Photorefractive Keratectomy for Myopia

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PURPOSE. To investigate the optical quality of the anterior cornea during a 6-year follow-up after photorefractive keratectomy (PRK) for myopia.

METHODS. Forty-nine patients (98 eyes) underwent PRK using an excimer laser platform. Patients were subdivided into three groups according to their preoperative spherical equivalent refraction and amount of cylinder component: the low-myopia, the high-myopia, and the astigmatism group. Preoperative and 1-, 3-, and 6-year postoperative root-mean-square values of coma, spherical aberration (SA), and total high-order aberrations (HOA) were calculated over 3.50- and 6.00-mm pupil diameters. Modulation transfer function (MTF) values and point spread functions were calculated to describe the impact of myopic PRK on the optical performance of the cornea during follow-up.

RESULTS. The amount of postoperative SA was higher (P < 0.05) than the preoperative state in both the low- and the high-myopia groups over 3.50- and 6.00-mm pupil sizes. The postoperative increase of coma was statistically significant (P < 0.05) only in the high-myopia group over both pupil sizes. Total-HOA increased (P < 0.05) after PRK in all the study groups over 6.00-mm pupil. A distinct increase in the ratios of MTF was calculated over 6.00-mm pupil, at low and middle spatial frequencies in the range between 5 and 15 c/deg, especially after the deepest myopic ablations.

CONCLUSIONS. The high-order wavefront aberration of the anterior cornea stabilized 1-year after PRK for the treatment of myopia up to −9.00 D. The effect of induced HOA on the image optical quality of the cornea was increased mainly after the correction of high myopia over scotopic pupil. (Invest Ophthalmol Vis Sci. 2011;52:846–857) DOI:10.1167/iovs.10-5905

Excimer laser surgery is an established procedure for correcting refractive error, enabling surgeons to give patients a high quality of unaided vision. Several works1–10 have globally assessed the long-term safety and efficacy of photorefractive keratectomy (PRK) for the treatment of myopia. On the other hand, most of the studies were focused on the analysis of manifest refraction and visual acuity after surgery, with limited information on the optical performance of the treated cornea in a period longer than 3 years after surgery.11

In a previous work,11 we analyzed the wavefront aberration (WA) architecture and the relative image optical quality of the cornea in a population of 30 myopic patients who were followed up to 3 years after surgery. In general, the high-order corneal WA was shown to stabilize 1 year after surgery. An induction of corneal high-order aberrations was measured after PRK, especially after the treatment of high myopia. Moreover, using a new metric of optical quality—the modulation transfer function (MTF)—we demonstrated a distinct decline in the optical quality of the postoperative cornea at low and middle spatial frequencies, between 6 and 19 c/deg, over 5.00-mm and 7.00-mm pupil diameters.

The aim of the present work was to extend our knowledge of the long-term changes of the high-order corneal WA after PRK, providing data from a population of myopic eyes (different from those of the previous 3-year study11) during a 6-year follow-up. A control group of age-matched patients with stable myopia was examined to observe changes in the optical performance of the cornea during the same period.

MATERIALS AND METHODS

A total of 49 consecutive patients, 20 men and 29 women, who underwent PRK for myopia or myopic astigmatism between September 2002 and June 2003 was included in this study. Patients were considered eligible for the study if they were at least 21 years old and free of ocular disease, underwent no previous ocular surgery, and had at least 2 years of refractive stability. Patients wearing contact lenses were asked to discontinue their use for at least 4 weeks before surgery. The study followed the tenets of the Declaration of Helsinki. Informed consent was obtained from all patients. Institutional review board approval was not required for this study. Patients were subdivided into three groups according to the preoperative spherical equivalent (SE) cycloplegic refraction and the amount of cylinder component: the low-myopia group (range, −1.25 to −4.00 D) and the high-myopia group (range, −4.10 to −9.00 D), in whom the cylinder component was lower than 1.75 D, and the astigmatism group, in whom the cylinder component ranged between −2.00 and −5.00 D.

Either of two experienced surgeons (ML and SS) performed the procedures. PRK was performed with an excimer laser platform (Technolas 217 C; Bausch & Lomb, Dornach, Germany) with an ablation zone diameter of 6.00 mm (transition zone up to 9.00 mm in diameter) in all eyes. The smoothing technique was performed immediately after the procedure, using a viscous 0.25% sodium hyaluronate solution for masking the cornea.12 With the laser in PTK mode, the ablation depth was set at 10 μm (divided into four intervals for a total of 428 spots), and the maximum diameter of the ablation zone was set at 9.00 mm. A spatula was used to spread the masking fluid onto the corneal surface. The astigmatism was corrected using the cross-cylinder technique to homogenize the treatment across the steepest and flattest corneal meridians. The technique consists of treating half the cylinder component with hyperopic ablation and the other half with SE refraction using myopic ablation. In all cases, a 6.00-mm ablation zone (with a transition zone up to 9.00 mm in diameter) was used.

All patients included in the study underwent complete ocular examination before surgery and 1, 3, and 6 years after surgery. Mon-

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ocular uncorrected (UCVA) and best-corrected (BCVA) photopic visual acuities were assessed preoperatively and postoperatively. Corneal topography and pupillometry were performed with a topographer (Keratron Scout; Optikon 2000 SpA, Rome, Italy). For each eye, measurements were repeated three times to assess the repeatability of the topography; the best image was then chosen for analysis. The topographer software calculates corneal WA on the corneal elevation with respect to an ideal aspherical corneal shape with eccentricity 1/n (where n = 1.3375) and centered on the corneal vertex. The WA was then computed with respect to the line of sight (i.e., the center of the entrance pupil) using the move axis function of the topographer and was obtained from the derivatives using a least squares best-fit procedure to the desired pupil area of analysis and described as a seventh-order Zernike polynomial expansion.11 Corneal aberation data output were exported and processed into custom software written in technical computing software (MatLab, version 7.0; The MathWorks, Inc., Natick, MA) for analysis. Preoperative and postoperative high-order corneal aberation data were computed over simulated pupils of 3.50-mm and 6.00-mm diameters. Root mean square (RMS) of the corneal aberration data were computed up to the seventh order, the RMS of coma (the square root of the sum of the squared coefficients of Z4, Z6, and Z8), and the RMS of the spherical aberration (SA; the square root of the sum of the squared coefficients of Z2 and Z4). The MTF and the point spread function (PSF) of the anterior corneal optics were computed from the corneal WA at 555 nm wavelength of light, excluding first- and second-order terms. The mean preoperative and postoperative radial MTFs and the ratio between the preoperative and postoperative MTFs (i.e., the MTF ratio) were used to evaluate the relative optical effect induced on the corneal optics by the surface ablation procedures. Detailed information on the calculation of objective metrics of optical quality can be found in a previous review article.15

**Statistical Analysis**

One-way analysis of variance (ANOVA) was used to statistically compare the differences between the preoperative and postoperative data in each study group. When statistical significance was found, the differences between each postoperative period were further compared using the Tukey-Kramer test for pairwise comparisons. The Pearson correlation test was performed to analyze the changes of refractive correction in simple myopic treatments. Statistical comparison of preoperative data between the study groups and control group was again performed using ANOVA and the Tukey-Kramer test.

**RESULTS**

Table 1 provides preoperative characteristics of the study groups. Two female patients were anisomyopic, and those eyes were split into the low- and high-myopia groups respectively; the eyes of one male patient were split into the high-myopia and astigmatism groups. A group of 10 age-matched patients, with stable myopia and no history of ocular disease or previous ocular surgery, was used as a control to examine the physiologic change of the high-order corneal WA during the same follow-up period.

**Refractive and Visual Acuity Data**

All procedures were uneventful, and no eye underwent repeat surgery during follow-up; only one patient in the low-myopia group missed the 6-year postoperative examination. A statistically significant myopic regression in the mean SE refraction was measured between 1 and 6 years either in the low-myopia (−0.24 D; P < 0.001) or the high-myopia (−0.30 D; P < 0.001) group. Three eyes (7%) in the low-myopia group, four eyes (10%) in the high-myopia group, and two eyes (13%) in the astigmatism group experienced a mean refractive regression of −0.50 D or higher between 1 year and 6 years after surgery. One eye in either the low-myopia (2%) or the high-myopia (2%) group had a mean refractive regression higher than −1.00 D in the same period. At 6 years after surgery, 40 eyes in the low-myopia group (91%), 31 eyes in the high-myopia group (80%), and seven eyes in the astigmatism group (47%) were within ± 0.50 D of emmetropia. Postoperative SE refraction data are summarized in Table 2. Vector analysis of refractive cylinder was performed using adjusted axes for the left eye (adjusted axis = 180° − original axis) and doubled angles to determine the change in both direction and magnitude of refractive cylinder from the preoperative to the 6-year postoperative visit.16,17 The astigmatic refractive change was +0.22 at 13° in the low-myopia group, +0.39 at 18° in the high-myopia group, and +2.36 at 11° in the astigmatism group (P < 0.001). The direction change of refractive astigmatism was not statistically significant in any study group. The vector change in refractive cylinder has been plotted using a double-angle format, as illustrated in Figure 1. At 6 years after surgery, 95% and
87% of the population of vectors in the low- and high-myopia groups, respectively, were within 0.50 D of the origin; 86% of vectors in the astigmatism group were within 1.00 D of the origin.

All eyes (100%) in the low-myopia group had 20/20 BCVA before surgery, whereas 56% and 53% of eyes in the high-myopia and the astigmatism group, respectively, had 20/20 BCVA before surgery. At 6 years after surgery, 95% of eyes in the low-myopia group, 52% in the high-myopia group, and 36% in the astigmatism groups had UCVA of 20/20 or better (100%, 97%, and 87% had UCVA of 20/40 or better, respectively). The BCVA was unchanged or improved in 100% of eyes in all study groups at the end of follow-up (Fig. 2). No eye lost one or more lines of Snellen visual acuity in this series. During the first year after surgery, traces of haze were observed in six eyes (14%) during the long-term follow-up in any study group.

High-Order Corneal Wavefront Aberration Data

On average, the mean mesopic and scotopic pupil sizes were approximately 3.40 mm and 5.80 mm, respectively, in all study groups (Table 1). For this reason, we chose to represent the optical quality of the anterior cornea in mesopic and dim light conditions over simulated pupils of 3.50-mm and 6.00-mm diameters, respectively. The small pupil area further ensured that we would analyze changes of HOA within the ablation zone rather than over larger area, including the edge of ablation.

Preoperative mean RMS values of all determined combinations of high-order aberrations were more similar between the study groups for either 3.50-mm or 6.00-mm pupils, with the exception of higher values of total RMS-HOA (P < 0.05) and coma (P < 0.01) in the astigmatism group, than in the other study groups for 6.00-mm pupils (Table 1).

For 3.50-mm pupil diameters, the increase in total RMS-HOA and coma values was statistically significant (P < 0.01) after the deepest myopic ablations 1 year after surgery and was almost stable during follow-up. The amount of SA increased in both the low-myopia (P < 0.05) and the high-myopia (P < 0.01) groups after surgery and remained stable during follow-up. Corneal high-order aberrations were not statistically significantly changed after PRK for the treatment of myopic astigmatism. Figure 3 illustrates high-order RMS values during follow-up in all the study groups over 3.50-pupil diameters.

At the 6.00-mm pupil diameter, total RMS-HOA and SA increased both in the low-myopia (P < 0.001) and high-myopia (P < 0.001) groups at 1-year after surgery and were stable during follow-up. Coma values did not differ between the preoperative and postoperative states in the low-myopia group, whereas a statistically significant increase of coma was measured after deeper myopic ablations (P < 0.001). A statistically significant increase of total RMS-HOA (P < 0.05) was measured in the astigmatism group 1 year after surgery and

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TABLE 2. Postoperative Refractive and Corneal Thickness Data of Study Groups

<table>
<thead>
<tr>
<th>Postoperative Variables</th>
<th>Low Myopia</th>
<th>High Myopia</th>
<th>Myopic Astigmatism</th>
<th>Control</th>
</tr>
</thead>
<tbody>
<tr>
<td>1-Year SE refraction, D</td>
<td>−0.03 ± 0.30</td>
<td>−0.15 ± 0.49</td>
<td>−0.35 ± 0.66</td>
<td>−4.98 ± 2.64</td>
</tr>
<tr>
<td>3-Year SE refraction, D</td>
<td>−0.20 ± 0.25</td>
<td>−0.32 ± 0.45</td>
<td>−0.34 ± 0.89</td>
<td>−4.99 ± 2.68</td>
</tr>
<tr>
<td>6-Year SE refraction, D</td>
<td>−0.27 ± 0.22* (n = 42)</td>
<td>−0.45 ± 0.40*</td>
<td>−0.35 ± 0.64</td>
<td>−5.04 ± 2.61</td>
</tr>
<tr>
<td>1-Year central corneal thickness, µm</td>
<td>485 ± 41</td>
<td>447 ± 33</td>
<td>470 ± 21</td>
<td>544 ± 21</td>
</tr>
<tr>
<td>3-Year central corneal thickness, µm</td>
<td>487 ± 29</td>
<td>466 ± 20</td>
<td>465 ± 33</td>
<td>542 ± 22</td>
</tr>
<tr>
<td>6-Year central corneal thickness, µm</td>
<td>501 ± 42 (n = 42)</td>
<td>453 ± 34</td>
<td>462 ± 32</td>
<td>541 ± 21</td>
</tr>
</tbody>
</table>

All values are mean ± SD unless otherwise indicated.
* Statistically significant differences (P < 0.05) between 1 year and 6 years after surgery.

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FIGURE 1. Double-angle plot of the preoperative (black circles) and 6-year postoperative (gray circles) refractive astigmatism for all study groups. Each point represents a single eye astigmatism uniquely characterized by a pair of values in the x- and y-coordinates. Squares: represent the means (centroids) of the preoperative and postoperative astigmatism: the amount of improvement can be seen directly on the doubled-angle plots by how much closer the postoperative centroid is to the origin than the preoperative one. In the low-myopia group, most astigmatism vectors were calculated to be 0 D, and the symbols overlapped each other.
remained stable during follow-up. The postoperative amounts of SA and coma values were not statistically significant different from the preoperative values after astigmatic photoablation. Figure 4 illustrates high-order RMS values during follow-up in all the study groups over a 6.00-mm pupil diameter.

A statistically significant linear correlation between the amount of refractive correction and the change in total RMS-HOA, coma, and SA values was determined over either 3.50-mm or 6.00-mm pupil sizes at each postoperative examination period (Fig. 5).

Mean radial MTF was calculated to quantitatively compare the preoperative and postoperative MTFs in each study group (Fig. 6). Two-dimensional mean MTF was converted from rectangular to polar coordinates, and then the MTF values were averaged across meridians. A higher postoperative decrease, though not statistically significant (P > 0.05), of the mean radial MTF was calculated in the high-myopia group compared with the low-myopia and astigmatism groups, over both pupil diameters. The ratio between the preoperative and postoperative MTFs for spatial frequencies up to 85 cyc/deg was calculated, with the highest values in the high-myopia group.

Two-dimensional corneal PSFs were calculated as the average of the PSFs of all the eyes in the population study. High-quality corneal PSFs were obtained over the 3.50-mm pupil diameter, and very subtle differences were measured between the preoperative and postoperative states in all the study groups. Over the 6.00-mm pupil diameter, there was a clearly increased effect of spherical aberration on the optical image quality, primarily in the high-myopia group (Fig. 8).

**Control Data**

The control group was homogeneous with regard to mean age and mean SE refraction with the study groups. Refractive and corneal pachymetry data are summarized in Tables 1 and 2. Corneal WA data during follow-up are illustrated in Figures 2 and 3. High-order RMS values of the anterior cornea were stable during follow-up over the 3.50-mm and the 6.00-mm pupil diameters.

**Discussion**

Although PRK is a widespread established procedure for the correction of myopia and myopic astigmatism, no work...
has yet aimed to analyze the optical performance of the anterior cornea in the very long-term period. In this study, we provided information on the image optical quality of the anterior cornea in a population of 49 myopic patients (98 eyes) who were followed up for 6 years after surgery.

Between 1 and 6 years after surgery, a mean refractive regression of $-0.24$ D and $-0.30$ D in the low-myopia and high-myopia groups, respectively, was measured. This myopic shift, though statistically significant, did not achieve clinical significance because all the patients were spectacle independent. Mean refractive regression was in accordance with the long-term data of previous reports, in which a mean myopic regression between $-0.20$ D and $-1.00$ D up to 14 years after surgery was measured. After PRK for the correction of myopic astigmatism, however, mean postoperative SE refraction of approximately $-0.35$ D tended to stabilize 1 year after surgery. Vector analysis of refractive astigmatism revealed how PRK was effective in minimizing the amount of cylinder, without inducing change in direction, in all study groups.

The preoperative values of determined combinations of HOAs were similar between groups over mesopic pupils, here set at 3.50-mm diameter; on the other hand, over
scotopic pupils (6.00-mm diameter), total RMS-HOA and coma were significantly higher in the astigmatism group than in the other study groups. These data were consistent with several population studies on normal eyes.15,20–26

After surface ablation, the increase in corneal HOA was confirmed to be dependent on either the magnitude of refractive correction or the pupil diameter, as previously discussed.11,27–29 The high-order WA of the anterior cornea was confirmed to stabilize 1 year after surgery.11

In the 3.50-mm pupil, the increase of total HOA-RMS was statistically significant only in the high-myopia group; on the other hand, the postoperative amount of SA was higher than the preoperative state either in the low- or the high-myopia group. In the 6.00-mm pupil, the increase in total-HOA RMS, coma, and SA was twofold after deeper myopic ablations; a slight, though statistically significant, increase in total-HOA was measured in both the low-myopia and the astigmatism groups after surgery. It should be considered how the effect of induced high-order aberrations could be higher than those reported for eyes with scotopic pupil diameters larger than 6.00 mm; this was verified in nine eyes (20%) the low-myopia group, five eyes (13%) in the high-myopia group, and any eye in the astigmatism group.

**FIGURE 4.** Preoperative and postoperative RMS values (mean ± SD) of determined combinations of high-order aberrations in the study groups over a 6.00-mm diameter pupil. *P ≤ 0.05 or less, statistically significant (Tukey test).**

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Ablation design and parameters, epithelial healing, and biomechanics of the corneal tissue are indicated as the main causes that may influence the definite optical result after PRK. The increase of SA within the ablation zone (over 3.50-mm pupil) after simple myopic ablations has been related to various factors—including variable predictability of ablation because of variations in the energy per pulse, spatial and temporal positioning and distribution of the laser spots, ablation frequency, ablation plume dynamics, loss of ablation efficiency at nonnormal incidence, temperature increases in the stroma.

**FIGURE 5.** Correlation scattergram between the achieved correction and the change in total-HOA, SA, and coma over 3.50- and 6.00-mm diameter pupils at the end of follow-up. Each line represents the linear fit to the data.
during ablation, corneal hydration, and environmental temperature and humidity—other than the biomechanical response of the tissue.\textsuperscript{30–44} SA did not increase after photoastigmatic procedures, most likely because of the hyperopic ablation step used during the cross-cylinder technique.\textsuperscript{45} The different regional biomechanical response induced in the cornea by the proprietary laser system ablation design, the ablation parameters discussed, the depth of ablation, and the corresponding wound healing of the individual cornea should be considered as the sources of coma and asymmetric HOA.\textsuperscript{11,12,27,46–51}

\textbf{FIGURE 6.} Averaged one-dimensional radial profiles of the MTFs at different spatial frequencies (0–85 cyc/deg) in all the study groups. Preoperative and postoperative radial MTFs were calculated over 3.50-mm and 6.00-mm diameter pupils. The low-myopia and astigmatism groups did not experience a clear decline in MTF values after surgery; this was not the case for the high-myopia group, in whom postoperative mean radial MTF values were lower than preoperative values. No clear differences between the mean MTF values, at all spatial frequencies, were measured in the control group during follow-up.
The WA architecture of the anterior cornea was shown to remain stable between 1 year and 6 years after surgery, suggesting that neither epithelial healing nor corneal biomechanics played any significant role long after the surface ablation procedure.11,44,45

One should bear in mind how the results of this prospective study cannot be generalized to other excimer laser platforms and how the induction of corneal HOA could be less pronounced with current PRK treatments with wider optical zones or wavefront-guided surface ablation procedures than reported in this series.8,52–54 Differences may also be encountered in LASIK eyes because of flap-related optical and mechanical effects.

The effect of postoperative induction of HOA on the optical performance of the anterior cornea was evaluated using two
image plane metrics, the MTF and the PSF. MTF indicates how the contrast of the various spatial frequencies in the object are reduced in the image. The mean radial MTF demonstrated a decline, though it was not statistically significant, in the high-quality performance of the corneal optics after PRK for high myopia over 3.50- and 6.00-mm pupil diameters. To highlight differences in the image optical quality between preoperative and postoperative corneas and between the amount of dioptric correction, we calculated the MTF ratio, showing a distinct decline in the optical performance of the cornea between 5 and 15 cyc/deg over a scotopic pupil, especially after the treatment of high myopia. This result was consistent with previous clinical studies performed using either the MTF ratio or contrast sensitivity function tests as metrics to quantitatively characterize the optical performance of the eye after refractive surgery. We can confirm how the MTF ratio may be a useful optical performance index to quantify the change in optical quality of postsurgical corneas in determined spatial frequencies.

The PSF describes the effect of aberrations in the spatial domain. In the 3.50-mm diameter pupil, high-quality corneal PSFs, with high contrast and compact forms, were calculated in all the study groups before and after surgery, whereas over a 6.00-mm pupil, spherical aberration dominated the effect. Figure 8. Average PSFs computed over a 6.00-mm diameter pupil. Corneal PSFs subtend to an angle of 30 arc min. Preoperative corneal PSFs of the astigmatism group were more defocused than those of the other study groups (Table 1). During follow-up, the effect of spherical aberration on the image increased in the high-myopia group. No discernible differences between the various corneal PSFs of the control group were determined during follow-up.

Figure 7. Ratios of MTF for preoperative and 1-year (black symbols) and 6-year (gray symbols) postoperative data over 3.50- and 6.00-mm diameter pupils in all the study groups. Data are shown at different spatial frequencies (0–85 cyc/deg). The MTF ratio gives an easy overall value of the effect on the eye’s (or corneal, if using a corneal aberrometer) optical-image quality induced by surgery. A value $>1$ of the parameter indicates that a decline in the optical image quality has occurred in ocular (or corneal) optics, whereas a value $<1$ indicates an improvement in optical quality. Higher values of MTF ratios were calculated for the high-myopia group than for the other two study groups over both pupils. Over the 3.50-mm diameter pupil, the MTF ratio was close to 1 at all spatial frequencies in the low-myopia and astigmatism groups; values higher than 1.2 were measured for the high-myopia group between 5 and 60 cyc/deg. Over the 6.00-mm diameter pupil, a distinct increase in MTF ratios was calculated, particularly at low and middle spatial frequencies in the range between 5 and 15 cyc/deg. The highest values were measured in the high-myopia group. No differences were determined between ratios at 1 year and 6 years after surgery. In the control group, the MTF ratio showed values scattered around 1 both at 1 and 6 years after surgery over the 3.50-mm diameter pupil. Over the 6.00-mm diameter pupil, the MTF ratio was slightly increased between 5 and 60 cyc/deg.
optical image quality of the corneal optics, especially after the deepest myopic ablations.

The WA and the relative optical performance of the anterior cornea in a control group of 10 age-matched patients with stable myopia have been investigated during the same follow-up period. High-order aberrations RMS values were demonstrated to be very stable in young myopic patients, as reported in large population studies.15-26

A couple of limitations should be considered in this work. First, an additional factor other than high-order aberrations, such as corneal scattering, has been reported to negatively influence the individual optical performance of the cornea after PRK.36,39 On the other hand, the relationship between specularly reflected light, as measured by the corneal topographer, and forward scatter is complex and must be further investigated.15 Second, the role of intraocular optics has not been considered here. It has been widely discussed how corneal and lenticular aberrations may interact to improve vision in young and middle-aged patients.15,60-63 This interaction may accordingly be changed after standard photoablation procedures.

Although myopic PRK increased corneal high-order aberrations, it was demonstrated to be effective in terms of optical performance for low-myopia treatments over mesopic pupil size in the long term.

References


Six Years of Corneal WA after PRK 857