Long-term corneal wavefront aberration variations after photorefractive keratectomy for myopia and myopic astigmatism

Sebastiano Serrao, MD, PhD, Giuseppe Lombardo, MEng, PhD, Pietro Ducoli, MD, Marco Lombardo, MD, PhD

PURPOSE: To analyze the higher-order corneal wavefront aberration during an 8-year follow-up after photorefractive keratectomy (PRK).

SETTING: IRCCS Fondazione G.B. Bietti, Rome, Italy.

DESIGN: Case series.

METHODS: Patients having PRK using the Technolas 217C excimer laser platform were divided into 3 groups according to the preoperative refraction as follows: low myopia, high myopia, and astigmatism. The preoperative and 1-, 4-, 6-, and 8-year postoperative root mean square (RMS) values of coma, spherical aberration, and total higher-order aberrations (HOAs) were calculated with 3.5 mm and 6.0 mm simulated pupils. The mean preoperative and postoperative higher-order corneal wavefront aberration maps, point-spread functions, and radial modulation transfer functions (MTFs) were represented to describe the impact of PRK on the optical quality of the anterior cornea.

RESULTS: The study enrolled 33 patients (66 eyes). Corneal spherical aberration was statistically significantly higher after PRK for simple myopia with 3.5 mm and 6.0 mm pupils ($P<.05$). The postoperative increase in coma was statistically significant in the high-myopia group with both pupil sizes ($P<.05$). Total RMS HOAs increased postoperatively with a 6.0 mm pupil in all groups ($P<.05$). The mean radial MTF was almost stable in all groups between preoperatively and postoperatively.

CONCLUSIONS: Higher-order corneal wavefront aberrations stabilized 1 year after PRK to treat myopia or myopic astigmatism. The effect of induced corneal HOAs tended to increase after correction of high myopia with large pupils, although without degrading the image optical quality of the cornea over the long term.

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a change in the asphericity of the cornea with aging. The anterior cornea tends to become less prolate with age, whereas there is no significant or accurate information on age-related changes in the posterior corneal shape. The net effect of the increase in total corneal HOAs is that the coupling of optical aberrations between the cornea and lens tends to decrease with age, with an ultimate decline in the whole eye’s optical performance, even in healthy eyes.

After a standard surface ablation procedure, the HOA architecture of the cornea changes and the aberrations of the optical components are also decoupled. Spherical aberration becomes the dominant corneal HOA with, in general, a 2-fold increase over the preoperative state under dim-light conditions when the pupil becomes larger than 5.0 mm. Coma and other HOAs also increase after surgery, and the increase is linearly related to the amount of refractive correction.

Thousands of young people have excimer laser refractive procedures each year. Considering the expected longevity of this population, it is of clinical interest to evaluate the optical properties of the ablated cornea over the very long term and to develop a quantitative description of the cornea’s optical performance. In the present study, we describe the 8-year fluctuation in anterior corneal wavefront aberrations in eyes that had PRK to correct myopia or myopic astigmatism.

**PATIENTS AND METHODS**

This study enrolled patients who had PRK for myopia or myopic astigmatism between November 2001 and May 2002. Patients were eligible for the study if they were at least 21 years old, were free of ocular disease, had 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. All patients provided informed consent.

Patients were divided into 3 groups according to the preoperative spherical equivalent (SE) refraction and the amount of cylinder. In the low-myopia group and the high-myopia group, the cylinder was lower than 1.75 diopters (D). In the astigmatism group, the cylinder ranged between \( \pm 2.00 \) D and \( \pm 5.00 \) D. A 1:1 allocation scheme was used to obtain equal sample sizes (patients/eyes) in the low-myopia group and the high-myopia groups. The cutoff between simple myopia groups was set at \( \pm 4.50 \) D SE refraction.

### Surgical Technique

A flying-spot excimer laser platform (Technolas 217C, Bausch & Lomb) was used to perform the PRK procedure. The epithelium was removed using an Amoils brush, and the ablation zone was set at 6.0 mm diameter (transition zone up to 9.0 mm in diameter) in all eyes; a standard ablation algorithm was used. The smoothing technique was performed immediately after the procedure; the laser was set in phototherapeutic keratectomy mode with an ablation depth of 10 \( \mu \)m and an ablation zone diameter of 9.0 mm. A sodium hyaluronate 0.25% solution was used to mask the stromal surface while the fluid was spread with a cylindrical spatula (7.0 mm radius of curvature) during the procedure. The eyes in the astigmatism group were treated using the technique described in Table 1.

### Table 1. Preoperative patient characteristics.

<table>
<thead>
<tr>
<th>Characteristic</th>
<th>Low Myopia</th>
<th>High Myopia</th>
<th>Astigmatism</th>
</tr>
</thead>
<tbody>
<tr>
<td>SE refraction range (D)</td>
<td>-1.25 to -4.40</td>
<td>-4.50 to -9.00</td>
<td>-1.00 to -7.25</td>
</tr>
<tr>
<td>Patients/eyes (n)</td>
<td>13/26</td>
<td>13/26</td>
<td>7/14</td>
</tr>
<tr>
<td>Mean age (y) ( \pm ) SDyrs</td>
<td>30.71 ± 5.73</td>
<td>34.14 ± 7.50</td>
<td>32.75 ± 5.34</td>
</tr>
<tr>
<td>Sex (n)</td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Male</td>
<td>4</td>
<td>5</td>
<td>4</td>
</tr>
<tr>
<td>Female</td>
<td>9</td>
<td>8</td>
<td>3</td>
</tr>
<tr>
<td>Mesopic pupil (mm)</td>
<td>Mean ± SD</td>
<td></td>
<td></td>
</tr>
<tr>
<td></td>
<td>3.51 ± 0.41</td>
<td>3.47 ± 0.45</td>
<td>3.33 ± 0.41</td>
</tr>
<tr>
<td></td>
<td>Range</td>
<td>2.51, 4.38</td>
<td>2.48, 4.43</td>
</tr>
<tr>
<td>Scopotic pupil (mm)</td>
<td>Mean ± SD</td>
<td></td>
<td></td>
</tr>
<tr>
<td></td>
<td>5.63 ± 0.89</td>
<td>5.49 ± 0.81</td>
<td>5.22 ± 0.33</td>
</tr>
<tr>
<td></td>
<td>Range</td>
<td>3.53, 6.87</td>
<td>3.61, 7.01</td>
</tr>
</tbody>
</table>

SE = spherical equivalent

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cross-cylinder technique, splitting the total amount of the cylinder correction (with the SE refraction) in hyperopic ablations and myopic ablations.

**Corneal Wavefront Aberration Analysis**

Monocular uncorrected (UDVA) and corrected (CDVA) visual acuities were assessed under photopic conditions preoperatively and postoperatively. Corneal topography and pupillometry were performed with the Keratron Scout topographer (Optikon 2000 SpA). In each eye, the measurements were repeated 3 times to assess the repeatability of the topography; the best image was chosen for analysis. The topographer software calculates the corneal wavefront aberration on the corneal elevation with respect to an ideal aspheric corneal shape with eccentricity 1/n (where n = 1.3375) and centered on the corneal vertex. The wavefront aberration was then computed with respect to the line of sight (ie, the center of the entrance pupil, using the move-axis function of the topographer) and obtained from the derivatives using a least-squares best-fit procedure to the desired pupil area of analysis and described as a 7th-order Zernike polynomial expansion. The corneal aberration data were exported and processed into a purpose-written program in Matlab software (7.0, Mathworks, Inc.) for analysis.

Preoperative and postoperative higher-order corneal aberration data were computed for simulated pupils of 3.5 mm and 6.0 mm. The root mean square (RMS) of the higher-order corneal wavefront aberrations was computed from the Zernike coefficients, and the more recent recommended notation was used.\textsuperscript{26,27} The parameters analyzed included (1) the total RMS HOAs up to the 7th order; (2) the RMS of coma, calculated as the square root of the sum of the squared coefficients of Z(−1,3) and Z(1,3); and (3) the RMS of the spherical aberration, calculated as the square root of the sum of the squared coefficients of Z(0,4) and Z(0,6).

Composite mean corneal higher-order wavefront aberration maps were created preoperatively and postoperatively for each study group to describe the optical variations at the first corneal surface during the follow-up. The sign of odd symmetric Zernike terms about the y-axis (ie, terms having positive m values when the orders n were odd numbered and negative m values when the orders n were even numbered) were flipped in the left eye. This approach was applied to correct for enantiomorphism in the wavefront error maps of the eyes.\textsuperscript{28}

The modulation transfer function (MTF) and the point-spread function (PSF) of the anterior cornea were computed from the corneal higher-order wavefront aberrations at λ = 555 nm before and after surgery.\textsuperscript{29} The mean radial MTF was calculated to quantitatively compare the preoperative MTF and postoperative MTF in each group. The 2-dimensional corneal PSFs were calculated as the mean of the PSF values in all eyes in the study. Detailed information on the calculation of the objective metrics of optical quality are reported in the Appendix (available at http://jcrsjournal.org).

**Statistical Analysis**

The 1-way analysis of variance (ANOVA) was used to compare the differences between the preoperative and

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**Table 2.** Mean preoperative and postoperative SE refraction by study group.

<table>
<thead>
<tr>
<th>Examination Interval</th>
<th>Low Myopia (n = 26)</th>
<th>High Myopia (n = 26)</th>
<th>Astigmatism (n = 14)</th>
</tr>
</thead>
<tbody>
<tr>
<td></td>
<td>Mean (D) ± SD</td>
<td></td>
<td></td>
</tr>
<tr>
<td>Preoperative</td>
<td>−2.82 ± 0.86</td>
<td>−6.30 ± 1.27</td>
<td>−3.03 ± 2.09</td>
</tr>
<tr>
<td>Postoperative (y)</td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>1</td>
<td>−0.01 ± 0.31</td>
<td>−0.09 ± 0.36</td>
<td>−0.37 ± 0.66</td>
</tr>
<tr>
<td>4</td>
<td>−0.15 ± 0.28</td>
<td>−0.27 ± 0.37</td>
<td>−0.35 ± 0.59</td>
</tr>
<tr>
<td>6</td>
<td>−0.24 ± 0.21</td>
<td>−0.41 ± 0.39</td>
<td>−0.39 ± 0.48</td>
</tr>
<tr>
<td>8</td>
<td>−0.28 ± 0.16*</td>
<td>−0.56 ± 0.57*</td>
<td>−0.48 ± 0.70</td>
</tr>
</tbody>
</table>

n = number of eyes

*Statistically significant differences between 1 year and 8 years postoperatively (P < .05, Tukey-Kramer)
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 used to analyze the changes in determined combinations of corneal HOAs depending on the amount of refractive correction in simple myopic treatments.

Statistical comparison of the postoperative curvature data between the low-myopia group and the high-myopia group was performed using multivariate ANOVA for repeated measurements. Differences with a $P$ value of 0.05 or less were considered statistically significant. Kyplot software (KyensLab Inc.) was used for all statistical testing.

**RESULTS**

The study enrolled 38 patients (13 men, 25 women). Five patients (2 each in the low-myopia and high-myopia groups and 1 in the astigmatism group) did not complete the study’s follow-up protocol and were unavailable at the last postoperative examination; their data were removed from the series. The final analysis included 33 patients. Table 1 shows the patients’ characteristics.

**Refractive**

All procedures were uneventful, and no eye had repeat surgery during the follow-up period. Table 2 shows the mean preoperative and postoperative SE refraction by study group over time. A slight, although statistically significant, refractive regression ($P < .05$) occurred between 1 year and 8 years in the low-myopia group and the high-myopia group.

**Visual Acuity**

Preoperatively, the CDVA was a 20/20 in 25 eyes (97%) in the low-myopia group, 15 eyes (58%) in the high-myopia group, and 7 eyes (50%) in the astigmatism group. Eight years postoperatively, all eyes in the low-myopia group, 25 eyes (97%) in the high-myopia group, and 12 eyes (87%) in the astigmatism group achieved a UDVA of 20/40. The UDVA was 20/20 or better in 22 eyes (88%) in the low-myopia group, 8 eyes (31%) in the high myopia group, and 2 eyes (14%) in the astigmatism group. No eye lost 1 or more lines of Snellen visual acuity. Figure 1 shows
the efficacy index and safety index values during the follow-up. The mean safety index was greater than 1.0 at all visits in all groups. The mean efficacy index varied from a low of 0.76 at 8 years in the astigmatism group to a high of 1.08 at 4 years in the low-myopia group.

**Higher-Order Corneal Wavefront Aberrations**

Because the mean mesopic pupil size and the mean scotopic pupil size were approximately 3.4 mm and 5.5 mm, respectively, in all study groups (Table 1), the optical quality of the anterior cornea under mesopic and dim-light conditions was assessed with a simulated 3.5 mm pupil and a simulated 6.0 mm pupil, respectively. The small pupil area of analysis further ensured that the changes in corneal HOAs would be analyzed within the ablation zone rather than over a larger area that included the edge of ablation.

With a 3.5 mm pupil, the increase in total RMS HOAs was statistically significant ($P < .05$) in the high-myopia group 1 year after surgery and was almost stable during follow-up. The RMS of coma was statistically significantly higher 1 year postoperatively in the high-myopia group ($P < .01$), after which it decreased toward preoperative values during long-term follow-up. The amount of spherical aberration increased in the low-myopia group and the high-myopia group (both $P < .01$) and remained stable thereafter. With a 3.5 mm pupil, the postoperative amount of corneal HOAs was not different from the preoperative amount after PRK for myopic astigmatism.

Figure 3 shows the higher-order RMS values in all groups with a 6.0 simulated pupil over time. With a 6.0 mm pupil diameter, the total RMS HOAs and spherical aberration were statistically significantly higher in the low-myopia group and the high-myopia group 1 year after surgery (both $P < .001$); both stabilized thereafter. There was no

Figure 3. Preoperative and postoperative RMS values (mean ± SD) of combinations of HOAs in the study groups with a 6.0 mm simulated pupil (* = $P < .05$, Tukey test) (HOA = higher-order aberrations; RMS = root-mean-square; SA = spherical aberration).
significant difference in coma between preoperatively and postoperatively in the low-myopia group, whereas there was a statistically significant increase in coma in the high-myopia group \( (P < .001) \). The astigmatism group had a statistically significant increase in total RMS HOAs \( (P < .05) \) 1 year after surgery; it remained stable thereafter. The postoperative spherical aberration and coma values were not different from the preoperative values in the astigmatism group. Figure 3 shows the 6.0 mm pupil higher-order RMS values by group over time.

At the end of follow-up, there was a statistically significant linear correlation between the amount of refractive correction and the change in total RMS HOAs, coma, and spherical aberration with a 3.5 mm pupil and a 6.0 mm pupil (Figure 4).
The contribution of spherical aberration to the overall postoperative HOA architecture of the anterior cornea increased after the correction of simple myopia, especially with a larger pupil and higher treatment, as shown in the mean composite corneal higher-order wavefront aberration maps (Figure 5).

High-quality postoperative corneal PSFs were obtained with a 3.5 mm pupil in all groups; faint preoperative to postoperative differences were noticeable only in the high-myopia group. With a 6.0 mm pupil, spherical aberration had an increased effect on optical image quality, mainly in the high-myopia group (Figure 6). Figure 7 shows the mean 1-dimensional radial profiles of the MTFs at different spatial frequencies by group. There was a minor improvement, although not a statistically significant improvement in optical quality of the anterior cornea between 5 cycles per degree (cpd) and 20 cpd with a 3.5 mm pupil after correction of simple myopia. The mean MTF values were stable between preoperatively and postoperatively in both simple myopia groups with both pupil diameters. No discernible differences between the preoperative and postoperative states were seen in the astigmatism group with either pupil diameter ($P > .05$).

### DISCUSSION

In this study, we evaluated the optical quality of the anterior cornea with simulated pupil diameters of 3.5 mm and 6.0 mm in patients who had PRK for myopia or myopic astigmatism. This allowed us to delineate the optical performance of photoablated corneas under mesopic and scotopic light conditions and to differentiate between changes in corneal HOAs within the ablation zone and those over larger areas, including the edge of ablation.

The effect of postoperative induction of HOAs on the optical performance of the cornea was evaluated using pupil-plane or image-plane metrics. The pupil-plane metric, here the RMS error, describes the optical properties of the cornea, whereas the image-plane metrics, here the MTF and PSF, describe the effect of those properties on image quality. The MTF describes how the contrast of various spatial frequencies in the object are reduced in the image, whereas the PSF represents image quality for point objects.

The mean refractive regression, although less than $-0.50$ D, was statistically significant between 1 year and 8 years postoperatively in the simple myopia groups. This myopic shift, however, did not achieve clinical significance because all patients were spectacle independent. No statistically significant changes in the

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![Figure 5](image)

**Figure 5.** Mean corneal higher-order wavefront aberration maps with a 6.0 mm pupil diameter. Corneal spherical aberration increased postoperatively, mainly after the correction of high myopia. Asymmetrical HOAs contributed more to the total higher-order corneal wavefront aberrations in the astigmatism group than in the other 2 groups before and after surgery. A fixed color scale, visually similar to that of commercial aberrometers, was developed for easy interpretation (scale bar in microns; range between $-2.75 \mu m$ and $+2.25 \mu m$).
mean SE refraction (−0.11 D) occurred in the astigmatism group during the follow-up.

After surface ablation, the increase in corneal HOAs is dependent on the magnitude of the refractive correction and the pupil diameter.23,24,30–32 With a 3.5 mm pupil, the increase in total RMS HOAs was statistically significant in the high-myopia group only; on the other hand, the postoperative spherical aberration was higher than the preoperative value in the low-myopia and high-myopia groups. With a 6.0 mm pupil, the increase in total RMS HOAs, coma, and spherical aberration in the high-myopia group was 2-fold that of the preoperative values. A slight, although statistically significant, postoperative increase in total RMS HOAs occurred in the low-myopia group and the astigmatism group.

The relative contribution of spherical aberration to the overall corneal higher-order wavefront aberration map was greater postoperatively in both simple myopia groups. This effect was primarily evident in the high-myopia group with a 6.0 mm pupil.

The wavefront aberration architecture of the anterior cornea was markedly stable between 1 year and 8 years after surgery, suggesting that the optical remodeling of the anterior cornea can be considered completed 1 year after surface ablation.33–35 When the central portion of the anterior cornea has mechanically stable curvature in the very long-term postoperative period, as reported previously,23,24,33,34 it contributes to the stability of corneal optical performance.

With a 3.5 mm pupil, high-quality corneal PSFs with high contrast and a compact form were calculated in all groups before and after surgery. With larger pupils, spherical aberration dominated the optical image quality of the corneal optics, especially for deeper myopic ablations. The mean radial MTF was almost stable after surgery in all groups with both pupil sizes, showing how the high-quality performance of the corneal optics is preserved after PRK performed using a smoothing technique to treat myopia up to −9.00 D SE refraction.

The ablation design and parameters,36–43 epithelial healing, and biomechanics of the corneal tissue33–35 are the main sources of HOA induction, which can influence the optical result after PRK. The increase in spherical aberration in the optical ablation zone after simple myopic ablations could be due to causes other
than the biomechanical response of the tissue. These include variable predictability of the ablation because of variations in the energy per pulse, spatial and temporal positioning and distribution of the laser spots, ablation plume dynamics, loss of ablation efficiency at non-normal incidence (i.e., at oblique angle with respect to the normal to the corneal apex), the temperature increase of the stroma during ablation,
corneal hydration, and environmental temperature and humidity. Spherical aberration did not increase after photoablation procedures, likely because of the hyperopic ablation step used in the cross-cylinder technique.

The different regional biomechanical response induced in the cornea by the proprietary laser system ablation design, the ablation parameters discussed above, the ablation depth, the ablated surface regularity, and the corresponding wound healing of the individual cornea should be considered as the sources of coma and other asymmetric HOAs. Submicron irregularities induced on the photoablated increase as more tissue is removed, contributing to the induction of asymmetric HOAs. In addition, current ablation profiles assume the anterior cornea as a rotationally axis-symmetric surface and do not take into account local asymmetries along meridians; this leads to further asymmetries at the first surface of the cornea.

The results in this prospective study cannot be generalized to other excimer laser platforms or other excimer laser procedures, such as LASIK. In addition, the induction of corneal HOAs found in our study could be less pronounced with current PRK treatments with ablation zones diameters wider than 6.0 mm and with wavefront-guided surface ablation procedures.

A limitation of this study was that it did not evaluate the effect of scattering on corneal optical quality. Indeed, beyond HOAs, corneal scattering can negatively affect the effect of scattering on corneal optical quality. In particular, axis-symmetric surface and do not take into account local asymmetries along meridians; this leads to further asymmetries at the first surface of the cornea.

In conclusion, PRK with smoothing to treat myopia and myopic astigmatism provided good corneal optical performance. Higher-order aberrations of the anterior cornea stabilized 1 year after surgery. The high optical performance of photoablated corneas was preserved over the very long-term follow-up.

REFERENCES


