Long-Term Changes of the Anterior Corneal Topography after Photorefractive Keratectomy for Myopia and Myopic Astigmatism

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PURPOSE. To analyze the anterior corneal topography changes after 8 years after photorefractive keratectomy (PRK) for the correction of myopia and myopic astigmatism.

METHODS. Sixty-six eyes (33 patients) underwent PRK using an excimer laser platform. Patients were subdivided into three groups: the low myopia (13 patients; range, −1.25 to −4.40 diopters [D]), the high myopia (13 patients; −4.50 to −9.00 D), and astigmatism (7 patients; cylinder component between −2.00 and −5.00 D) groups. The preoperative and 1-, 2-, 4-, 6-, and 8-year postoperative average corneal maps were computed for each study group. Changes inside and outside the optical zone, which was 6.00 mm in diameter for all eyes, during follow-up were further investigated.

RESULTS. The topographic central region, 2.00-mm diameter, was almost stable in all study groups, with changes < 0.39 D between 1 and 8 years. The postoperative variations at the peripheral region, 6.00- to 8.00-mm diameter, were related to the type and amount of refractive correction: a higher flattening (P < 0.05) has been assessed in the high-myopia group (−0.85 D) in comparison with the low-myopia group (−0.42 D) between 1 and 8 years. On the contrary, corneal periphery steepened (+2.22 D; P < 0.05) in the astigmatism group during follow-up, mainly at the superior and inferior meridians.

CONCLUSIONS. The anterior corneal topography continues to change configuration even long term after PRK. Changes are confined outside the functional optical zone of the cornea. PRK for the correction of myopia was shown not to influence the mechanical stability of the corneal tissue at 8 years after surgery. (Invest Ophthalmol Vis Sci. 2011;52:6994 –7000) DOI:10.1167/iovs.10-7052

Long-term refractive and mechanical stability of the cornea is of paramount importance in refractive surgery. Corneal topography represents the most objective method for assessing the shape and optical properties of the anterior cornea. For this reason, dedication to collection of postoperative data has been adopted by many surgeons since the beginning of the excimer laser surgery era.

After photorefractive keratectomy (PRK), curvature changes can manifest clinically as either immediate modification of surface topography or as long-term shape variations.1,2 A few works have thoroughly characterized long-term shape changes over the whole anterior cornea, including the peripheral portion of the tissue.3–9 Most of the long-term clinical studies have, in general, targeted their scope at assessing stability and predictability of the surgical outcome by measuring refraction and mean simulated keratometry values during follow-up.10–25 The results from these works have reported, as common occurrence after PRK, a mean postoperative refractive regression of −0.50 diopters (D) during the first 1 to 2 years after treatment and a slow myopic regression for up to 14 years postoperatively. However, this information is not exhaustive, since it does not take into account how refraction of the eye optics, besides the main role of the anterior cornea, depends on various parameters including the posterior corneal interface or the age-related changes of lens and vitreous.26–31 In addition, the anterior corneal topography has been shown to change with aging, even in the normal cornea.32–35 The surface topography tends to become steeper and less prolate with increasing age, with changes of approximately 0.25 D in the mean simulated keratometry value between 20 and 40 years.

In previous studies,8,9 we described the topographic response of the cornea to PRK for myopia and demonstrated how the anterior cornea undergoes minimal changes of the central optical portion up to 6 years after surgery. In the present study, we describe the long-term variation of the whole anterior corneal morphology over an 8-year follow-up after PRK for the correction of myopia or myopic astigmatism.

MATERIALS AND METHODS
Thirty-eight patients, 13 males and 25 females, who underwent PRK for myopia or myopic astigmatism between November 2001 and May 2002 were included in this study. Patients were considered eligible for the study if they were at least 21 years old and free of ocular disease, had no previous ocular surgery, and 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. An institutional review board approval was not required for this study. Patients were subdivided into three groups according to the preoperative spherical equivalent (SE) refraction and the amount of cylinder component: the low-myopia group (range, −1.25 to −4.40 D) and the high-myopia group (range: −4.50 to −9.00 D), where the cylinder component was < 1.75 D, and the astigmatism group, with the cylinder component ranging between −2.00 and −5.00 D. A scheme with 1:1 allocation was used to have equal sample size (patients/eyes) in the low- and high-myopia groups.

Surgical Procedure
One of two experienced surgeons (ML and SS) performed the procedures. The epithelium was removed using an Amoils brush in all cases.
Corneal Topographic Changes 8 Years after PRK

Table 1. Mean (±SD) Preoperative and Postoperative Spherical Equivalent Refraction (D) of the Three Study Groups

<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>Preoperative</td>
<td>-2.82 ± 0.86</td>
<td>-6.30 ± 1.27</td>
<td>-3.03 ± 2.09</td>
</tr>
<tr>
<td>1 Year postoperative</td>
<td>-0.01 ± 0.31</td>
<td>-0.09 ± 0.36</td>
<td>-0.37 ± 0.66</td>
</tr>
<tr>
<td>2 Years postoperative</td>
<td>-0.08 ± 0.25</td>
<td>-0.15 ± 0.30</td>
<td>-0.36 ± 0.57</td>
</tr>
<tr>
<td>4 Years postoperative</td>
<td>-0.15 ± 0.28</td>
<td>-0.27 ± 0.37</td>
<td>-0.35 ± 0.59</td>
</tr>
<tr>
<td>6 Years postoperative</td>
<td>-0.24 ± 0.21</td>
<td>-0.41 ± 0.59</td>
<td>-0.39 ± 0.48</td>
</tr>
<tr>
<td>8 Years postoperative</td>
<td>-0.28 ± 0.16*</td>
<td>-0.56 ± 0.57*</td>
<td>-0.48 ± 0.70*</td>
</tr>
</tbody>
</table>

Tukey-Kramer: * P < 0.05 (between 1 and 8 years after surgery).

Corneal Topographic Changes 8 Years after PRK

Topographic Analysis

Corneal topography and pupillometry were performed with corneal topographer software (Keratron Scout; Optikon 2000 Spa, Rome, Italy) and central corneal thickness (CCT) was obtained with an ultrasound pachymeter (Pacline; Optikon 2000 Spa). For each eye, measurements were repeated three times to assess the repeatability of the topography: the best image, with full corneal coverage and no eyelash artifacts, was chosen for analysis. All the preoperative and postoperative topographies were taken by a single observer (ML).

The topographer software (versions 3.5 to 3.7) allows the exportation of topographic measurements computed from 28 rings and 256 meridians, for a maximum area of analysis of 5.00-mm radius from the corneal apex for each patient’s eye. The preoperative and postoperative tangential curvature data were exported to custom software (Matlab, version 7.0; The MathWorks, Inc., Natick, MA). The mathematical algorithm computed the preoperative and postoperative average tangential curvature map with respect to the reference axis for each study group. Interpolation to the same spaced referenced cornea grid was necessary for this purpose, as discussed in previous works.8,9 A central zone with radius (r) of 1.00 mm from the corneal apex and a peripheral annular zone with 3.00 ≤ r ≤ 4.00 mm from the apex were delineated for detailed regional analysis of anterior corneal topography changes during follow-up. The choice of the regions’ width was based on results of previous studies.8,9 The average difference between the preoperative and postoperative curvature values, or between early postoperative and late postoperative, were calculated for each corneal zone.

Statistics

The one-way ANOVA was used to statistically compare the differences between the preoperative and postoperative SE refraction data in each study group. When statistical significance was found, the differences between each postoperative period were further compared using the Tukey test for pairwise comparisons. Statistical comparison of postoperative curvature data between the low- and high-myopia groups was performed using multivariate analysis of variance for repeated measurements.

The Pearson correlation test was performed to investigate the correlation between postoperative changes of either central or peripheral curvature values and the amount of refractive correction in simple myopic treatments.

Differences with a value of P ≤ 0.05 were considered statistically significant. A software program (KyPlot; KyensLab Inc., Tokyo, Japan) was used for all statistical testing.

Results

In all, 33 patients (66 eyes), 13 males and 20 females, completed the study protocol follow-up. Two patients either in the low- or high-myopia groups and one patient in the astigmatism group were unavailable at the last postoperative examination and were removed from the series. The mean mesopic and scotopic pupil sizes were 3.41 ± 0.43 mm (range, 2.81–4.43 mm) and 5.40 ± 0.73 mm (range, 3.53–7.01 mm), respectively.

Figure 1. Double-angle plot of the preoperative (black circles) and 8 years postoperative (gray squares) 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. The star symbols 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 simple myopic groups, the majority of astigmatism vectors were calculated to be zero and symbols overlapped each other.
Refractive Data

All the procedures were uneventful and no eye was reoperated during follow-up. Complete reepithelialization occurred within 72 hours after surgery in all eyes. At 1 year after surgery, the mean SE refraction was almost plano (< −0.10 ± 0.30 D) in both simple myopic groups and −0.37 ± 0.66 in the astigmatism group. A statistically significant myopic regression in the mean SE refraction was measured between 1 and 8 years postoperatively both in the low-myopia (−0.27 ± 0.22 D, \( P < 0.05 \)) and high-myopia (−0.47 ± 0.41 D, \( P < 0.01 \)) groups. SE refraction was stable in the astigmatism group during follow-up (−0.11 ± 0.50 D). At 8 years, 24 eyes in the low-myopia group (92%), 19 eyes in the high-myopia group (73%), and 6 eyes in the astigmatism group (43%) were within ±0.50 D of emmetropia. Follow-up refractive data are summarized in Table 1.

Changes in both direction and magnitude of refractive cylinder induced by surgery and between early postoperative and late postoperative states were determined using vector analysis. The preoperative to 1-year postoperative astigmatic refractive change was 0.44 (±0.40) at 70° in the low-myopia group, 0.87 (±0.63) at 91° in the high-myopia group, and 3.09 (±0.94) at 89° in the astigmatism group; the induced direction change (against-the-rule and anticlockwise torque) of refractive astigmatism was not statistically significant in any study group. Changes in astigmatism vector magnitude < 0.40 D (range, 0.30–0.39 D), with no significant changes in vector direction, were measured between 1 year and 8 years after surgery in all study groups. The definite vector change in refractive cylinder has been plotted using a double-angle format, as illustrated in Figure 1: at 8 years, 100% and 84% of the population of vectors in the low- and high-myopia groups were within 0.50 D from the origin, respectively; 86% of vectors in the astigmatism group were within 1.00 D from the origin.

Table 3. Preoperative and Postoperative Anterior Tangential Average Curvature (D, ±SD) of the Central and Peripheral Corneal Zones in Each Study Group

<table>
<thead>
<tr>
<th>Corneal Zone (diameter, mm)</th>
<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>Central zone (within the optical zone), 2.00 mm</td>
<td>Preoperative</td>
<td>4.49 ± 1.35</td>
<td>4.58 ± 1.70</td>
<td>4.31 ± 1.55</td>
</tr>
<tr>
<td></td>
<td>1 Year postoperative</td>
<td>4.61 ± 1.53</td>
<td>4.24 ± 2.75</td>
<td>4.03 ± 1.13</td>
</tr>
<tr>
<td></td>
<td>2 Years postoperative</td>
<td>4.58 ± 1.47</td>
<td>4.09 ± 2.50</td>
<td>4.19 ± 1.12</td>
</tr>
<tr>
<td></td>
<td>4 Years postoperative</td>
<td>4.59 ± 1.60</td>
<td>4.09 ± 2.57</td>
<td>4.66 ± 1.01</td>
</tr>
<tr>
<td></td>
<td>6 Years postoperative</td>
<td>4.72 ± 1.69</td>
<td>4.05 ± 2.31</td>
<td>4.83 ± 1.21</td>
</tr>
<tr>
<td></td>
<td>8 Years postoperative</td>
<td>4.64 ± 1.26</td>
<td>4.29 ± 2.39</td>
<td>4.27 ± 1.11</td>
</tr>
<tr>
<td>Peripheral zone (outside the optical zone), 6.00 to 8.00 mm</td>
<td>Preoperative</td>
<td>4.02 ± 1.84</td>
<td>4.22 ± 3.49</td>
<td>4.00 ± 3.07</td>
</tr>
<tr>
<td></td>
<td>1 Year postoperative</td>
<td>4.25 ± 1.52</td>
<td>4.13 ± 2.78</td>
<td>3.56 ± 2.18</td>
</tr>
<tr>
<td></td>
<td>2 Years postoperative</td>
<td>4.18 ± 1.37</td>
<td>4.42 ± 2.72</td>
<td>4.08 ± 3.53</td>
</tr>
<tr>
<td></td>
<td>4 Years postoperative</td>
<td>4.21 ± 1.33</td>
<td>4.29 ± 3.19</td>
<td>4.60 ± 3.19</td>
</tr>
<tr>
<td></td>
<td>6 Years postoperative</td>
<td>4.18 ± 1.24</td>
<td>4.41 ± 3.63</td>
<td>4.18 ± 3.31</td>
</tr>
<tr>
<td></td>
<td>8 Years postoperative</td>
<td>4.12 ± 1.13</td>
<td>4.28 ± 2.69</td>
<td>4.18 ± 3.21</td>
</tr>
</tbody>
</table>

ANOVA: * \( P < 0.05 \) (1- and 8-year postoperative differences between the low- and high-myopia groups). Tukey-Kramer: † \( P < 0.05 \) (between 1 and 8 years after surgery).

Tukey-Kramer: * \( P < 0.05 \) (between preoperative and 8 years after surgery).

Corneal Topographic Data

The surgically induced 1-year postoperative flattening of the central corneal zone was statistically significant correlated to the amount of SE refraction treated (\( R = 0.52, P < 0.001 \)). The 1-year postoperative steepening of the peripheral annular zone was also statistically significantly correlated to the amount of refractive correction (\( R = -0.38, P < 0.01 \)). Tables 2 and 3 summarize the average topographic values for each analyzed corneal zone both preoperatively and postoperatively and the relative average differences between topographic data in all study groups.

The anterior central corneal region was measured to be remarkably stable between 1 and 8 years after the treatment of simple myopia and myopic astigmatism. A slight steepening (<0.40 D), although not statistically significant, of the central region was measured in the high-myopia group up to 2 years after surgery, then surface topography stabilized.

Late postoperative curvature changes of the peripheral anterior cornea were influenced by the type and amount of refractive correction: a more pronounced flattening of the peripheral region was measured in the high-myopia group in comparison with the low-myopia group (−0.85 D vs. −0.42 D;
between 1 and 8 years postoperatively. The peripheral cornea was shown to steepen (2.22 D; $P < 0.05$) in the astigmatism group during follow-up (1 to 8 years postoperatively), mainly in the superior and inferior emimeridians after 4 years. Differences in the peripheral corneal response to surgery between study groups are summarized in Figure 2. In all, 76% of eyes that underwent PRK for the correction of low myopia had peripheral curvature changes within $\pm 0.50$ D between 1 and 8 years postoperatively; larger changes were measured in the high-myopia and astigmatism groups, where only 27% and 43% of eyes had changes within $\pm 0.50$ D, respectively.

The composite average corneal topography maps and difference maps of all study groups are represented in Figures 3 and 4, respectively. No statistically significant differences in CCT values were assessed during follow-up in any group, as summarized in Table 4.

**DISCUSSION**

The aim of the present study was to investigate the topography changes occurring inside and outside the optical zone of the anterior cornea over a period of 8 years in a population of eyes that have been treated with PRK plus smoothing for myopia or myopic astigmatism. For this reason, we developed custom software to delineate a central region, 2.00 mm in diameter, and a peripheral annular region, from 6.00 to 8.00 mm in diameter, of the anterior corneal topography, both centered to the corneal apex. The topography changes after the treatment of low myopia and high myopia have been further directly compared with detected differences correlated to the amount of refractive correction.

Five of 38 patients did not return for the last postoperative examination and have not been included in the statistics. They did not return for reasons unrelated to laser treatment.
No eye has been reoperated or have lost one or more visual acuity lines in this series. A mean refractive regression of $-0.27$ D and $-0.47$ D between 1 and 8 years postoperatively in the low-myopia and high-myopia groups respectively was measured. This myopic shift, although statistically significant, did not achieve clinical significance, since all the patients were spectacle independent. No statistically significant change in the mean SE refraction ($-0.11$ D) was measured in the astigmatism group during follow-up.

The anterior central topography has been assessed to be stable during follow-up in all study groups, with changes confined to a high of $0.38$ D between 1 and 8 years postoperatively. A different response, in relation to the amount of refractive correction, has been measured in the peripheral cornea during follow-up: a higher flattening of the peripheral region has been measured in the high-myopia group ($-0.85$ D) than that in the low-myopia group ($-0.42$ D) between 1 and 8 years postoperatively. These results are in accordance with our previous works, in which we investigated the topography changes in two different populations of myopic eyes up to 4 and 6 years after PRK.1,9 After the expected steepening measured in the first year after surgery, the peripheral portion of the cornea tends to flatten in the long-term postoperative course.

Differences in the postoperative changes of the peripheral portion of the anterior cornea may depend on various factors, associated with the ablation profile and laser parameters as well as with the epithelial and stromal response of the corneal tissue to surface ablation.1,34 The different response of the peripheral cornea in relation to the amount of refractive correction could be related to the different meridional (central/peripheral regions) and depth-varying (anterior/posterior regions) organization of the stromal microstructure and thus to the regional mechanical properties of the cornea.7–9,55–59 The portion of the corneal tissue confined between the central cornea and limbus (i.e., the peripheral region in our study) has been measured to be the more susceptible to strain in various

**Figure 4.** Average composite tangential curvature difference maps of the three study groups (color scale bar: diopters). The effective optical zone diameter appeared to slightly narrow in all study groups. Changes in the peripheral portion of the anterior cornea can be better evidenced using tangential difference maps.
The postoperative changes in CCT values were not statistically in any group.

experimental studies in both unoperated and operated eyes.\textsuperscript{21,32}\textsuperscript{21,32} The cutting of a variable amount of anterior collagen lamellae (dependent on the refractive correction) from the central cornea could enhance these biomechanical inhomogeneities in the stroma.\textsuperscript{41,42}\textsuperscript{41,42}

A completely different response of the corneal periphery has been assessed after the correction of myopic astigmatism in comparison with simple myopic treatments. The corneal periphery steepened after the correction of myopic astigmatism during follow-up, although showing a higher variability than that of spherical treatments both preoperatively and postoperatively. Changes were mostly confined in the superior and inferior meridians. This may be related to the effect of cross-cylinder technique, which consists, in the case of compound myopic astigmatism with the rule, in treating half of the cylinder, with a hyperopic treatment, along the horizontal (flattest) meridian and the remaining half, using a myopic treatment, along the vertical (steepest) meridian. The astigmatic ablations performed by the excimer laser platform (Technolas 217) use elliptical ablation profiles elongated in the direction of the astigmatic axes. Since the hyperopic ablation consists in removal of tissue peripherally along the flat meridian, it blends with the myopic ablation transition zone. A smoother transition zone slope can thus be obtained along the flat than the steep meridian of the anterior cornea: this factor can influence subsequent wound healing. A differential relaxation in stromal lamellar tension, due to the combination of central and peripheral ablations of collagen lamellae at various depths along the principal meridians, may thus be responsible for the continuous non-axisymmetric anterior corneal steepening of the periphery measured during follow-up, although without resulting in ectasia.\textsuperscript{7,43,44}\textsuperscript{7,43,44}

It should be considered how changes in the peripheral portion of the cornea do not hold a refractive role since all eyes in this series, except 8 eyes (none in the astigmatism group), had scotopic pupils < 6.00 mm.

Wound healing may play a role in the changes measured in the present work, resulting in an additional variable that may influence the long-term shape of the cornea after PRK.\textsuperscript{24,45}\textsuperscript{24,45} On the other hand, it has been evidenced that the epithelial stromal healing is almost completed at 1 year postoperatively.\textsuperscript{46,47}\textsuperscript{46,47} Considering the distinct curvature variations between the central and peripheral portions of the anterior cornea in relation to the type and amount of refractive correction, it is accordingly reasonable that the long-term changes may be biomechanical in nature.

Although all ablation profiles are designed with the assumption of a rotationally axis-symmetric corneal plane, the results from this study cannot be generalized to other excimer laser platforms: a different curvature response of the anterior cornea for the same amount of refractive correction can be a common occurrence when comparing the results from two or more laser platforms.\textsuperscript{48,49}\textsuperscript{48,49} At the same time, the optical zone diameter can dramatically affect long-term results.\textsuperscript{50–52}\textsuperscript{50–52} in this work all eyes were treated using the same optical zone diameter to minimize this bias effect. Differences can ultimately be encountered in laser-assisted in situ keratomileusis eyes due to the flap-related mechanical effects and the removal of deeper stroma in comparison with PRK.\textsuperscript{53}\textsuperscript{53}

The lack of information on posterior corneal curvature changes and on regional corneal thickness measurements are possible limitations of the present study. A larger population of eyes could enhance the power significance of statistical analysis for 1- to 8-year corneal region changes.

Long-term studies on photoablated corneas are beneficial in widening our knowledge on the response of the corneal tissue and thus may lead to new strategies for optimizing refractive results over the life of the individual. In conclusion, PRK for the correction of low to moderate myopia up to −9 D of SE refraction was shown to be an effective refractive procedure during an 8-year postoperative period. The anterior cornea was shown to maintain a stable central curvature profile, with no significant changes in the long-term postoperative period. Major changes were confined to the peripheral portion of the anterior corneal topography.

### References


