Photorefractive keratectomy in patients with suspected keratoconus: Five-year follow-up

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PURPOSE: To assess the long-range outcomes of photorefractive keratectomy (PRK) using functional and topographic criteria in myopic eyes with suspected keratoconus.

SETTING: Rothschild Foundation, Paris, France.

DESIGN: Retrospective interventional case series.

METHODS: Eyes of patients classified as keratoconus suspects or keratoconus by the Corneal Navigator software of the OPD-Scan II device were included. They were treated with myopic PRK using an EC-5000 excimer laser between 2004 and 2007. The main outcome measures were refractive stability, mean corneal keratometry, mean central pachymetry, mean thinnest point value, and the occurrence of postoperative complications such as corneal ectasia.

RESULTS: The study evaluated 62 eyes of 42 patients. The mean patient age was 34.6 years ± 15.1 (SD) and the mean spherical equivalent (SE), −3.96 ± 3.05 diopters (D). The mean central pachymetry was 529.4 ± 32.8 μm and the mean simulated keratometry, 45.75 ± 1.75 D. The percentage of similarity to keratoconus suspects or keratoconus was positive in all 62 eyes and exceeded a 50% similarity score in 30 eyes (48.4%). The mean follow-up was 4.8 ± 1.4 years. The mean magnitude of the SE was −0.53 ± 1.35 D over the follow-up. Two patients required glasses postoperatively because of significant myopic regression. No case of corneal ectasia was reported.

CONCLUSION: Photorefractive keratectomy in eyes with suspected keratoconus based on a Placido neural network may be safe and effective for myopia and astigmatism in carefully selected patients.

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True keratoconus-suspect corneas are an absolute contraindication to laser in situ keratomileusis (LASIK) and are generally held to be a contraindication to photorefractive keratectomy (PRK). Corneal ectasia after PRK as a treatment modality to prevent progression has been described in a few case reports in which the affected corneas presented preoperatively with obvious characteristics of keratoconus suspect or a family history of keratoconus.4 Other studies report encouraging results using PRK alone or associated with crosslinking to reduce irregular astigmatism in patients with keratoconus or in keratoconus suspects.

Keratoconus is a well-defined pathology that is described as noninflammatory progressive localized thinning and protrusion of the cornea; it is characteristically recognizable in its advanced stages. On the other hand, keratoconus suspect is an unclarified entity with no specific definition and no consensual diagnostic criteria. In particular, localized steepening on Placido corneal topography or slight bowing of the posterior corneal surface on elevation topography has been used to characterize keratoconus suspects. Reaching appropriate sensitivity levels for screening methods is crucial to identify patients with mild forms of subclinical keratoconus and to prevent iatrogenic keratectasia.
The classification of corneal topographies as suspect for keratoconus can be performed by neural networks, such as the Corneal Navigator software of the OPD-Scan II aberrometer/corneal topographer (Nidek Co., Ltd.).17-19 This software uses an artificial intelligence technique to train a computer neural network to recognize specific classifications of corneal topography. The software first calculates various indices representing corneal shape characteristics. The indices are used by the software to score the measurement’s similarity to 9 clinical classification types as follows: normal, astigmatism, keratoconus suspect, keratoconus, pellucid marginal degeneration, postkeratoplasty, myopic refractive surgery, hyperopic refractive surgery, and unclassified variation. These diagnostic results are estimated based on the relationship between many corneal indices and cases. For each diagnostic condition, the percentage of similarity is indicated in a range from 0% to 99%. The indicated result for each topographic condition is independent of that of other categories.17-19

The purpose of our study was to assess the long-term safety, effectiveness, and the occurrence of complications such as corneal ectasia following PRK performed in eyes with fully diagnosed or forme fruste keratoconus, according to the Corneal Navigator OPD system algorithm.

PATIENTS AND METHODS

The study comprised consecutive eyes that had PRK between January 2004 and December 2006 at the Rothschild Foundation, Paris. The same experienced operator (D.G.) performed all surgeries using the EC-5000 excimer laser (Nidek).

Eyes were selected as suitable for PRK based on the evaluation of Placido and elevation topographies as well as the patient’s refraction. All patients received an explanation of the risks of the procedure and the recovery time, and all provided informed consent. Data were collected from the patient’s files. Placido topography and elevation topography were obtained with the OPD-Scan II aberrometer/corneal topographer and Orbscan IIz scanning-slit topographer/tomographer (Bausch & Lomb), respectively, and the databases of the 2 machines were extracted. All tests were performed in the same clinic, and the same instruments were used during the course of the study.

Of the operated eyes, all classified as keratoconus suspects or keratoconus based on Placido topography analysis by the OPD-Scan II Corneal Navigator neural-network software were retrospectively selected (Figure 1). At the time of the surgery, the software was not available in the clinic; thus, the keratoconus and keratoconus suspect scores were retrospectively assessed.

The following were assessed.

1. Patient demographics.
2. Mean follow-up time.
3. Refractive stability: the mean preoperative and postoperative refraction, sphere, cylinder, axis group (with the rule [WTR], against the rule [ATR], or oblique, performed on the Automatic Refracto-Keratometer ARK 530A [Nidek]).
4. Preoperative corrected distance visual acuity (CDVA) and postoperative uncorrected distance visual acuity (UDVA) measured by 2 trained optometrists in the same room. The proportion of patients wearing glasses at the final follow-up was also assessed.

![Figure 1. A scan of a keratoconus-suspect patient with major inferior steepening on curvature map and keratoconus suspect scores of 92.7% in the right eye (left) and 51.7% in the left eye (right).](image-url)
5. Keratometry: preoperative and postoperative mean corneal keratometry measured using the automatic refractor/keratometer.

6. Corneal thickness: preoperative and postoperative mean central pachymetry, mean thinnest point value, and pachymetry mean delta (central thickness – thinnest point value) measured using the scanning-slit topographer/tomographer.

7. The mean keratoconus suspect and keratoconus score per eye and proportion of eyes with a keratoconus suspect or keratoconus score over 50%, measured using the neural-network software of the aberrometer/corneal topographer.

8. Topography: elevation topography and keratometric irregularity on Placido topography of the aberrometer/corneal topographer (according to investigators’ judgment).

Classifications were regular astigmatism, asymmetric bowtie, inferior–superior (I–S) value as defined by Rabionowitz, oblique astigmatism, skewed radial axis, or undefined topographic irregularity (Figure 2). The I–S value is an expression of inferior–superior dioptric asymmetry, and the skewed radial axis index is an expression of irregular astigmatism; the methods for calculating the 2 parameters have been described.

9. Occurrence of postoperative complications as corneal ectasia judged by the investigators.

Patients were systematically examined at least 1 week and 1 month postoperatively. The examination included UDVA, slitlamp evaluation, and assessments with the aberrometer/corneal topographer and the scanning-slit topographer/tomographer.

At the most recent examination, 14 of the included patients were examined (topography and aberrometry) at the Foundation Rothschild center, 11 patients were examined by their private practice ophthalmologist, 8 patients who did not recently consult an ophthalmologist were telephoned by investigators to make sure no complication had occurred, and 9 patients were lost to follow-up after a variable amount of time (Figure 3).

Statistical Analysis

Continuous variables were reported as the median and interquartile range and were compared using Wilcoxon rank-sum or matched-pair signed-rank tests, as appropriate. Categorical variables were reported as the number and percentage and were compared using chi-square or Fisher exact test, as appropriate. Comparisons between similarity to a keratoconus or keratoconus suspect score less than 50% and similarity to a keratoconus or keratoconus suspect score 50% or higher were performed after stratification by eye side to avoid the potential correlation between 2 eyes of the same patient. Statistical analyses were 2 sided, and a P value less than 0.05 was considered statistically significant. Analyses were performed using Stata software (version 11.0, StataCorp LP).

Figure 2. Scanning-slit topographer quad maps of 2 patients with keratoconus suspects in both eyes. Asymmetric bowtie on the curvature map and temporal pachymetry thinning are obvious.
RESULTS

Three hundred thirty eyes of 165 patients had PRK during the study period. Of those, 62 eyes (42 patients) were classified as keratoconus or keratoconus suspect at baseline. There was a slight female predominance (sex ratio 1.47). Table 1 shows the refractive outcomes and Table 2, the preoperative and postoperative pachymetry at the central and thinnest points. The mean preoperative spherical equivalent (SE) was \(-3.96 \pm 3.14\) D. Subgroups based on the mean preoperative refractive cylinder axis orientation were as follows: WTR (0 to 30 degrees or 150 to 180 degrees), which comprised 239 eyes (72.6%); ATR (60 to 120 degrees), which comprised 48 eyes (14.5%); oblique (30 to 60 degrees or 120 to 150 degrees), which comprised 43 eyes (12.9%). The mean simulated keratometry was 45.75 \pm 1.75\) D. A keratoconus suspect or keratoconus score was present in all 62 eyes (Table 1); keratoconus or keratoconus suspect exceeded a 50% value in 30 eyes (48.4%).

Based on the curvature shape analysis with the aberrometer/corneal topographer, 22 eyes had asymmetric bowtie, 10 eyes had skewed radial axis, 6 eyes had oblique astigmatism, 2 eyes had ATR asymmetric astigmatism, 9 eyes had indefinable irregularity, and 13 eyes had regular astigmatism (Figure 4).

The mean manifest refraction SE at the last visit was \(0.53 \pm 1.35\) D. The mean central pachymetry thinning measured with the scanning-slit tomographer was 61.7 \pm 39.3 \mu m at 5 years, which was consistent with the mean value of the corrected SE (\(-4.00\) D).

The mean UDVA at 5 years was 0.05 \pm 0.20 logMAR. Three patients required glasses because of significant myopic regression. The first patient had been operated for a mild myopic error (\(-3.75 \pm 1.00\) in both eyes) and had a postoperative refraction of \(-0.50 \pm 0.75\) in the right eye and \(-1.00 \pm 0.50\) in the left eye at 5 years. The second patient had PRK for high myopia (\(-8.25 \pm 2.25\) and \(-8.00 \pm 2.25\), respectively) but had a major regression to \(-5.25 \pm 1.50 \times 15\) in the right eye and \(-3.50 \pm 1.25 \times 15\) in the left eye at 5 years.
−0.50 × 90 in the left eye. Corneal topography performed with the scanning-slit topographer/tomographer and aberrometer/corneal topographer showed no topographic signs of corneal ectasia (Figure 5).

No case of corneal ectasia was reported over the study period, and no unusual problems were encountered in the 49 eyes of the 33 patients who could be contacted. The 13 eyes of the 9 patients lost to follow-up had no significant difference at baseline for the keratoconus-suspect score (\( P = .322 \)) and keratoconus score (\( P = .693 \)). The only significant differences preoperatively were a higher mean central pachymetry (555 μm), a higher thinnest point (546 μm), and a flatter curvature (44.2 D) in the group lost to follow-up.

### DISCUSSION

It is established that cases of topographic suspicion of keratoconus that are believed to have subclinical keratoconus are absolute contraindications to LASIK.\(^1\) It is uncertain whether there is a strict contraindication to PRK in these cases based on historical results, which give variable outcomes. With the current diagnostic tools, the classification of a cornea as normal may not indicate the absence of a subclinical keratoconus because the sensitivity of computer-assisted Placido-based videokeratography is not 100%. Similarly, an abnormal inferior keratometry minus a superior keratometry (I−S) value, as defined by Rabinowitz and Rasheed,\(^12\) or a steep keratometry (>47.0 D) may merely represent a false positive and may not necessarily be an indicator of a keratoconic subtype. Thus, the specificity of subclinical keratoconus detection-based Placido topography is not 100%. Therefore, some included corneas may correspond to false positives, possessing physiologic variations of normal corneas.\(^16\) In our study, no case of ectasia was reported and the PRK did not lead to a progression or acceleration of the suspected keratoconus or any other complication.

In 2006, Malecaze et al.\(^21\) reported the first case of bilateral iatrogenic ectasia after uneventful PRK.

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**Table 2. Preoperative versus postoperative pachymetry values (central and thinnest point).**

<table>
<thead>
<tr>
<th>Statistic</th>
<th>Central Pachymetry Delta (μm)</th>
<th>Thinnest Point Delta (μm)</th>
</tr>
</thead>
<tbody>
<tr>
<td>Eyes (n)</td>
<td>21</td>
<td>21</td>
</tr>
<tr>
<td>Mean (μm)</td>
<td>61.7</td>
<td>60.7</td>
</tr>
<tr>
<td>SD</td>
<td>39.3</td>
<td>42.5</td>
</tr>
<tr>
<td>p25</td>
<td>42</td>
<td>42</td>
</tr>
<tr>
<td>p50</td>
<td>53</td>
<td>48</td>
</tr>
<tr>
<td>p75</td>
<td>64</td>
<td>66</td>
</tr>
<tr>
<td>( P ) value</td>
<td>( &lt;10^{-4} )</td>
<td>( &lt;10^{-4} )</td>
</tr>
</tbody>
</table>

\( p = \) percentile
preoperative Placido topography of 1 of the treated eyes showed a skewed radial axis and some degree of irregularity. Most post-PRK ectasia cases described in the literature\(^2\)–\(^4,21\)–\(^23\) are subjectively diagnosed as suspect for keratoconus (Table 3). The automated detection software may be more sensitive in detecting early keratoconus suspect; thus, the cases we report may represent an earlier form of the disease.

The myopic regression of 2 patients in our study was not different from the regression observed after PRK in patients with regular corneal topographies in the first case and was related to the magnitude of the photoablation depth in the second case, in which the high myopia (−8.0 D) associated with thin corneas was a clear contraindication to LASIK. The differential axial topographies between 3 months and 5 years postoperatively showed central steepening in both eyes, which was more severe in the right eye and was correlated with the myopic regression (Figure 6). This central steepening was present 2 years postoperatively and did not evolve in the right eye. In the left eye, slight central steepening occurred between 2 years and 6 years postoperatively. The bilateral regression was attributed to stromal wound healing and epithelial hyperplasia (Figure 7).

We became interested in retrospectively analyzing all outcomes of PRK in eyes with corneas at risk for ectasia because we had noticed in our common practice that corneas classified as keratoconus suspect based on computerized Placido analysis did not develop unusual complications or ectatic evolution after surface-ablation techniques. Today, there are no biochemical or chemical tests to identify keratoconus in corneas with atypical topographies. Topography and tomography remain the best discriminatory methods.\(^13,14,16\)

The Corneal Navigator software, as most diagnostic and classification criteria, is based on anterior corneal curvature\(^12,19\) and does not consider the pachymetry profile or elevation parameters. Thus, even very steep

### Table 3. Description of the reported cases of post-PRK ectasia.

<table>
<thead>
<tr>
<th>Study*</th>
<th>Date</th>
<th>Pt Age (Y)</th>
<th>Preop Refraction</th>
<th>Preop Central Pachymetry (μm)</th>
</tr>
</thead>
<tbody>
<tr>
<td></td>
<td></td>
<td></td>
<td>RE</td>
<td>LE</td>
</tr>
<tr>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Malecaze(^21)/2006</td>
<td>22</td>
<td>−1.50 –1.00 × 105</td>
<td>−1.50 –1.00 × 65</td>
<td>495 495</td>
</tr>
<tr>
<td>Chiou(^2)/2006</td>
<td>42</td>
<td>−9.25 –1.25 × 65</td>
<td>−8.25 –2.00 × 160</td>
<td>477 481</td>
</tr>
<tr>
<td>Randelman(^3)/2006</td>
<td>37</td>
<td>−4.00 +2.50 × 160</td>
<td>−8.00 +3.00 × 180</td>
<td>472 441</td>
</tr>
<tr>
<td>Randelman(^3)/2006</td>
<td>40</td>
<td>−8.50 +3.75 × 123</td>
<td>−9.25 +4.00 × 77</td>
<td>509 508</td>
</tr>
<tr>
<td>Leccisotti(^2)/2007</td>
<td>38</td>
<td>−7.00 –3.00 × 0</td>
<td>−6.00 –4.00 × 0</td>
<td>520 510</td>
</tr>
<tr>
<td>Leccisotti(^2)/2007</td>
<td>31</td>
<td>−4.50 –1.75 × 175</td>
<td>PKP</td>
<td>487</td>
</tr>
<tr>
<td>Leccisotti(^2)/2007</td>
<td>31</td>
<td>−3.75 –0.75 × 10</td>
<td>−3.75 –0.50 × 150(^2)</td>
<td>506 492</td>
</tr>
<tr>
<td>Leccisotti(^2)/2007</td>
<td>38</td>
<td>−2.50 –0.75 × 130</td>
<td>−1.50 –1.25 × 130</td>
<td>510 509</td>
</tr>
<tr>
<td>Navas(^2)/2007</td>
<td>35</td>
<td>NA</td>
<td>NA</td>
<td>NA NA</td>
</tr>
<tr>
<td>Reznik(^23)/2008</td>
<td>25</td>
<td>−5.75 –1.75 × 95</td>
<td>−7.50 –1.25 × 80</td>
<td>500 460</td>
</tr>
</tbody>
</table>

FFKC = forme fruste keratoconus; I-S = inferior–superior value; KC = keratoconus; KCS = keratoconus suspect; PKP = penetrating keratoplasty; SRAX = skewed radial axis

*First author

Figure 6. Differential maps comparing the 3-month and 6-year postoperative axial keratometry. A severe and moderate central steepening can be seen in the right eye and left eye, respectively.
corneas (>47.0 D), especially with oblique or irregular astigmatism, will in most cases be classified as keratoconus suspect by the software. Combining tomographic and pachymetric maps with the usual Placido topographic index might improve the sensitivity and specificity of a comprehensive algorithm to detect corneas that should not have refractive surgery. In addition, viscoelasticity measurements with the Ocular Response Analyzer (Reichert, Inc.) provides additional information for screening for subclinical keratoconus, with an accurate analysis of the corneal biomechanical properties according to central corneal thickness, air pressure, and infrared curves; however, it is difficult to significantly discriminate keratoconic from normal corneas using corneal hysteresis and the corneal resistance factor index only.

Finally, it is possible that the inflammation induced by PRK halts the progression of keratectasia and plays a part in localized crosslinking, thereby strengthening the corneal collagen fibers by linking 1 polymer chain to another. If this were the case, the use of riboflavin and ultraviolet-A collagen crosslinking may further stabilize these corneas.

However, our results are restricted to a 5-year study period; safety over a longer follow-up must be assessed and the results compared with those of combined crosslinking techniques. The loss of some patients to follow-up did not likely significantly affect our results because in our experience, unhappy patients tend to return for follow-up more often than happy patients.

In summary, PRK in eyes with suspected keratoconus diagnosed with an automated system was a safe and effective therapy for mild myopia and astigmatism in carefully selected patients (age, preoperative characteristics, family history, magnitude of myopia, refractive stability, tomographic data, biomechanical properties). Visual function was improved with refractive and corneal stability. However, treatment indications remain to be discussed on a case-by-case basis.
WHAT WAS KNOWN

- Corneas with topographic suspicion of keratoconus are an absolute contraindication to LASIK.
- Cases of corneal ectasia after PRK are rare. The long-range safety of this procedure in corneas at risk for ectasia (keratoconus suspect) had not been studied in large samples.

WHAT THIS PAPER ADDS

- Photorefractive keratotomy was a safe and effective procedure for keratoconus-suspect corneas over a 5-year follow-up.
- Moreover, because no unusual complication was encountered, PRK may play a protective role on the evolution of ectasia in corneas at risk.

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