Contribution of the corneal epithelium to anterior corneal topography in patients having myopic photorefractive keratectomy

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PURPOSE: To assess the variations in corneal topographic characteristics after removal of the epithelium in patients having myopic photorefractive keratectomy (PRK).

SETTING: Rothschild Foundation, Paris, France.

METHODS: Forty-four eyes of 25 patients with myopia had corneal topography examination with the Orbscan II device (Bausch & Lomb) before removal of the corneal epithelium preoperatively and after removal of the corneal epithelium during PRK. On each examination, elevation, curvature, and pachymetry parameters were recorded and analyzed (paired 2-sided Student *t* test).

RESULTS: The mean difference in central pachymetry between preoperative and epithelial removal was 37.84 μm ± 9.82 (SD) (range 19 to 58 μm). The mean best-fit spherical surface radius was 7.75 ± 0.28 mm (range 7.25 to 8.42 mm) before removal of the epithelium and 7.92 ± 0.29 mm (range 7.39 to 9.16 mm) after removal of the epithelium (P<.0001). The mean simulated K-value difference increased from 0.75 ± 0.55 diopter (D) (range 0.1 to 4.7 D) before removal to 1.21 ± 0.66 D (range 0.2 to 4.7 D) after removal (P<.0001). The mean simulated value decreased from 43.77 ± 1.83 D (range 40.25 to 47.00 D) to 42.44 ± 1.73 D (range 37.05 to 45.50 D), respectively. The mean power (3.0 mm) decreased from 44.42 ± 1.59 D (range 40.4 to 47.2 D) before removal to 43.46 ± 1.37 D (range 39.7 to 46.9 D) after removal. The mean irregularity index increased from 1.07 ± 0.35 D (range 0.5 to 2.5 D) to 2.03 ± 0.38 D (range 1.3 to 3.3 D), respectively (P<.0001). The mean asphericity value (Q) changed from −0.44 ± 0.14 (range −0.72 to −0.20) to −0.65 ± 0.46 (range −1.04 to 0.14), respectively (P = .003).

CONCLUSIONS: The epithelium affected the topographic properties of the cornea by significantly reducing corneal topographic astigmatism and irregularity. This might prove to be important in the assessment of patient candidacy for and treatment planning in refractive surgery.

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Conventional or customized photoablative techniques used to modify the optical power of the cornea achieve their effect by altering the anterior corneal surface contour. In customized surface ablation techniques, preoperative wavefront measurements, corneal topography measurements, or both are performed with the epithelial layer in place, while the laser ablation is performed on the underlying stroma after epithelial removal. Studies have found that the thickness of the epithelial layer is not constant over the entrance pupil[1,2] and that simply removing the epithelium can alter the refractive and geometric properties of the cornea before ablation.[3] Similarly, the epithelial remodeling in PRK and other surface techniques may modify the specific effect induced by any customized profile after laser ablation.[4]

The human corneal epithelium has a refractive index that differs from that of the underlying corneal tissue,[5] and its thickness distribution is uneven from the center of the cornea to the periphery.[3,6] Simon et al.[4] measured corneal keratometry with an automated keratometer in 10 fresh human eye-bank eyes with and without the epithelium. They found that the corneal epithelium accounts for an average of 1.03 diopters (D) of the power of the eye at a central 2.0 mm zone. This power was 0.85 D at the 3.6 mm zone, suggesting that the corneal epithelium makes an individual contribution to the prolate aspherical nature of the cornea typically attributed to the corneal stromal surface alone. In addition, a change in astigmatism power and axis was observed between the epithelium and Bowman's surface in most eyes.

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Patel et al.[1] studied central epithelial thickness distribution in 14 normal human corneas by in vivo measurements using high-frequency ultrasound digital signal processing with a measurement precision of 2 μm. The mean radius of Bowman's layer was 7.34 mm ± 0.17 (SE). Its shape was hyperbolic, with a mean shape factor, p, of 0.22 ± 1.81 (SE), ranging from a prolate ellipse to a hyperbola.

Zipper et al.[2] obtained topographic data from 16 fresh human cadaver eyes using a PAR corneal topography system (PAR Vision Systems Corp.) before and after removal of the epithelium with a blunt knife. They found that the difference in the apical radius of curvature before and after removal of the epithelium corresponded to a power of approximately 0.5 D within the central 7.0 mm zone. In addition, Bowman's surface was slightly more prolate than the epithelial surface.

To our knowledge, there has been no previous study using anterior elevation and Placido video topography to characterize the role of the corneal epithelium on the anterior corneal shape and curvature in living human eyes. In the present study, Placido and elevation topography using the Orbscan II device (Bausch & Lomb) was used to assess the topographic changes induced by the removal of the corneal epithelial layer in patients having photorefractive keratectomy (PRK) for myopia.

PATIENTS AND METHODS

In this study, 25 consecutive patients having PRK for the correction of myopia or compound myopic astigmatism were enrolled. The reasons for choosing PRK were (1) the presence of a thin cornea (calculation of a residual stromal bed less than 250 μm after subtracting the sum of the planned laser in situ keratomileusis [LASIK] flap and laser ablation thickness); (2) patient preference when both LASIK and PRK were proposed. All patients provided written informed consent.

Patients with general conditions such as diabetes or collagen disease were excluded, as were those who had worn rigid gas-permeable (RGP) lenses in the 12 months before the preoperative examination. Patients who presented with keratoconus or suspicion of form fruste keratoconus were excluded. Patients wearing soft contact lenses were asked not to wear their lenses for at least 3 weeks before surgery.

Preoperatively, patients had a routine refractive surgery screening and examination including the determination of uncorrected visual acuity, best corrected visual acuity, refraction, slitlamp examination, ultrasound (US) pachymetry, pupil measurement, and topography using the Orbscan II device.

Topography Data

The Orbscan II device uses 40 scanned slit images from throughout the cornea to measure the anterior and posterior corneal surfaces as well as a reflective Placido disk image to measure the curvature of the anterior corneal surface. By default, the Orbscan II device presents the best-fit spherical (BFS) surface calculated over the central 10.0 mm diameter of the corneal topography as 1 measure of the corneal shape. To avoid interference from the remaining peripheral epithelium ring in this calculation, a smaller area of data calculation was used for preoperative and postoperative measurements: The points outside the inner 7.0 mm central zone were not considered in the calculation of elevation. A central zone fit of 7.0 mm was selected to determine the area used for anterior elevation BFS calculations.

The Orbscan wide-field pachymetry maps were calculated as the difference in elevation from the anterior surface to the posterior surface of the cornea. The acoustic factor (a standard correction factor in the instrument software that corrects the Orbscan pachymetry values to those typically found with US pachymetry[7,8]) was set to the manufacturer default value of 0.92. This acoustic factor reduces all pachymetry values by 8%.

The Orbscan II device calculates the 3.0 mm irregularity index and mean curvature using an algorithm that defines sampling for each zone as follows: Nine concentric rings are defined in the 3.0 mm zone. Each ring is divided into segments using a general formula for sampling to ensure uniform sampling density (eg, first ring has 3 segments, second ring has 9 segments, third ring has 15 segments). The following data from each of the obtained topographies were recorded: (1) central mean optical pachymetry in the 2.0 mm diameter zone; (2) anterior BFS radius (calculated over the central 7.0 mm zone with the floating mode); (3) keratometric astigmatism (given as the absolute value of the difference between the values of the simulated K-values; (4) central 3.0 mm mean curvature; (5) apical curvature and asphericity. These data were calculated by fitting an aconic surface to the set of anterior central 7.0 mm corneal data points. The aconic surface is an aspherical and toric surface constructed by multiplying a 2-fold axisymmetric saddle with a conoidal surface over the central 7.0 mm.

Surgical Technique

On the day of surgery, Orbscan topography was repeated in the surgical suite 10 minutes before surgery and administration of surface anesthesia. To limit the influence of overnight swelling,[9] the surgical procedures were performed at least 4 hours after the patient's awakening. All measurements were done using the same Orbscan topographer by the same examiner.

After standard disinfection and draping, an 8.0 mm Hanna corneal trephine blade (Moria) was used to apply 20% alcohol for 20 seconds on the central cornea. After it was rinsed with a balanced salt solution, the epithelium was removed completely over the central 8.0 mm corneal surface using a blunt forceps. Meticulous care was given to the removal

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of small epithelial debris to obtain a fully exposed Bowman membrane over the central 8.0 mm of the corneal surface.

The surgical drape and eyelid speculum were removed, allowing the patient to blink. The patient then sat up and was immediately placed in front of the Orbscan device. Two Orbscan topographies were acquired, and the patient was returned to the surgical bed and draped again. Excimer laser ablation was performed using the Nidek EC-5000 unit. A soft contact lens bandage was applied at the end of surgery, and a topical antibiotic agent was instilled into the eye. The same process was used for the second eye in cases in which surgery was required. Postoperative care consisted of topical antibiotics and corticosteroids.

On the Orbscan device, only topographies with no or minimum data loss were included. Visual inspection of the Orbscan software eye image during acquisition allowed the quality of the ocular surface during measurements to be checked. Given the smoothness and macroscopic regularity of the human Bowman's layer, the Placido disk reflection images always appeared to be smooth and distinct. Saving the 40 corneal slit images acquired by the instrument during acquisition of the corneal elevation enabled the accuracy of detection of the edges of the scanned slits to be checked.

Statistical Analysis

Pachymetry and topography parameters are presented as mean $\pm$ SD. A paired 2-sided Student t test was applied to check for significant differences (ie, $P < .05$).

RESULTS

There were no intraoperative or postoperative complications. There were no cases of visually significant haze, and no infection was recorded. The epithelialization rate was within normal limits in all patients. Forty-four eyes of 25 patients were included in the study. The mean patient age was 28.7 $\pm$ 7.9 years. The mean spherical equivalent before surgery was -3.56 ± 1.98 D (range -9.4 to 0.0 D) and the mean refractive cylinder magnitude, -0.49 ± 0.68 D (range -2.75 to 0.0 D).

Figure 1 shows an example of the topographic variation induced by the removal of the epithelium. Using 0.92 as the acoustic factor, the mean preoperative central Orbscan pachymetry was 518 $\pm$ 29.29 μm and was not statistically different from the mean US pachymetry of 516 $\pm$ 22.9 μm ($P = .65$). The mean difference in Orbscan pachymetry between before and after epithelial removal was 37.20 $\pm$ 9.43 μm (range 19 to 58 μm) in the 2.0 mm central area.

Table 1 summarizes the differences between parameters before deepithelialization and after deepithelialization. On average, the central cornea curvature was flatter after epithelial removal, as indicated by the change in the mean simulated K, 3.0 mm mean curvature, and the apical sphere radius values. The mean BFS radius calculated over the central 7.0 mm and the mean astigmatism derived from the simulated K values were statistically significantly different

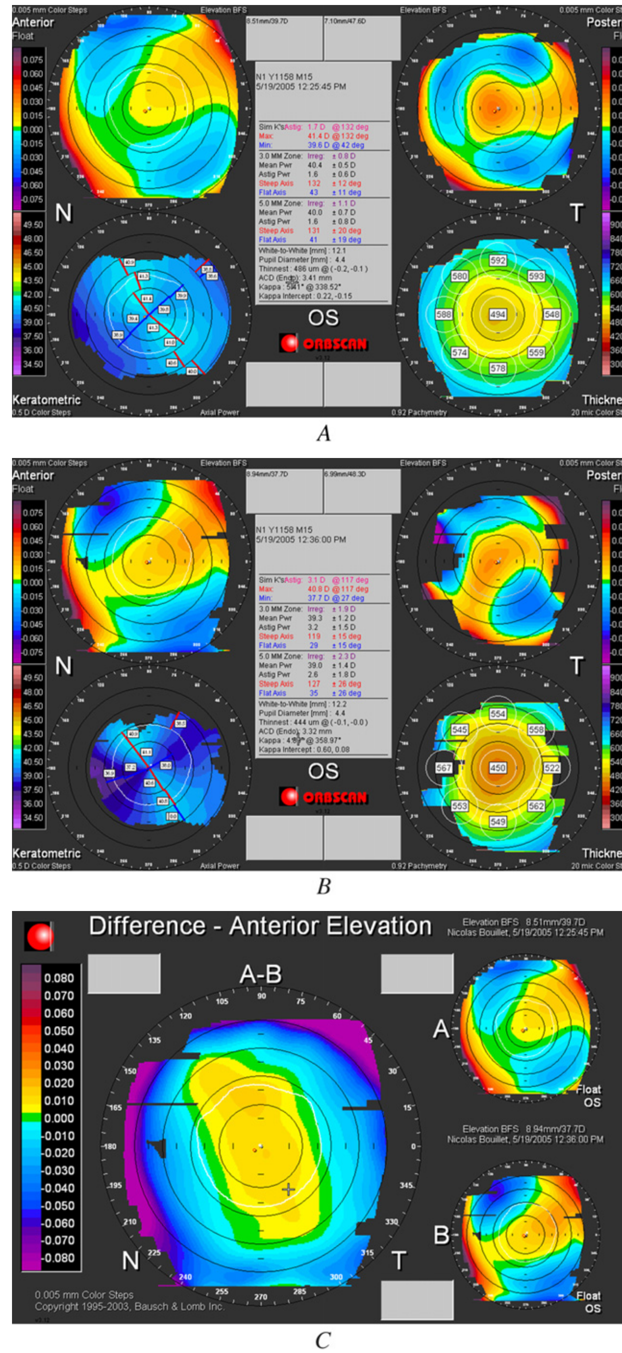

Figure 1. *A*: Preoperative Orbscan data. Color representation of anterior elevation map (*top left*), posterior elevation map (*top right*), axial curvature map (*bottom left*), and pachymetry map (*bottom right*). *B*: After epithelial removal. Note the increase in BFS radius, the reduction in the 3.0 mm central mean power, and the increased corneal astigmatism and irregularity index value. *C*: Anterior elevation difference map between the corneas before epithelial removal and after epithelial removal. This provides an approximate elevation shape of the epithelium.

between preoperatively and after removal of the epithelium (both $P < .0001$). The 3.0 mm irregularity index was significantly higher after removal of the epithelium ($P < .0001$). The asphericity (Q value) calculated

Table 1. Orbscan data before and after removal of epithelium.

Orbscan Data	Preoperative	Without Epithelium	*P* Value
Pachymetry (μm)			<.0001
Mean ± SD	519.73 ± 29.36	482.05 ± 30.89	
Range	466 to 604	420 to 565	
BFS, central 7.0 mm (mm)			<.0001
Mean ± SD	7.75 ± 0.28	7.92 ± 0.29	
Range	7.25 to 8.42	7.39 to 9.16	
Central keratometry (simulated K)			<.0001
Mean ± SD	43.77 ± 1.83	42.44 ± 1.73	
Range	40.25 to 47.00	37.05 to 45.50	
Astigmatism (D) (simulated K difference)			<.0001
Mean ± SD	0.75 ± 0.55	1.21 ± 0.66	
Range	0.1 to 4.7	0.2 to 4.7	
Mean power, 3.0 mm (D)			.0004
Mean ± SD	44.42 ± 1.59	43.46 ± 1.37	
Range	40.4 to 47.2	39.7 to 46.9	
Irregularity, 3.0 mm (D)			<.0001
Mean ± SD	1.07 ± 0.35	2.03 ± 0.38	
Range	0.5 to 2.5	1.3 to 3.3	
Apical sphere radius			$<10^{-7}$
Mean ± SD	44.54 ± 2.08	43.68 ± 2.01	
Range	40.31 to 48.06	36.95 to 46.47	
Asphericity (Q value)			.009
Mean ± SD	−0.44 ± 0.14	−0.65 ± 0.46	
Range	−0.72 to −0.20	−1.04 to 0.14	

BFS = best-fit sphere

over the central 7.0 mm also significantly changed toward a more prolate shape after epithelial removal ($P = .009$).

DISCUSSION

In this study, we measured significant variations in corneal pachymetry, anterior curvature, and elevation after epithelial removal over the 7.0 mm central corneal zone. The mean central thickness variation after removal of the epithelium was 37.84 ± 9.82 μm. This value is close to that reported by Ringvold et al.,[10] who conducted a morphologic study of the epithelium using human corneal specimens obtained from enucleated cadaver eyes and found a mean value of 36.6 μm.

On average, the corneal surfaces of our patients' eyes were flatter centrally, with an increased gradient of flattening toward the periphery as it was measured more prolate after deepithelialization in the 7.0 mm zone. The trend observed for the central curvature was the opposite of that reported in previous studies,[1,4] which found, on average, an increase in central keratometry after epithelial removal. The Orbscan device acquires keratometric and elevation data independently (Placido disk versus scanning slit); because both the keratometric parameter (mean of the simulated K value, mean central power) and elevation parameter (apical mean sphere) showed consistent results (average central corneal flattening), we are confident of the validity of these results. The floating BFS was calculated using the elevation data in the 7.0 mm central zone. Therefore, the increase in its radius may reflect the tendency toward central and peripheral flattening.

This discrepancy in the central keratometry change may be the result of different causes. First, the difference in measurement protocols may have influenced the results. We could obtain measurements in living eyes and in routine examination conditions without ocular globe preparation such as dextran irrigation. The brief alcohol exposure allowed us to avoid excessive epithelial scraping and subsequent damage to Bowman's surface. Second, our eyes were measured from a living population that was probably younger than that in the previous studies and all presented with a myopic, spherocylindrical refractive error. Some of our patients were counseled to have PRK because they had thinner than average corneas. Hayashi et al.[11] studied the change in corneal shape with age using corneal topography. They concluded that the mean refractive power of the cornea increases with age because the normal cornea becomes steeper and shifts from with-the-rule to against-the-rule astigmatism over time.

The refractive index of the epithelium is slightly higher than that of the corneal stroma. However, to estimate the total corneal power, the index used by the Orbscan software to calculate the curvature numbers parameters, expressed in diopters, is a standard keratometric index of 1.3375. Thus, these differences in curvature, expressed in diopters, cannot be used to estimate the change in the paraxial optical power.

We found a trend toward increased anterior prolateness after epithelial removal. This trend is similar to that reported by Patel et al.[1] and Zipper et al.[2] However, the mean asphericity of Bowman's layer that we measured before and after epithelial removal was less prolate than that reported by Patel et al. and Zipper et al. This may, in part, be explained by the difference in the methods of acquisition and fitting of the corneal data. Patel et al.[1] used high-frequency scanning to measure the epithelial thickness from the center of the cornea to a peripheral location along a radius.

This procedure was limited to a 3.0 mm of central chord. Zipper et al.[2] used an intraoperative PAR corneal topography system and performed the curve fits over a central 7.0 mm diameter optical zone of the cornea along the hemimeridian at 5-degree intervals. The difference in the diameter of the analyzed areas between the studies of Patel et al. and Zipper et al. (3.0 mm versus 7.0 mm) may be a major factor in the differences in the calculated shape factor values. The estimation of the anterior surface asphericity with the Orbscan device is performed by fitting an osculating aconic surface to the surface data points. This differs from the nonlinear conic fitting procedure used by Zipper et al. over the central 7.0 mm cornea, which may give less weight to the central points and result in a more negative Q value given the peripheral corneal flattening.[12]

Our results should not be extrapolated to the general population because some of our patients presented with compound myopic astigmatism and had corneas that were slightly thinner than average. Oshika et al.[13] studied the changes in corneal wavefront aberrations with aging. They report that coma-like aberrations correlate with age, implying that the corneas become less symmetrical with aging. Because we observed that the epithelium was compensating for irregularities at the Bowman's layer level, one may hypothesize that the increase in corneal coma-like aberrations with age is at least partly a result of changes in the distribution of the epithelium.

The ability of the epithelium to remodel the anterior corneal surface has been well established. Using very high-frequency (VHF) ultrasound corneal analysis, Reinstein et al.[14] suggest that the epithelium has the ability to remodel itself to compensate for stromal surface abnormalities caused by flap irregularities or irregular stromal ablation after lamellar refractive surgery. The wound-healing process in PRK and rearrangement of the flap in LASIK may result in partial compensation of the sculpted pattern onto the corneal surface after laser ablation.[15–19] The corneal thickness changes during overnight orthokeratology with reverse-geometry RGP contact lenses worn over a 3-month period has been studied.[20] Central corneal thinning (-9.3 ± 5.3 μm; $P < .001$), which was epithelial in origin, was found from day 1, whereas central stromal change was negligible. Analysis by Munnerlyn et al.'s formula[21] indicates that corneal sagittal height change resulting from the thickness changes could account for the refractive effect. Our results show that the epithelium has the ability to significantly modify the aspect of the anterior elevation and the curvature corneal topography map. The significant increase in astigmatism and topographical irregularity after removal of the epithelium shows that the epithelium smoothes some of the topographic features of the shape of Bowman's layer. This represents a major difference from the posterior surface, where no compensatory effect from a tissue layer can occur.

That the epithelium reduces the topographical irregularities of Bowman's membrane in myopic eyes supports the hypothesis that the variations in epithelial thickness may mask some early corneal anomalies that might otherwise identify some corneas in the early stages of keratoconus.[22] Rao et al.[23] report that patients with positive keratoconus screening tests have higher anterior and posterior elevation on Orbscan II topography. Fam and Lim[24] report that the topographical index derived from the anterior elevation was a better indicator than posterior elevation to distinguish between keratoconus and keratoconus-suspect eyes. However, other studies[25,26] conclude that the increased posterior elevation may be indicative of an early stage of keratoconus. Some epithelial remodeling may be involved to explain these discrepancies between anterior and posterior elevations in patients presenting with early stage of corneal ectasia.

Considering that the epithelium may have little or no influence on the structural integrity and strength of the cornea, should corneal topography look at the shape and curvature of the underlying stroma, or perhaps at Bowman's layer? Because of large subject intervariability, in practice, it might be difficult to predict the specific contribution of the epithelium to the corneal topography in a given patient. Even though no imaging device is capable of accurately mapping Bowman's layer or the epithelium with the level of precision of corneal topography, other techniques can be used to evaluate corneal epithelium distribution. By providing layered anatomical mapping, techniques combining VHF digital ultrasound scanning[27] and/or optical coherence tomography[28] may provide anatomic diagnostic information to explain clinical observations and enable more accurate preoperative and postoperative assessment and surgical planning.

Corneal topography is commonly used to calculate the amount and distribution of the optical aberrations generated by the eye's anterior surface. The subtraction of corneal aberration from the total aberrations of the eye (measured, for instance, with a Hartmann-Shack aberrometer) allows calculation of aberrations generated by the internal optical surfaces of the eye (posterior surface of the cornea, anterior and posterior surfaces of the crystalline lens).[29] A similar principle could be applied to our data to evaluate the role of the corneal epithelium in the optical quality of the retinal image. These calculations may also help us understand the epithelium's influence on postoperative phenomena such as sphere and cylinder regression and perhaps help develop better treatment algorithms.

Relatively few studies have evaluated the shape of the peripheral cornea. A recent study[12] found that the cornea is significantly flatter and slightly less toric in the periphery than in the center. Our data were limited to the central 7.0 mm of the corneal surface, and therefore we could not study the influence of the epithelium in the corneal periphery.

In conclusion, we have shown that the corneal epithelium has an important contribution to the anterior corneal topographical features. The cellular basis for these changes requires additional research, and further studies are needed to study the anatomy of the corneal epithelium, its variation among individuals, and its influence on preoperative evaluation of corneas before refractive surgery.

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