3-D Characterization of the Corneal Shape in Fuchs Dystrophy and Pseudophakic Keratopathy

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PURPOSE. To characterize the 3-D corneal shape deformation incurred by Fuchs corneal dystrophy and pseudophakic bul- lerous keratopathy by using the integrated analysis of Orbscan (Bausch & Lomb Surgical, Rochester, NY) topographic maps of affected and normal corneas.

METHODS. One hundred thirty-seven patients with Fuchs dystrophy or pseudophakic keratopathy were divided into three groups according to the severity of the disease: mild (central corneal thickness [CCT], 500–710 μm; n = 46); moderate (710–775 μm; n = 45), and severe (775–1100 μm; n = 46). A control group included 411 normal subjects matched for age and refractive spherical equivalent (three control subjects for each subject with Fuchs or pseudophakic keratopathy). The four groups were compared by using 3-D corneal shape atlases illustrating mean anterior elevation, posterior elevation, and pachymetry.

RESULTS. Whereas the atlases showed little anterior surface deformation, the posterior surface presented a significant central bulging toward the anterior chamber. The thinnest point was displaced away from the center, toward the superior nasal midperiphery. The corneal periphery remained relatively unaffected by the disease, except in the final stage.

CONCLUSIONS. 3-D atlases provided detailed new information on the 3-D corneal shape deformation incurred by Fuchs corneal dystrophy throughout disease progression. (Invest Ophthalmol Vis Sci. 2011;52:206–214) DOI:10.1167/iovs.09-4101

Fuchs endothelial dystrophy and pseudophakic keratopathy represent the leading indications for corneal transplantation, being responsible for 42.4% of the 42,000 grafts performed each year in North America.1–3 Since their initial description,4 both entities have been well studied from clinical, histologic, and genetic perspectives. Fuchs dystrophy is a primary corneal endothelial cell disease, whereas pseudophakic bullous keratopathy results from mechanical or microenvironmental cellular stress generated at the time of cataract surgery. In both cases, as the endothelial decapsulation evolves, stromal edema progresses, corneal thickness increases, and fluid accumulates beneath the epithelium, creating painful subepithelial bullous detachment and vision loss.

Disease progression can be clinically assessed and quantified, either subjectively (visual acuity measurement, quality of life assessment, slit lamp examination) or objectively (corneal pachymetry, anterior or posterior surface corneal topography, optical coherent tomography). However, tools able to characterize the impact of corneal endothelial decapsulation on the overall corneal shape and to follow its progression at a population scale were missing.

We approached Fuchs dystrophy and pseudophakic bullous keratopathy, the two most frequent diseases involving corneal endothelial decapsulation, from a 3-D corneal shape perspective. Our research hypothesis was that the 3-D corneal shape deformation incurred by Fuchs corneal dystrophy and pseudophakic bullous keratopathy could be characterized based on the integrated analysis of consecutive Orbscan (Bausch & Lomb Surgical, Rochester, NY) topographic maps of affected and normal corneas. To the best of our knowledge, there has been no report on the effect of endothelial decapsulation on the overall 3-D shape of the cornea.

METHODS

Fuchs and PBK Patients

One hundred thirty-seven patients with a diagnosis of Fuchs corneal dystrophy or pseudophakic corneal decapsulation were studied, 72 from the Devers Eye Institute (Portland, OR; MAT) and 65 from the Department of Ophthalmology, Maisonneuve-Rosemont Hospital (Montreal, QC, Canada; IB). One topography per patient was studied. As several topographies were usually available for each patient, only the latest one of the most affected eye was retained. None of these eyes had undergone corneal transplantation. The research protocol adhered to the tenets of the Declaration of Helsinki and was approved by the Maisonneuve-Rosemont Hospital human experimentation committee. All patients signed an institutional review board–approved research consent form (HIPAA-compliant for Devers Eye Institute).

Fifty-nine of these 137 eyes were pseudophakic, of which 38 (64.4%) had a confirmed diagnosis of Fuchs dystrophy. For simplification purposes, the term Fuchs herein globally refers to all eyes affected by irreversible endothelial decapsulation, whether caused by Fuchs dystrophy, pseudophakic decapsulation, or both. A comparison of phakic and aphakic eyes is also reported.

Normal Subjects

A control group consisting of 411 normal subjects with no corneal disease or previous ocular surgery was used for comparison purposes. For each Fuchs subject enrolled in the study, three normal controls...
matching for age and spherical equivalent were selected from a pool of 11,361 normal subjects. Only one topography per subject was selected: the right eye preferably or the left eye if the right eye was not available.

**Atlas Construction Methodology**

The methodology used for the construction of the atlases is described in detail elsewhere. The following is a summary of the method and specifics for this study. All topographies were obtained with the Orbscan II anterior segment analysis system (ver. 3.12; Bausch & Lomb Surgical). A topography consisted of an array of 101 × 101 points (10 × 10-mm surface) depicting the 3-D elevation of the anterior or posterior surface. Because of the mirror symmetry of the right and left eyes with respect to the sagittal plane (enantiomorphism), the left eyes were swapped to right-eye configuration. For each topography, a best-fit sphere (BFS) was calculated (i.e., the sphere that best adjusts to the anterior or posterior surface of the cornea in the least-squares sense).

The first step in atlas construction was topography normalization, a process that consisted of the scaling and translation of each cornea to a reference size and location in space. This process minimized the variations due to global corneal size and location in space while keeping each cornea local variations and individual features. For each cornea, the spatial alignment was initiated at the level of its anterior surface. The corneal anterior BFS was aligned on the reference anterior BFS. This generated a transformation matrix (isometric scaling and x, y, z plane translations) that was then applied to the corneal posterior surface. The cornea was thus treated as a volume, keeping the anterior and posterior surfaces in interrelation. In the present study, the average anterior BFS of the normal control subjects was used as the reference for the normal and Fuchs atlases. Once normalized, the topographies were then averaged to construct the atlases.

Four atlases were constructed: the normal control atlas and the mild, moderate, and severe Fuchs atlases. Each atlas was characterized by its mean anterior elevation, posterior elevation, and pachymetry maps. A standard deviation (SD) map was generated for each pachymetry map. SD maps were preferred to standard error of the mean (SEM) or coefficient of variation maps, although any one of them could have been used. Differences between groups were expressed by computing a point-by-point difference between the atlas elevation maps. The same color scales used by the Orbscan were used for the atlases: 5-μm color steps for the elevation maps (green representing a point on the steps for the difference maps. A scale ranging from 0 to 0.1 was used. Differences between groups were expressed in red and statistically significant differences were represented in red and nonsignificant differences in green.

**Orbscan Parameters**

Several parameters generated by the Orbscan software and meant to describe the anatomy of the anterior segment of the eye were also studied. These included the pupil diameter (Pup Dil [millimeters]) and several parameters related to astigmatism, such as keratometric astigmatism, simulated maximum and minimum K readings, and their corresponding meridian (Astig [KD] and Astig [deg]; Max K [KD] and Max K [deg]; and Min K [KD] and Min K [deg]). The mean power, the astigmatism power, and the steep and flat axes were also studied successively for the 3-mm central area and for the 3- to 5-mm ring shaped paracentral areas (Mean Pwr [KD]; Astig Pwr [KD]; Steep Axis [deg]; Flat Axis [deg]). Surface irregular astigmatism was quantified directly (Irreg [KDI]) and indirectly by assessing the percentage of missing values on anterior elevation, posterior elevation, and pachymetry maps. All pupil diameter and keratometric values were obtained from the Orbscan software and thus were not subject to any isometric scaling (normalization). This information is also routinely available to the clinician on the regular topography printout.

**3-D Corneal Shape in Fuchs Dystrophy**

As ultrasound pachymetry (US-CCT) was not available for all corneas (available for the HMR patients only), central corneal thickness (CCT) measurements were obtained from all the topographies before normalization, by averaging the central 2-mm pachymetry values. The correlation between the two parameters was high (r = 0.878; P < 0.001). Throughout the text, CCT refers to the averaged 2-mm central pachymetry.

**Corneal Parameters**

The corneal radius of curvature (R) and asphericity (Q) were also studied. These parameters were generated by fitting a conicoid in the least-squares sense to the anterior and posterior Orbscan elevation maps. Since corneal surface can be described by a conic section, Baker’s formula was used to model the corneal profile as an optical conicoid that can be expressed as

\[ x^2 + y^2 + (1 + Q)z^2 = 2Rz = 0 \]

where \( R \) is the apical radius of curvature, \( Q \) is a conic constant representing the conicoid asphericity, the z-axis corresponds to the optical axis, and \( x \) and \( y \) represent lateral distances from the optical axis. When \(-1 \leq Q < 0\), the ellipsoid is said to be prolate, with the major axis in the z-axis; when \( Q = 0 \) the ellipsoid becomes a plane, and when \( Q > 0 \), the ellipsoid is said to be oblate, with the major axis in the x – y plane.

**Statistical Analysis**

Student’s t-tests with Welch’s correction were used for the point-by-point comparisons of the various topographic maps (normal, mild, moderate, and severe Fuchs). All P values were adjusted according to the correction for multiple comparisons of Benjamini and Hochberg. P < 0.05 was considered to be statistically significant. ANOVA was used to assess intergroup differences, followed where necessary by a Tukey test for contrasts. Correlations between the different topography and CCT parameters were assessed with Pearson correlation coefficients. These correlations were calculated for all Fuchs groups together, as well as for each of the four groups separately (normal and mild, moderate and severe Fuchs). Pearson χ² tests were used to compare phakic and pseudophakic eyes.

**RESULTS**

Fuchs patients were aged from 45.5 to 89.7 years (mean ± SEM, 70.4 ± 0.90). The refractive spherical equivalent ranged from −6.75 to +6.38 D (mean ± SEM, −0.14 ± 0.21) and the refractive cylinder from 0 to +5.0 D (mean ± SEM, 1.22 ± 0.08). Best corrected visual acuity (BCVA) ranged from 0.04 to 3.00 logMar units (mean ± SEM, 0.66 ± 0.04; Snellen acuity, 20/22 to hand motion; mean, 20/91). Intraocular pressure was available in 46 eyes (HMR) and ranged from 8 to 22 mm Hg (mean ± SEM, 14.85 ± 0.54). In this study, CCT was used for staging and categorization of the disease. Figure 1 shows that the CCTs among the Fuchs patients followed a normal distribution that covered the entire range of the disease. Categorization was necessary to construct the atlases. The patients were divided into three tertiles, which were named according to disease severity (i.e., tertile 1, mild Fuchs [500 μm ≤ CCT < 710 μm; n = 46]; tertile 2, moderate Fuchs [710 μm ≤ CCT < 775 μm; n = 45]; and tertile 3, severe Fuchs [775 μm ≤ CCT < 1100 μm; n = 46]). This subdivision was also thought to be clinically acceptable.

The 411 normal subjects were aged from 45.2 to 89.9 years (mean ± SEM, 63.0 ± 9.1). Their refractive spherical equivalent ranged from −6.00 to +3.50 D (mean ± SEM, −0.06 ± 2.48), with a mean refractive cylinder of 0.94 ± 1.09 D.
and covered the entire range of the disease. Irreg [KD] as a function of CCT, it was corroborated by a basement membrane irregularities. This difference was more irregularity as the disease progressed, with a loss of smoothness between each Fuchs group and the normal control subjects. In the normal subjects, the average anterior surface revealed a typical concentric pattern, in which the apex in warm colors (i.e., above the BFS) was surrounded by cold colors (under the BFS), themselves surrounded by another ring of increasingly warmer colors toward the periphery (Fig. 2A1). An isthmus joined the central cornea to the temporal periphery. The apex lay 10 μm above the BFS and was slightly centered in the inferior temporal direction (−0.5, −0.5 mm; x, y).

In Fuchs patients, the same concentric pattern with a temporal isthmus was seen on the anterior surface (Figs. 2A2-2A4). The apex height and position remained unchanged (i.e., within 1.5 μm in elevation and 0.4 mm on the x-y plane) from its position in normal subjects. The main difference between the four groups consisted of an increase in anterior surface irregularity as the disease progressed, with a loss of smoothness in the concentric pattern due to epithelial bullae and basement membrane irregularities. This difference was more apparent on individual corneas than it was on atlases, because of the averaging smoothing effect. It was corroborated by a significant increase in the central index of surface irregularity (Irreg [KD]) as a function of CCT (r = 0.558, P < 0.001; Table 1). It was also accompanied by a significant increase in the percentage of missing data as the CCT increased (all Fuchs, r = −0.212, P = 0.013; severe Fuchs, r = −0.372; P = 0.011).

Overall, as shown by the P-value maps (Figs. 2B1-2B3), no differences in anterior elevation were found between Fuchs dystrophy and normal atlases.

### Posterior Corneal Surface Maps

In normal subjects, the average posterior surface presented a concentric pattern similar to that of the anterior surface, with an isthmus joining the central cornea to the temporal periphery. The posterior apex lay 26 μm above the BFS and was slightly displaced by (−0.4, −0.4 mm) with respect to the center of the map.

One of the main characteristics of Fuchs atlases consisted of a reversal of the typical normal posterior surface pattern, with a posterior shift of the apex behind the BFS, toward the anterior chamber. This shift increased in severity and extent with the progression of the disease. In Fuchs patients, the posterior apex was thus redefined as the most posterior elevation point in the 5-mm central area. The posterior apex lay 74, 151, and 245 μm below the BFS in the mild, moderate, and severe Fuchs atlases, respectively. In the three groups, the lateral apex displacement remained less than 0.4 mm.

Differences in posterior surface elevation between the normal and the Fuchs subjects were significant, as shown by the red areas covering 75%, 82%, and 99% of the P-value maps, in the mild, moderate, and severe Fuchs atlases, respectively (Fig. 2B, row 2). In patients with severe Fuchs, only a thin (0.1-mm) rim remained nonsignificant in the temporal periphery.

### Pachymetry Maps

In normal subjects, the pachymetry atlas (Fig. 2A9) showed a standard concentric pattern, thinner in the center and thicker in the periphery. The thinnest point measured 554 μm and was almost centered (−0.2, −0.3 mm).

Unlike the atlases of normal subjects, no central thinning was seen in the Fuchs atlases. In patients with mild Fuchs (Fig. 2A10), this zone was replaced by a 640- to 650-μm-thick area covering 31% of the map. In patients with moderate Fuchs (Fig. 2A11), pachymetry reached an average maximum of 723 μm in the inferotemporal paracentral area (−0.4, −1.8 mm). This zone was encircled by a large, crescent-shaped, thinner area in the superior nasal midperiphery area. The thinnest point measured 652 μm and was positioned nasally at (2.8, 0.5 mm). This pattern reached its maximum in the severe Fuchs group (Fig. 2A12), with an average maximum of 803 μm in the inferior temporal paracentral area (−0.1, −1.6 mm) and a minimum of 706 μm in the nasal area (3.5, 0.6 mm). More than 34% of the cornea was thicker than 770 μm.

The difference in pachymetry between the normal and Fuchs groups was statistically significant over 80%, 86%, and 99% of the surface in the mild, moderate, and severe Fuchs groups, respectively (Fig. 2B7-2B9).

### 2-D Corneal Profile

Figures 3A and 3B represent the corneal profile in the transverse (horizontal) and sagittal (vertical) planes. Both figures confirm that as the severity of the disease increased, the posterior profile became flatter, mainly due to a shift in the central posterior surface toward the anterior chamber. This shift appeared to be asymmetrical, slightly more pronounced temporally and inferiorly.

Each corneal profile is accompanied by a pachymetry graph indicating corneal thickness as a function of distance from the center of the average corneal atlas. Although central pachymetry was shown to clearly increase with disease progression, the peripheral cornea was only minimally affected by the disease, except in the most severe cases. In Figures 3C and 3D, slit lamp photographs of a cornea of a 55-year-old woman with Fuchs dystrophy show the typical central bulge of the posterior surface and the more uniform, less disturbed anatomy of the peripheral cornea.

### R, Q, and Astigmatism Parameters

For the anterior surface, no significant intergroup difference in R was found between the four groups (normal and Fuchs; ANOVA, P > 0.05; Table 2). A correlation was found, however, between R and CCT (r = 0.291, P = 0.001). Intergroup differences in Q were significant (ANOVA, P < 0.001), Q being significantly higher in severe Fuchs than in mild Fuchs or
FIGURE 2. 3-D topographic atlases of normal and Fuchs corneas. (A) Average elevation and pachymetry maps. First row: anterior elevation; second row: posterior elevation; third row: pachymetry; fourth row: SD map was generated for each pachymetry map. Column 1: average maps of the normal control subjects (411 eyes of 411 normal subjects). Columns 2–4: the three Fuchs atlases. Mild Fuchs: 500 μm ≤ CCT < 710 μm, n = 46; moderate: 710 μm ≤ CCT < 775 μm, n = 45; and severe: 775 μm ≤ CCT < 1100 μm, n = 46. The number at the bottom right of (A1) and (A5) is the atlas BFS radius (in millimeters). (B) P-value maps of the differences between the normal atlas and the mild, moderate, and severe Fuchs atlases.
normal control. A correlation was found between Q and CCT (r = 0.319, P < 0.001), with asphericity progressively evolving from a prolate to a more spherical and even oblate shape as the disease progressed (Tables 1, 2; Fig. 4).

In the case of the posterior surface, significant intergroup differences in R and Q were found (ANOVA, P < 0.05) and the correlations with CCT were significant (r = 0.300, P < 0.001; Q: r = 0.227, P < 0.001). The posterior surface became flatter and severely oblate as the disease progressed (Tables 1, 2; Fig. 4).

Figure 4 illustrates the increase in R and Q values as a function of CCT for the anterior and posterior surfaces. The posterior surface presented higher data dispersion and a steeper linear trend for both parameters.

For each surface, the two shape parameters R and Q correlated strongly (anterior surface: r = 0.669, P < 0.001; posterior surface: r = 0.917, P < 0.001). The correlations between anterior and posterior surface parameters were not as strong (R: r = 0.271, P = 0.001; Q: r = 0.184, P = 0.032).

No intergroup difference in keratometric power was found (Mean Pwr [KD, 0–3 mm] and Mean Pwr [KD, 3–5 mm]: ANOVA, P > 0.05). Within the severe Fuchs group, however, the keratometric power correlated negatively with CCT: Mean Pwr [KD, 0–3 mm]: r = −0.366, P = 0.012; and Mean Pwr [KD, 3–5 mm]: r = −0.432, P = 0.005).

The three parameters that characterize astigmatism also mildly but significantly correlated with CCT: Astig (KD) (r = 0.354; P < 0.001), Astig Pwr (KD, 0–3 mm) (r = 0.252; P = 0.003), and Astig Pwr (KD, 3–5 mm) (r = 0.182; P = 0.033; Table 1). This increase in astigmatism was particularly marked in the severe Fuchs group (Astig [KD]: r = 0.526, P < 0.001; Astig Pwr [KD, 0–3 mm]: r = 0.306; P = 0.039). It appeared to be related to a decrease in minimum K readings (Min K [KD]: r = −0.251; P = 0.003), while maximum K readings remained unchanged. No change in mean astigmatism orientation was found.

**Phakic versus Pseudophakic Corneal Edema**

To compare the 3-D shape of the edematous cornea in phakic and pseudophakic eyes, atlases were constructed for two subgroups of Fuchs eyes with a confirmed diagnosis of phakia (n = 70) or pseudophakia (n = 59) (maps not shown). Comparison of these two atlases revealed a mild flattening of the horizontal meridian and a relative steepening of the vertical meridian on the anterior surface elevation map in the pseudophakic group compared with the phakic group. This mild difference was suggestive of a postphacoemulsification surgery astigmatism pattern in the pseudophakic group. Corneas of the pseudophakic eyes were also thicker. However, none of the differences was statistically significant (entirely green P-value maps for the anterior elevation, posterior elevation, and pachymetry comparisons).

**Severity of the Disease**

Pupil diameter decreased with disease progression (r = −0.227, P = 0.008; Table 2). This progressive miosis was mostly marked in the group with advanced disease (severe Fuchs: r = −0.371, P = 0.011) and was not observed in the control group paired for age. CCT in Fuchs patients correlated mildly to moderately with age, BCVA, anterior and posterior surface R and Q values, and indices of surface irregularity (Table 1). The correlation between CCT and age was strongest when only eyes with severe Fuchs were considered (r = 0.346; P = 0.018). Merging all Fuchs and control eyes yielded stronger correlations for the following three parameters: posterior surface Q (r = 0.509, P < 0.001), posterior surface R (r = 0.515, P < 0.001), and Irreg (KD, 0–3 mm; r = 0.462, P < 0.001).

**Discussion**

The 3-D atlases, with their difference and P-value maps, allowed overall characterization of the corneal shape on a population level. They allow balanced interpretation of differences between cohorts of patients, taking into account the magnitude, distribution, and statistical significance of the changes observed across the entire cornea. With 3-D average models, the risk of giving excessive weight to a few localized measures on the cornea is minimized and interpretation of clinical relevance is simplified. Atlases allow for the description of complex topographical patterns that no single parameter could express. They can be used with any topography unit for which raw data are available.

In the present study, detailed new information is given on the evolution of the 3-D shape of the cornea in Fuchs dystrophy and pseudophakic keratopathy. The use of the anterior surface as the reference for the atlas spatial alignment was justified by the absence of significant difference in R values between the four groups (normal and Fuchs groups; Table 2) and by the low dispersion of R and Q values compared with posterior values (Fig. 4).

**Parameter Used for Staging and Categorization of the Disease**

In the present study, CCT was used for disease staging and categorization for the following reasons: (1) an increased cor-
neal thickness is the first clinical sign of endothelial decomposition; (2) CCT is routinely used to observe the severity of endothelial decomposition in Fuchs and PBK patients; and (3) CCT is intimately related to the patient’s functionality, corneal edema resulting in decreased vision, increased discomfort, photophobia, and pain. Other parameters such as BCVA or endothelial cell counts were not used for classification purposes. BCVA may not correlate closely with disease stage, in that it is dependent on several other confounding parameters not necessarily related to the actual stage of corneal decomposition (e.g., cataract, AMD, glaucoma, and retinal detachment). Also, because of light scattering and decreased visibility, specular microscopy becomes impossible to perform early in the course of the disease (i.e., as soon as mild central edema occurs).

CCT measurements obtained from the Orbscan topographies before normalization were very useful for staging the disease and categorizing the topographic maps. These topography-derived CCTs correlated highly with the ultrasound pachymetries. Although little is still known about Orbscan’s performance in edematous corneas, Martin et al. demonstrated high reproducibility of the Orbscan for the monitoring of corneal swelling and posterior corneal surface flattening in contact lens (hypoxia)-induced corneal edema. Orbscan also showed higher repeatability than ultrasound for central and peripheral corneal thickness measurements in edematous corneas.

To construct the atlases, categorization was necessary. Three classic methods of categorization were considered: (1) equal distribution of the number of subjects in each group; this method was retained and the study group was divided into three tertiles; (2) equal progression of the CCT staging intervals: The data were also analyzed by 100-μm CCT slices. The evolution of these successive atlases being slowly progressive and unidirectional, conclusions were the same as those reported for the three tertile atlases; and (3) categorization according to defined clinical parameters, which could not be used because of the lack of recognized algorithms for the clinical staging of corneal endothelial decomposition. It should be remembered that, in addition to categorization of the data for the purpose of atlas construction, all statistical analyses were performed on a continuous basis, using the pool of all Fuchs patients as a whole group (Table 2).

Although the atlases showed little anterior surface deformation, the posterior surface presented an inverted pattern, with significant central bulging toward the anterior chamber. The thinnest point was displaced quite far from the center, toward the superior nasal midperiphery. The corneal periphery remained relatively unaffected by the disease, except in the final stage. Topography parameters analysis brought interesting complementary information, showing that the anterior surface became less prolate and the posterior surface considerably flatter and oblate as the disease progressed.

It should be noticed that if the flattening of anterior surface K readings seen in Fuchs patients has any effect on intraocular lens calculation, it would theoretically result in overestimation of the intraocular lens power and induced postoperative myopia. In the case of combined surgery with in Descemet’s stripping automated endothelial keratoplasty (DSAEK), the induced myopia would compensate at least in part for the hyperopic shift typically induced by lenticular shape.
TABLE 2. Descriptive Statistics

<table>
<thead>
<tr>
<th></th>
<th>Normal Mean ± SEM</th>
<th>Fuchs Mild Mean ± SEM</th>
<th>Fuchs Moderate Mean ± SEM</th>
<th>Fuchs Severe Mean ± SEM</th>
<th>Intergroup ANOVA P value</th>
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<tr>
<td><strong>Group size, n</strong></td>
<td>411</td>
<td>46</td>
<td>45</td>
<td>46</td>
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<tr>
<td><strong>Clinical data</strong></td>
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<tr>
<td>Patient age</td>
<td>62.95 ± 0.44</td>
<td>70.85 ± 1.60*</td>
<td>67.55 ± 1.53*</td>
<td>72.83 ± 1.49*</td>
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<tr>
<td>Spherical equivalent</td>
<td>−0.06 ± 0.12</td>
<td>0.25 ± 0.44</td>
<td>0.09 ± 0.34</td>
<td>−0.68 ± 0.31</td>
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<td>BCVA, logMAR</td>
<td>0.53 ± 0.06</td>
<td>0.62 ± 0.05</td>
<td>0.79 ± 0.07</td>
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<td><strong>Topography data</strong></td>
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<td>Pupil Dia, mm</td>
<td>3.53 ± 0.05</td>
<td>3.32 ± 0.10</td>
<td>3.30 ± 0.09</td>
<td>3.11 ± 0.10*</td>
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<tr>
<td><strong>Percentage of missing data</strong></td>
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<td>Anterior surface</td>
<td>27.99 ± 0.39</td>
<td>31.37 ± 1.37</td>
<td>31.62 ± 1.48*</td>
<td>34.69 ± 1.65*</td>
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<tr>
<td>Posterior surface</td>
<td>43.73 ± 0.46</td>
<td>47.38 ± 1.47</td>
<td>45.23 ± 1.40</td>
<td>49.37 ± 1.55*</td>
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<tr>
<td>Pachymetry</td>
<td>43.73 ± 0.46</td>
<td>47.40 ± 1.47</td>
<td>45.23 ± 1.41</td>
<td>49.42 ± 1.55*</td>
<td>*</td>
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<td><strong>R</strong></td>
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<td>Anterior surface</td>
<td>7.62 ± 0.02</td>
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<td>Posterior surface</td>
<td>6.24 ± 0.02</td>
<td>6.89 ± 0.09*</td>
<td>7.37 ± 0.13*</td>
<td>7.54 ± 0.16*</td>
<td>*</td>
</tr>
<tr>
<td><strong>Q</strong></td>
<td></td>
<td></td>
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<td></td>
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<tr>
<td>Anterior surface</td>
<td>−0.31 ± 0.01</td>
<td>−0.34 ± 0.03</td>
<td>−0.26 ± 0.04</td>
<td>−0.17 ± 0.06*</td>
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<td>Posterior surface</td>
<td>−0.48 ± 0.02</td>
<td>0.10 ± 0.10*</td>
<td>0.46 ± 0.11*</td>
<td>0.73 ± 0.16*</td>
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<td>Astig, KD</td>
<td>0.95 ± 0.04</td>
<td>1.77 ± 0.23*</td>
<td>1.85 ± 0.23*</td>
<td>2.71 ± 0.31*</td>
<td>*</td>
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<tr>
<td>Astig, deg</td>
<td>262.56 ± 2.38</td>
<td>259.91 ± 8.69</td>
<td>263.50 ± 7.69</td>
<td>271.87 ± 8.40</td>
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<td>Max K, KD</td>
<td>44.43 ± 0.09</td>
<td>45.03 ± 0.31</td>
<td>44.82 ± 0.27</td>
<td>45.19 ± 0.34*</td>
<td>*</td>
</tr>
<tr>
<td>Max K, deg</td>
<td>262.56 ± 2.38</td>
<td>259.91 ± 8.69</td>
<td>263.50 ± 7.69</td>
<td>271.87 ± 8.40</td>
<td>*</td>
</tr>
<tr>
<td>Min K, KD</td>
<td>43.48 ± 0.08</td>
<td>43.26 ± 0.27</td>
<td>42.98 ± 0.23</td>
<td>42.49 ± 0.31*</td>
<td>*</td>
</tr>
<tr>
<td>Min K, deg</td>
<td>264.73 ± 2.94</td>
<td>271.65 ± 7.20</td>
<td>271.68 ± 8.41</td>
<td>260.13 ± 7.28</td>
<td></td>
</tr>
<tr>
<td>Irreg. KD, 0–3 mm</td>
<td>1.52 ± 0.04</td>
<td>2.04 ± 0.19*</td>
<td>3.27 ± 0.30*</td>
<td>3.51 ± 0.39*</td>
<td>*</td>
</tr>
<tr>
<td>Mean Pwr. [KD](0–3 mm)</td>
<td>43.89 ± 0.08</td>
<td>44.04 ± 0.27</td>
<td>43.93 ± 0.24</td>
<td>43.77 ± 0.25</td>
<td></td>
</tr>
<tr>
<td>Astig Pwr. [KD] (0–3 mm)</td>
<td>0.95 ± 0.04</td>
<td>1.50 ± 0.16*</td>
<td>1.60 ± 0.17*</td>
<td>2.08 ± 0.25*</td>
<td>*</td>
</tr>
<tr>
<td>Steep Axs* (0–3 mm)</td>
<td>79.52 ± 2.29</td>
<td>80.06 ± 8.52</td>
<td>92.55 ± 7.47</td>
<td>78.99 ± 7.35</td>
<td></td>
</tr>
<tr>
<td>Flat Axs* (0–3 mm)</td>
<td>92.65 ± 3.05</td>
<td>84.77 ± 7.58</td>
<td>105.28 ± 8.15</td>
<td>85.04 ± 7.54</td>
<td></td>
</tr>
<tr>
<td>Irreg [KD] (3–5 mm)</td>
<td>2.17 ± 0.07</td>
<td>2.71 ± 0.22</td>
<td>4.27 ± 0.52*</td>
<td>4.58 ± 0.54*</td>
<td>*</td>
</tr>
<tr>
<td>Mean Pwr [KD] (3–5 mm)</td>
<td>43.56 ± 0.07</td>
<td>43.62 ± 0.24</td>
<td>43.23 ± 0.24</td>
<td>43.24 ± 0.19</td>
<td>*</td>
</tr>
<tr>
<td>Astig Pwr [KD] (3–5 mm)</td>
<td>0.99 ± 0.04</td>
<td>1.41 ± 0.15</td>
<td>1.74 ± 0.23*</td>
<td>2.23 ± 0.40*</td>
<td>*</td>
</tr>
<tr>
<td>Steep Axs* (3–5 mm)</td>
<td>93.29 ± 2.49</td>
<td>80.25 ± 8.80</td>
<td>97.28 ± 8.42</td>
<td>73.05 ± 7.64</td>
<td></td>
</tr>
<tr>
<td>Flat Axs* (3–5 mm)</td>
<td>85.92 ± 2.96</td>
<td>87.74 ± 7.55</td>
<td>94.91 ± 8.96</td>
<td>93.51 ± 7.59</td>
<td></td>
</tr>
</tbody>
</table>

Data are expressed as the mean ± SEM.
* Significant (P < 0.05) difference to the normal group.

**FIGURE 4.** R and Q as functions of CCT in the anterior (A) and posterior (B) surfaces of the normal and the mild, moderate, and severe Fuchs corneas.
Progressive miosis was interpreted as sign of chronic irrita-
tion in eyes with advanced disease.

**Ultrastructure and Biomechanics of Corneal Deformation**

As corneal edema progressed, the anterior surface remained relatively stable in comparison to the major remodeling affect-
ing preferentially the central posterior surface. The cornea is a
3-D tissue with complex biomechanical interactions. Ultra-
structural architecture and distribution of mechanical and bio-
chemical properties across the cornea may explain in part the
surface deformation patterns in Fuchs dystrophy and pseu-
dophakic corneal edema.

Large bundles of striated collagen fibrils splay obliquely and
outward from the midstroma to the internal side of the Bow-
man’s amorphous matrix. Such an arrangement is thought to
prevent the anterior corneal surface from bending out of
shape when pathologic strength or shear stress is applied.
Compared with the posterior stroma, anterior collagen lamel-
lae are also more randomly distributed and more inter-
weaved, with interlamellae branching increasing in distrib-
ution and creating bridges between collagen lamellae, thus
providing a structural foundation for shear resistance by
distributing tensile loads.

The nonuniform swelling properties of the stroma also
participate in the volume distribution of the edema. In the
normal cornea, the anterior stroma is less hydrated than the
posterior stroma, with a higher keratocyte density and a
lower keratan sulfate (KS) to chondroitin/dermatan sulfate
ratio. The cohesive tensile strength of the stroma is
weaker in the anterior stroma. Consequently, the ante-
rior stroma swells less than the posterior stroma. Lamellar
interweave in the anterior stroma probably limits the extent
to which the lamellae can swell.

Limbal architecture also influences the 3-D shape of the
edematous cornea. Limbal collagen fibrils tend to adopt a
circumferential tangential orientation. They are more densely
distributed and the interlamellae cohesive forces and col-
lagen interweaving patterns are more extensive in the periph-
ery than in the central stroma, which may also support pre-
dominance of central swelling and preservation of the peri-
aphery, giving the typical 3-D shape of the edematous cornea in Fuchs dystrophy and pseu-
dophakic keratopathy.

To the best of our knowledge, this is the first study on the
3-D shape of edematous cornneas. This work illustrates the
functional and biomechanical responses of the human cornea
to endothelial decompensation. It also opens the door to sim-
ilar studies on ex vivo eye bank eyes. A better understanding of
the donor cornea 3-D shape may allow for the preparation of
donor tissues more suitable for posterior lamellar transplanta-
tion. In DSAEK, the donor button is presently cut with a
keratome blade, which results in a meniscus of excess tissue in
the graft periphery. This process induces hyperopia, a redu-
cion of endothelial cell spreading by the thick graft edges, and
excessive tissue presence in the narrow anterior chamber in
small eyes. Coupling the 3-D shape of the donor corneal post-

erior surface to a femtosecond laser may allow a much thinner
and more uniform cut.

3-D Corneal Shape in Fuchs Dystrophy

In conclusion, we described the 3-D corneal shape defor-
mation incurred by Fuchs corneal dystrophy throughout dis-
cease progression by using 3-D atlases, complemented by vari-
ous morphologic parameters.

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