• Clinical Research •

Assessment of tomographic parameters and detection of subclinical edema in Fuchs' endothelial corneal dystrophy pre-cataract surgery

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Abstract

● **AIM:** To assess tomographic changes and subclinical edema detection in Fuchs' endothelial corneal dystrophy (FECD) through Scheimpflug tomography in a group of phakic patients contemplating cataract surgery.

● **METHODS:** A retrospective study was conducted on 30 phakic eyes from patients diagnosed with FECD but without clinical edema, and 59 phakic eyes from a control group without corneal alterations. Comprehensive ophthalmic examinations were conducted, including slit-lamp biomicroscopy, corneal specular microscopy (CSM), and Scheimpflug tomography.

● **RESULTS:** The study encompassed 30 phakic eyes with FECD (mean age 59.8±13.1y) and 59 control eyes (mean age 61.3±7.7y). The best-corrected visual acuity was higher in the control group compared to the FECD group [0 (0, 0.08) *vs* 0.05 (0, 0.15) logMAR; *P*=0.042]. CSM revealed significant differences between the FECD and control groups in several parameters: number of analyzed cells (26±13 *vs* 135±42, *P*<0.001), cell density (2049±376 *vs* 2479±225 cells/mm^2, *P*<0.001), mean cell area [463 (434, 544) *vs* 397 (383, 431) μm^2; *P*<0.001], coefficient of variation (54.8%±18.7% *vs* 41.0%±7.2%, *P*<0.001), and hexagonal cells [0 (0, 47%) *vs* 47% (40%, 53%), *P*<0.001]. Although often used as a clinical parameter for detecting edema, central corneal thickness measured by CSM showed no significant difference between the FECD and control groups (530±57 *vs* 546±30 μm, *P*=0.179). Significant differences were noted in various Pentacam measurements between the groups. Specifically, parameters like loss of parallel isopachs (13 *vs* 0 eyes, *P*<0.001), displacement of the thinnest point (11 *vs* 0 eyes, *P*<0.001), posterior focal depression (25 *vs* 7 eyes, *P*<0.001), and increased light scatter [21.4 (17.6; 23.9) *vs* 18.0 (16.8, 21.8), *P*=0.01] were significantly more prevalent in FECD eyes, reflecting the presence of subclinical edema and loss of corneal transparency.

● **CONCLUSION:** Scheimpflug tomography allows for an objective assessment of FECD, offering the capability to detect subclinical edema at an early stage, monitor disease progression, and serve as a predictor of corneal decompensation following cataract surgery.

● **KEYWORDS:** anterior eye segment; cornea; endothelium; corneal; Fuchs' endothelial dystrophy; tomography

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INTRODUCTION

Fuchs' endothelial corneal dystrophy (FECD), first described by Austrian ophthalmologist Ernst Fuchs, is a non-inflammatory, sporadic or autosomal dominant, bilateral dystrophy involving the endothelial layer of the cornea[1]. Up to seventy percent of FECD cases are associated with an intronic trinucleotide repeat expansion in the transcription factor 4 (*TCF4*) gene, which plays a significant role in its pathogenesis[2-3]. In the early stages, changes include accelerated loss of endothelial cells and the formation of small extracellular matrix excrescences on the Descemet membrane, known as guttae. Over time, the compromised watertight seal provided by the endothelium results in fluid accumulation in the corneal stroma, leading to increased corneal thickness and causing light scattering[4]. This phenomenon is responsible for visual disturbances such as glare, halos, and reduced visual acuity. In advanced stages, epithelial layer edema may form bullae, and chronic edema can induce subepithelial fibrotic tissue formation, further contributing to corneal opacification[1]. While the diagnosis of FECD is generally straightforward, stratifying the severity of the disease remains largely subjective. Krachmer[5] initially introduced a grading system

to document FECD progression, where severity was assessed based on the confluence and number of guttae, along with the presence of corneal edema. Although most grading systems classify FECD into stages with and without corneal edema, and a stage with corneal scarring, the assessment of FECD severity through slit-lamp biomicroscopy remains subjective. This approach relies on endothelial morphology rather than function, overlooks the presence of subclinical corneal edema, and is incapable of predicting progression[6]. Moreover, it is crucial to acknowledge that subclinical edema is not necessarily asymptomatic; it can cause symptoms such as glare and a subjective lack of clarity in vision.

When penetrating keratoplasty was the preferred corneal transplantation technique, surgery was recommended for advanced cases where clinical evidence of corneal edema was apparent. However, endothelial keratoplasty (EK) has now enhanced transplantation outcomes, reducing risks such as graft rejection, and has become the preferred technique for FECD[7]. Naturally, lowering the threshold for intervention has introduced new challenges in determining which eyes will experience improved vision after EK, particularly when corneal edema is less clinically evident[8]. Similarly, assessing whether individuals with both FECD and cataracts can expect improved vision after cataract surgery alone poses a challenge when corneal edema is present but not visibly apparent during clinical examination[9]. Vision impairment, glare, and diminished contrast sensitivity may result from either corneal deterioration or cataracts. It is important to note that cataract surgery may also cause endothelial cell loss and worsen subclinical edema[3,10].

Beyond slit-lamp biomicroscopy, relying on central corneal thickness (CCT) assessment through corneal specular microscopy (CSM), ultrasound, or tomography as an indicator of corneal endothelial function may not consistently reflect the presence of subclinical corneal edema. While monitoring CCT can be valuable for tracking disease progression, interpreting isolated measurements may not accurately reflect FECD severity at a single time point. This is due to variations in corneal thickness within the normal population, making it challenging to differentiate corneas with subclinical edema from corneas that are naturally thicker in the absence of edema. Additionally, regional variations, particularly between guttata areas and observable cells within the limited field of view of CSM, introduce imprecision to corneal measurements[4,11].

Therefore, an objective clinical grading system would be valuable for monitoring the severity/progression of FECD, as well as determining the appropriate timing for intervention.

Various objective methods for assessing FECD severity have been investigated. A diagnostic approach for FECD utilizing custom-designed ultra-high-resolution anterior segment optical coherence tomography (AS-OCT) was suggested, as an increase in Descemet membrane thickness was observed in FECD patients compared to normal individuals[12-13]. Nevertheless, there is still a barrier to deploying this technology in clinical practice due to the lack of automated, reliable, and accurate analysis of AS-OCT scans[14].

Recently, Scheimpflug imaging, specifically with Pentacam® (Oculus Optikgeräte GmbH, Wetzlar, Germany), has emerged as an innovative approach for detecting subclinical edema in FECD and predicting the prognosis of the condition[15-19]. Integrated into Pentacam's software, corneal densitometry enables the measurement of the intensity of corneal backscatters at specified points in the captured images. Given that normal corneas typically exhibit minimal light backscatter, densitometry has been applied in assessing conditions such as postoperative corneal haze after photorefractive keratectomy or corneal collagen crosslinking, corneal opacity in bacterial keratitis, corneal clouding in patients with mucopolysaccharidosis, and corneal deposits in monoclonal gammopathies[20-24]. Pathological changes in corneal structures affecting light propagation into the eye, such as those observed in FECD, can be identified through the light backscatter detected by densitometry. This method has been utilized to assess the optical health of the cornea[25-26].

Furthermore, an objective functional index derived from the corneal pachymetric profile has identified the central-to-peripheral thickness ratio as a dependable metric for assessing FECD severity, exhibiting a correlation with endothelial function rather than morphology alone[6]. The Mayo Clinic has also reported that pachymetry maps and posterior corneal curvature patterns, specifically indicating irregular isopachs, displacement of the thinnest point of the cornea, and focal posterior surface depression, can facilitate the identification of subclinical edema in cases of FECD[15-16,27]. Additionally, the same group described that the posterior toricity of the cornea is abnormal in advanced FECD due to relatively greater horizontal than vertical corneal thickening[27].

The ability to detect subclinical edema and accurately stage FECD using Scheimpflug tomography could be highly beneficial in counseling patients about their disease and available treatment options, particularly before cataract surgery. In this study, our objective was to assess tomographic changes in corneal densitometry, pachymetry maps, and posterior corneal curvature patterns as an objective, quantitative tool for further categorizing phakic patients with FECD, particularly where corneal edema was not clinically obvious by slit-lamp biomicroscopy.

PARTICIPANTS AND METHODS

Ethical Approval This study adheres to the guidelines for human studies and was conducted ethically in accordance with

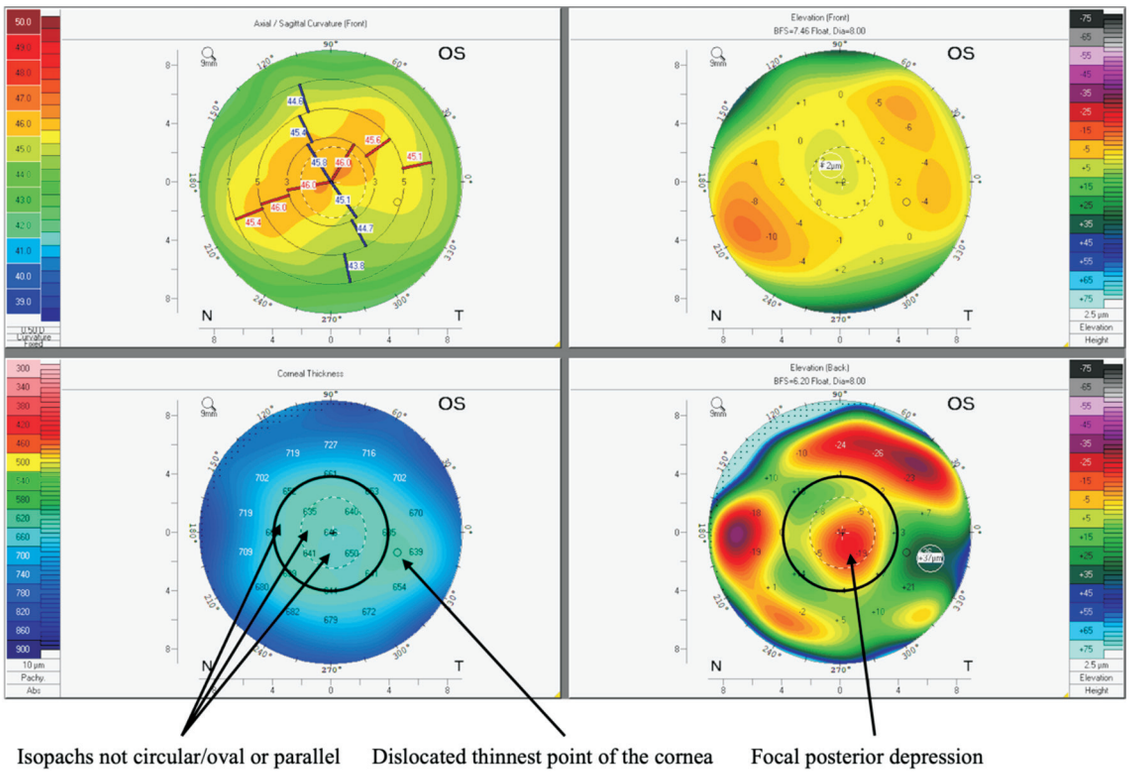

Figure 1 Mayo Clinic classification-tomographic features of corneal edema in Fuchs' endothelial corneal dystrophy The tomography maps of a left cornea affected by Fuchs' endothelial corneal dystrophy, utilizing Pentacam's "4 Maps Refractive" output. Key observations include 1) the loss of parallel and circular/oval isopachs and 2) the displacement of the cornea's thinnest point (indicated by a small black circle), both visible in the pachymetry map (lower left). Additionally, 3) a focal posterior depression of the posterior corneal surface (down to -19 relative to the best fit sphere) is evident in the posterior elevation map (lower right). The axial power (upper left) and anterior elevation (upper right) maps predominantly show oblique astigmatism. A large central black circle, with a diameter of 4 mm, is superimposed on the center of the lower maps for reference. The pupil center is denoted by a plus sign.

the tenets of the Declaration of Helsinki. Informed consent was waived due to the retrospective nature of the study and the absence of reported data that could identify individual patients. All cases have been anonymized in this manuscript.

A retrospective study was conducted on 30 phakic eyes diagnosed with FECD through slit-lamp biomicroscopy in conjunction with CSM. FECD severity was clinically classified based on the area and confluence of guttae. All patients included in the study did not exhibit clinically significant corneal edema, aligning with grades 0–4 in Krachmer's grading system[5]. However, it is important to acknowledge that interobserver agreement was demonstrated to be only fair when grading FECD using slit-lamp, especially when determining the presence of stromal edema[6]. Patients with microcystic or bullous epithelial edema were excluded. All patients underwent a complete ophthalmologic examination, which included CSM and Scheimpflug imaging.

A control group of 59 phakic eyes, undergoing routine ocular examination without corneal alterations, was also included. Specifically, 30 eyes from 15 patients underwent Scheimpflug tomography, and 29 eyes from 29 patients underwent CSM.

CSM was performed using the Tomey-EM 3000 (Tomey, Nagoya, Japan), and Scheimpflug tomography was carried out with the Pentacam (Oculus Optikgeräte GmbH, Wetzlar, Germany).

Scheimpflug imaging was conducted under the same controlled scotopic conditions. The tomographic images were analyzed for several parameters, specifically looking for three distinct features previously described by the Mayo Clinic classification, derived from the Pentacam's "4 Maps Refractive" output display: 1) loss of parallel isopachs on the pachymetry map; 2) displacement of the cornea's thinnest point; and 3) presence of a central focal posterior depression in the posterior elevation map (Figure 1)[15-16].

Isopachs are lines joining points of equal thickness, displayed in 10-mm steps, and tend to be almost circular/oval in normal corneas. The first feature was defined as any single isopach not being almost circular/oval or parallel to adjacent isopachs within the central 4 mm of the cornea relative to the pupil center. The typical location of the thinnest point of the cornea is inferotemporal to the visual axis. The second feature was defined as the thinnest point deviating from the inferotemporal quadrant (centered at the pupil center) or extended more than 1 mm from the pupil center in any quadrant. A focal posterior

depression involves a localized protrusion of the posterior corneal surface toward the anterior chamber. The third feature was identified using the posterior corneal elevation map, displayed in 5 mm steps. It was defined as any isolated area of depression (negative elevation relative to a sphere with the best-fit zone of 8 mm with a float function) within the central 4 mm of the cornea relative to the pupil center.

"Relative Pachymetry Map" display provides corneal thickness at a specific point as a percentage relative to the expected "normal" thickness, indicating the relative increase in CCT. The highest value within the central 3 mm was recorded. Additionally, corneal thickness at the apex (apical CT), at the center of the pupil (pupillary CT), and at the thinnest point (thinnest CT) were obtained from the default display, along with anterior chamber depth (ACD) from the corneal endothelium.

Moreover, the mean posterior corneal power and the posterior steep meridian (vertical, horizontal, oblique) were documented. Astigmatism was classified as horizontal if the steep corneal meridian was at 0º to 29º or 150º to 180º, vertical if the steep corneal meridian was at 60º to 119º, and oblique for the remaining meridians[27].

Nonstandardized corneal light backscatter measurements were evaluated using the densitometry display. Data is presented for four annular zones centered on the apex (0–2, 2–6, 6–10, and 10–12 mm in diameter). We focused on the first central annular zone, which has been demonstrated to be the most relevant in FECD[28]. Measurements are expressed in grayscale units (GSU) ranging from 0 (100% transparent) to 100 (completely opaque). The mean backscatter of a 2-mm diameter circle, centered on the apex, was measured for the anterior 120 μm of the cornea (A-backscatter), central cornea from 120 μm to 60 μm above the posterior surface (C-backscatter), the posterior 60 μm of the cornea (P-backscatter), and the total cornea (T-backscatter).

The data are presented as means±standard deviations or medians with interquartile range for the continuous variables, and as absolute and relative frequencies for categorical variables. Statistical analyses were conducted using IBM® SPSS® Statistics software (version 28.0 for MacOS; SPSS Inc., Chicago, IL, USA). The distribution normality of the variables was evaluated through skewness, kurtosis, and the Kolmogorov-Smirnov test. Depending on the distribution of the data, parametric or non-parametric tests were utilized for variable comparisons. The level of significance was defined at a P value <0.05.

RESULTS

Thirty phakic eyes from 18 patients with FECD (mean age 59.8±13.1y, 15 females) and 59 eyes from 44 patients (mean age 61.3±7.7y, 36 females) with healthy corneas were included (Table 1). In the control group, CSM was obtained for 29 eyes, while Scheimpflug tomography was performed for the remaining 30 eyes.

The best-corrected visual acuity (BCVA) was 0.05 (0, 0.15) logMAR and 0 (0, 0.08) logMAR (P=0.042) in FECD patients and the control group, respectively.

CSM revealed significant differences between the FECD and control groups in terms of the number of analyzed cells (26±13 *vs* 135±42, P<0.001), cell density (2049±376 *vs* 2479±225 cells/mm^2, P<0.001), mean cell area [463 (434, 544) *vs* 397 (383, 431) μm^2; P<0.001], coefficient of variation (54.8%±18.7% *vs* 41.0%±7.2%, P<0.001), and hexagonal cells [0 (0, 47)% *vs* 47 (40, 53)%, P<0.001]. Notably, CCT measured by CSM did not differ between the FECD and control groups (530±57 *vs* 546±30 μm, P=0.179).

Scheimpflug tomography measurements, including pupillary, apical, and thinnest point pachymetry, and relative increase in CCT, were as follows: 577±72 *vs* 541±27 μm (P=0.008), 577±70 *vs* 542±27 μm (P=0.008), 563±57 μm *vs* 537±28 μm (P=0.014), and 1.7 (-0.5, 4.3) μm *vs* 0.1 (-1.9, 0.9) μm (P=0.007), in the FECD *vs* control groups, respectively. A correlation was observed between CCT measured by CSM and apical pachymetry obtained by Pentacam (r=0.721; P<0.001). ACD differed significantly between both groups (2.42±0.32 *vs* 2.74±0.33 μm; P<0.001).

Patients with FECD, in comparison to the control group, exhibited significant differences in tomographic features: loss of parallel isopachs was observed in 13 eyes (43.3%) versus none in the control group (P<0.001), displacement of the thinnest point occurred in 11 eyes (36.7%) versus none (P<0.001), and posterior focal depression of the corneal surface was noted in 25 eyes (83.3%) compared to 7 eyes (23.3%) in the control group (P<0.001). Within the FECD group, 5 eyes (16.7%) did not display any of the specified features, 10 eyes (33.3%) exhibited one feature, 6 eyes (20.0%) had two features, and 9 eyes (30.0%) presented all three features. Conversely, in the control group, 23 eyes (76.7%) showed none of the tomographic features, while the remaining 7 eyes (23.3%) manifested only one feature.

Although no significant differences were observed in the mean posterior corneal power [-6.3 (-6.4, -6.0) *vs* -6.3 (-6.5, -6.2) D; P=0.137], the orientation of the posterior steepest meridian in dystrophic corneas varied significantly from the control group. Specifically, it was vertical in 22 eyes (73.3%) compared to 29 eyes (49.2%), horizontal in 2 eyes (6.7%) versus none in the control group, and oblique in 6 eyes (20%) versus 1 eye (1.7%) in the control group (P<0.001).

Light corneal backscatter values were significantly different between the FECD and control groups across several measurements: anterior [24.9 (23.4, 30.4) GSU *vs* 23.4 (22.5,

Table 1 Characteristics of eyes with Fuchs' endothelial corneal dystrophy compared to eyes with normal corneas

Characteristics	FECD (*n*=30)	Control (*n*=59)	*P*
Age, y	59.8±13.1	61.3±7.7	0.668
Female, *n* (%)	15 (83.3)	36 (81.8)	0.527
Right eye, *n* (%)	13 (43.3)	29 (49.2)	0.603
BCVA, logMAR	0.05 (0, 0.15)	0 (0, 0.08)	0.042
Corneal specular microscopy	FECD (*n*=30)	Control (*n*=29)	
Analyzed cells, *n*	26±13	135±42	<0.001
Cell density, cells/mm^2	2049±376	2479±225	<0.001
Mean cell area, µm^2	463 (434, 544)	397 (383, 431)	<0.001
SD, µm^2	252 (177, 306)	160 (145, 179)	<0.001
Maximum cell area, µm^2	1158 (862, 1424)	1026 (915, 1197)	0.188
Minimum cell area, µm^2	157 (136, 188)	118 (106, 139)	0.002
Coefficient of variation, %	54.8±18.7	41.0±7.2	<0.001
Hexagonal shape, %	0 (0, 47)	47 (40, 53)	<0.001
CCT, µm	530±57	546±30	0.179
Scheimpflug tomography			
Loss of parallel isopachs, %	13 (43.3)	0	<0.001
Displacement of the thinnest point, %	11 (36.7)	0	<0.001
Posterior surface depression, %	25 (83.3)	7 (23.3)	<0.001
No. of tomographic features, %			
0	5 (16.7)	23 (76.7)	
1	10 (33.3)	7 (23.3)	
2	6 (20.0)	0	
3	9 (30.0)	0	
Mean posterior corneal power, D	-6.3 (-6.4, -6.0)	-6.3 (-6.5, -6.2)	0.137
Posterior steep meridian, *n* (%)			<0.001
Vertical	22 (73.3)	29 (49.2)	
Horizontal	2 (6.7)	0	
Oblique	6 (20)	1 (1.7)	
ACD, µm	2.42±0.32	2.74±0.33	<0.001
Pupillary pachymetry, µm	577±72	541±27	0.008
Apical pachymetry, µm	577±70	542±27	0.008
Thinnest point pachymetry, µm	563±57	537±28	0.014
Relative increase in CCT	1.7 (-0.5, 4.3)	0.1 (-1.9, 0.9)	0.007
A-backscatter, GSU	24.9 (23.4, 30.4)	23.4 (22.5, 24.0)	<0.001
C-backscatter, GSU	15.1 (14.7, 16.5)	14.4 (13.8, 14.8)	<0.001
P-backscatter, GSU	12.8 (11.6, 15.9)	10.6 (10.0, 11.3)	<0.001
T-backscatter, GSU	21.4 (17.6, 23.9)	18.0 (16.8, 21.8)	0.010

ACD: Anterior chamber depth; A: Anterior 120 µm of the cornea; BCVA: Best-corrected visual acuity; C: Central from 120 to 60 µm above the posterior corneal surface; CCT: Central corneal thickness; D: Diopters; FECD: Fuchs' endothelial corneal dystrophy; GSU: Grayscale units; P: Posterior 60 µm of the cornea; SD: Standard deviation; T: Total corneal thickness.

24.0) GSU; *P*<0.001], central [15.1 (14.7, 16.5) GSU *vs* 14.4 (13.8, 14.8) GSU; *P*<0.001], posterior [12.8 (11.6, 15.9) GSU *vs* 10.6 (10.0, 11.3) GSU; *P*<0.001], and total corneal thickness [21.4 (17.6, 23.9) GSU *vs* 18.0 (16.8, 21.8) GSU; *P*=0.01].

DISCUSSION

This study exclusively enrolled phakic patients with FECD. Compared to the control group, individuals with FECD exhibited worse BCVA. This difference can be attributed to the presence of a cataract and/or subclinical corneal edema, as subclinical edema may contribute to visual symptoms such as glare and reduced visual acuity[10]. In fact, the primary objective of this study was to assess tomographic changes indicative of subclinical corneal edema, providing valuable insights for advising patients, especially before undergoing cataract surgery. This evaluation may help differentiate whether patients can expect improved vision after cataract

surgery alone, potentially guiding the decision for combined phacoemulsification with EK. Moreover, there is evidence suggesting that certain evaluated tomographic parameters may serve as predictors of the risk of corneal decompensation following phacoemulsification[15-16,18].

Despite the challenges in disease stratification, the diagnosis of FECD is typically straightforward through biomicroscopy alone, assisted by CSM. CSM parameters showed considerable variation between FECD patients and the control group, revealing the endothelial morphology differences that characterize this pathology[6,11]. Statistically significant differences were observed in the number of analyzed cells, cell density, mean cell area, coefficient of variation, and hexagonal cells. Interestingly, CCT measured by CSM did not differ between the FECD and control groups. This observation can be attributed to the absence of clinical corneal edema in FECD patients, as well as the inherent inaccuracy of the CSM method in measuring CCT, which is affected by both intra- and interpatient variability in corneal thickness.

Corneal thickness, as measured by Scheimpflug tomography, exhibited statistical differences between groups, particularly in pupillary, apical, and thinnest point pachymetry, and relative increase in CCT. The lack of difference in CCT when measured by CSM may be attributed to the use of a distinct subset of patients as the control group. This notion is further supported by the observed correlation between CCT measured by CSM and apical pachymetry obtained by Pentacam.

Statistical differences in ACD between both groups may be attributed to the bulging of the posterior corneal surface into the anterior chamber due to central edema in FECD patients. However, it remains uncertain whether this data holds clinical relevance, despite some residual literature suggesting shallower ACD in FECD patients[29-30].

Normal corneas exhibit greater thickness vertically than horizontally, leading to against-the-rule astigmatism induced by the posterior corneal surface[31]. Research indicates that central corneal edema in FECD can modify the normal ellipsoid posterior surface, primarily due to relatively greater horizontal than vertical corneal thickening. This transformation results in a more spherical shape, leading to reduced negative power and the loss of normal posterior surface toricity[27]. Consequently, the typically vertical orientation of the anterior and posterior surface meridians in normal corneas may become more oblique or horizontal in FECD[27]. These changes could, in part, account for the hyperopic shift following EK and may contribute to imprecise refractive outcomes after cataract surgery[27]. In our sample, despite no differences in the mean posterior corneal power, we observed a statistically significant difference in the posterior steep meridian, with a higher prevalence of horizontal and oblique astigmatism in individuals with FECD.

The Mayo Clinic classification has shown that subclinical corneal edema can be detected in eyes with FECD by using Scheimpflug imaging[15-16]. The subtle corneal thickening, which represents subclinical edema, can manifest as loss of parallel isopachs, displacement of the thinnest point of the cornea, and posterior corneal surface depression. Edema may emerge early in the course of the disease, indicating a decline in endothelial function and the potential for visual impairment[6]. Consequently, the onset of edema is a gradual phenomenon, emphasizing the need for a classification system that reflects this subtlety[16]. It is recommended that individuals with guttae but without clinically definite edema undergo tomography. Typically, if at least two features of the three previously described are present, subclinical edema may be diagnosed. In this study, of the 30 eyes diagnosed with FECD, 15 (50%) presented none or just one of the features described, while the other 15 (50%) showed two or three of the features. This observation may indicate the presence of subclinical edema in the latter individuals and greater severity of the disease, which could influence the decision to perform cataract surgery combined with EK. At least 1 of the tomographic features of interest was identified in 7 (23.3%) control eyes, suggesting potential variability in this method of analysis in the absence of clinical correlation.

In this study, we employed Pentacam densitogram to evaluate the corneal backscattering effects. In qualitative analysis, we identified the hanging-hammock pattern or camel's second hump sign in FECD patients, which exhibited a morphological difference from the high-back chair pattern observed in the control group (Figure 2). The second hump was found to correspond to corneal guttae at the Descemet membrane level, indicating that the diseased membrane significantly contributes to an increase in light backscattering of the cornea[32]. In quantitative analysis, we observed a statistically significant increase in corneal backscattering values in FECD compared to the control group in all layers of the cornea. This increase in corneal backscatter may be associated with disease severity, possibly attributed to the growing area and confluence of guttae[25].

One limitation of the study is the use of two distinct control groups–one for Scheimpflug imaging and another for CSM. This decision stemmed from logistical constraints encountered in a real-world scenario. Additionally, the FECD group was not substratified by disease severity, and Krachmer's grades 0–4 were not registered to avoid inconsistencies from fair interobserver agreement and to preserve statistical power.

There are concerns about extrapolating densitometry data due to the lack of homogeneous standardization of devices. Oculus has not developed a universal GSU standardization to account for variability in light source brightness and detection system

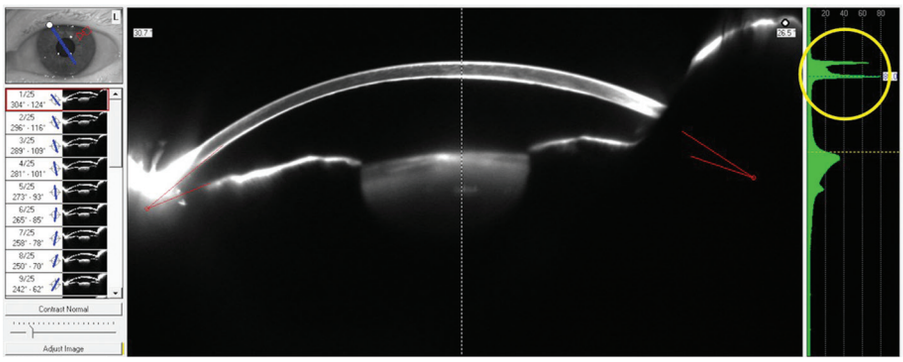

Figure 2 Densitometry analysis of Pentacam Scheimpflug images–general overview display This image depicts the left eye of a patient with Fuchs' endothelial corneal dystrophy, featuring a characteristic pattern resembling two spiking humps similar to a hanging hammock (yellow circle).

sensitivity. Despite attempts to find normative values, most densitometry studies do not adjust for these factors[26,33].

In summary, tomographic imaging serves as an objective and quantitative tool that can enhance clinical decision-making in FECD. The inclusion of corneal densitometry, pachymetry maps, and posterior corneal curvature patterns in clinical practice, especially for corneas lacking clinically evident edema, can aid in assessing the potential presence of subclinical edema. Despite being primarily inspired by and focused on validating the Mayo Clinic group's findings in a real-world scenario and European population, this study also contributes to the ongoing validation of the new classification method for FECD. The results highlight its clinical utility, offering valuable insights for clinicians who frequently evaluate patients with concomitant cataract and FECD. Further studies are needed to fully elucidate the role of tomographic parameters in gauging FECD severity and progression, determining the optimal timing for cataract surgery, selecting the most suitable procedure, and correlating these findings with visual function.

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