·Clinical Research·

# Ultrasound biomicroscopy in patients with unilateral pseudoexfoliation

*Erkan Ünsal, Kadir Eltutar, Ilkay Muftuoglu, Tulay Alpar Akcetin, Yildiz Acar*

Department of Ophthalmology, Istanbul Education and Research Hospital, Kasap Ilyas Mah, Org Abdurrahman Nafiz, Gurman Cd, Fatih, Istanbul 34098, Turkey

**Correspondence to:** Erkan Ünsal. Istanbul Education and Research Hospital, Kasap Ilyas Mah, Org Abdurrahman Nafiz, Gurman Cd, Fatih, Istanbul 34098, Turkey. erkanunsal@gmail.com

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## Abstract

**• AIM: To compare the anterior segment morphology evaluated using ultrasound biomicroscopy (UBM) in patients with clinical pseudoexfoliation syndrome (XFS) in one eye and no clinical XFS in the fellow eye.**

**• METHODS: Thirty patients with unilateral XFS were included in the study. All patients underwent evaluation of their anterior segment using UBM with and without dilatation with 1% cyclopentolate. The anterior chamber depth (ACD), lens thickness (LT), anterior chamber angle (ACA), ciliary body thickness (CBT), scleral thickness (ST), trabeculae –ciliary processes distance (T–CPD), and iris–ciliary processes distance (I–CPD) were measured using UBM scans. All results between the eyes with clinical XFS and their fellow eyes without clinical XFS were then compared.**

**• RESULTS: Before dilatation the eyes with XFS (4.350± 0.531 mm) were found to have a significantly thicker lens ($P$=0.002) than the eyes without XFS (4.238±0.540 mm). In addition after dilatation, the eyes with XFS (4.310 ± 0.500 mm) were found to have a significantly thicker lens than the eyes without XFS (4.160±0.480 mm) ($P$=0.019). The average ACD, for the group with XFS, comparing pre –dilatation (2.616 ±0.349 mm) and post –dilatation measurements (2.714±0.413) was found to be statistically increased ($P$=0.014). The average ACD, comparing pre–dilatation to post –dilatation measurements in patients without XFS (2.680±0.360), (2.720±0.500) was found to be statistically unchanged ($P$=0.450).**

**• CONCLUSION: Crystalline lenses tended to be thicker in the eyes with clinical pseudoexfoliation than their fellow eyes without pseudoexfoliation.**

**• KEYWORDS:** pseudoexfoliation syndrome; ultrasonic biomicroscopy; anterior segment morphology

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## INTRODUCTION

Pseudoexfoliation syndrome (XFS) is an age-related, generalized disorder of the extracellular matrix that is characterized by the production and progressive accumulation of an abnormal extracellular pseudoexfoliative material (PXM) in many intraocular and extraocular tissues. The presence of this material may contribute to important alterations in the anterior segment of the eye, particularly in the iridocorneal angle, iris and ciliary body, and crystalline lens and zonules [1]. Pseudoexfoliative material may also change the biomechanical structure of the tissue in which it is stored. The tensile strength of the zonular fibers is reduced because of the accumulation of PXM[2-4]. Clinically, eyes with XFS tend to have more-frequent complications during cataract surgery, related mostly to poor pupil dilation, subluxation, and vitreous loss. In addition, eyes with XFS have a higher risk of glaucoma, with a significant rise in IOP. Although histopathological studies have shown that PXM is usually accumulated in both eyes, the presence of PXM is frequently encountered as asymmetric, and clinically, XFS can be seen in only one eye of a patient. Differences in the severity of XFS may result in different morphology and biomechanical responses in both eyes of the same patient.

Ultrasound biomicroscopy (UBM) technology uses high-frequency ultrasound to produce images of the anterior segment in high resolution. Tissue penetration is approximately 5 mm in a lateral and an axial resolution approaching 50 μm and 25 μm respectively. Therefore anterior segment structures, including the crystalline lens, ciliary body, and lens zonules, can be morphologically assessed and quantitatively measured using this in vivo noninvasive imaging technique. The reported repeatability of UBM measurements is good if the measurements are performed by the same experienced observer[5-8].

The purpose of this study was to evalutate the anterior segment morphology of the eyes with clinical XFS and compare it to the same patients' fellow eyes, with no clinical XFS, which share the same genetic background and are exposed to the same environmental factors, using UBM.

## SUBJECTS AND METHODS

Between November 1, 2012 and April 30, 2013, patients with unilateral XFS and phakic eyes who were examined at the Istanbul Education and Research Hospital ophthalmology outpatient clinic were enrolled in this prospective study. The study was conducted in accordance with the tenets of the World Medical Association's Declaration of Helsinki. Approval of the ethics of the study protocol was obtained from the Ethics Committee of the Istanbul Education and Research Hospital. All the patients included in the study were informed about the details of the procedure and all signed the informed consent form.

Before UBM measurement, all patients were subjected to a complete ophthalmologic examination. Patients' detailed histories including age, gender, systemic disease, and drug use were recorded. Refractions were performed on the patients and according to the Snellen chart their best corrected visual acuities were determined. IOPs were measured using Goldmann tonometry. Anterior chamber angles were evaluated using the Goldmann three mirror lens.

The presence of clinical XFS was determined by slit-lamp examination, with the presence of fibrillin deposits on the anterior lens capsule and the pupillary margin.

No corneal pathology was noted in any of the patients included in the study according to their medical history and physical examination. Spherical refraction defect was less than 5 D, astigmatism was less than 3 D, and the best corrected visual acuity was 0.5 and above.

Subjects with cataracts that preventing fundus examination, and uveitis with evidence, systemic or topical steroid users, users of topical or systemic drugs that can potentially affect pupils or accommodation, previous ocular surgery, laser interference; and trauma with a history and general health status corrupt cases were excluded from the study.

To account for variable reproducibility by different observers, UBM examination was performed using the same device (SONOMED vumax II®) and the 35 MHz probe by one observer. All UBM examinations were made under environmental standards and conditions according to protocol. Subjects were placed in the supine position to prevent accommodative efforts and were asked to look at a red target hanging from the ceiling in a dim room, and the images were taken. After instillation of topical 0.5% proparacaine HCL (Alcaine®, Alcon), a soft silicone eye cup with the appropiate diameter (18, 20 or 22 mm) was inserted between the upper lid and the fornix conjoctiva of the lower lid. Using the same eye cup, scanning of every patient was performed before and after the dilatation. In order to prevent corneal contact the focus distance of the transducer was set at 12 mm. For the purpose of immersion, the eye cup was filled with an adequate amount of sterile physiological saline solution. Axial images of the anterior chamber and radial section of the angle images from the temporal quadrant were scanned. In order to obtain an ideal image and to have consistent pre- and post-dilatation measurements, we took care to have stable scanned axial images of the anterior segment (theoretically aligned with the central horizontal line and symmetrical to it) as well as stable images in the vertical alignment (cornea, lens, anterior and posterior capsule should be balanced with the referenced vertical central line). When taking radial cross-sectional images of the angle, we made sure that the probe was perpendicular to the limbus of the scanned quadrant, and we chose the images with the best reflectivity of the iris[9]. In regard to localization accuracy and ease of scleral spur, the interface between the sclera and ciliary body reflected markedly, and attention was paid to sufficient quality images in both the ciliary body and iris.

The anterior chamber depth and lens thickness were measured from the axial images of the anterior segment using the methods previously recommended by Pavlin *et al*[10,11] and the scales of the user guide for the device.

1) Axial ACD measurement: this was detected by measuring the distance between the posterior surface of the central cornea and the anterior surface of the lens in the midline of the pupil (Figure 1A).

2) Lens thickness (LT): the distance between the anterior and the posterior capsule of the lens (Figure 1A).Then from the radial cross-section images of the temporal quadrant.

3) Trabecular meshwork-iris angle (TIA): measured with the apex in the iris recess and the arms of the angle passing through a point on the trabecular meshwork 500 μm from the scleral spur and a point on the iris perpendicularly opposite (Figure 1B).

4) Ciliary body thickness (CBT), was measured in four regions: a) the distance 1 mm away from the scleral spure (CBT 1; Figure 1C); b) the distance 2 mm away from the scleral spure (CBT 2; Figure 1D); c) the distance 3 mm away from the scleral spure (CBT 3; Figure 1C); and d) the thickest location of the ciliary body (CBT max; Figure 1D).

5) Scleral thickness (ST): the distance of the episcleral surface measured perpendicularly to the scleral spure (Figure 1E).

6) Trabecular meshwork-ciliary process distance (T-CPD): measured as a line extending from a point 500 μm anterior to the scleral spur along the corneal endothelium and dropped perpendicularly through the iris to the most anterior ciliary process seen during scanning in that meridian (Figure 1E).

7) Iris-ciliary process distance (I-CPD): the distance measured between the iris pigment epithelium and ciliary processes (Figure 1F) .

The anterior segment examination was performed with UBM after the mydriatics were instilled [cyclopentolate hydrochloride (1%)], and UBM was performed again after 30min. The freeze images were saved on the computer's hard

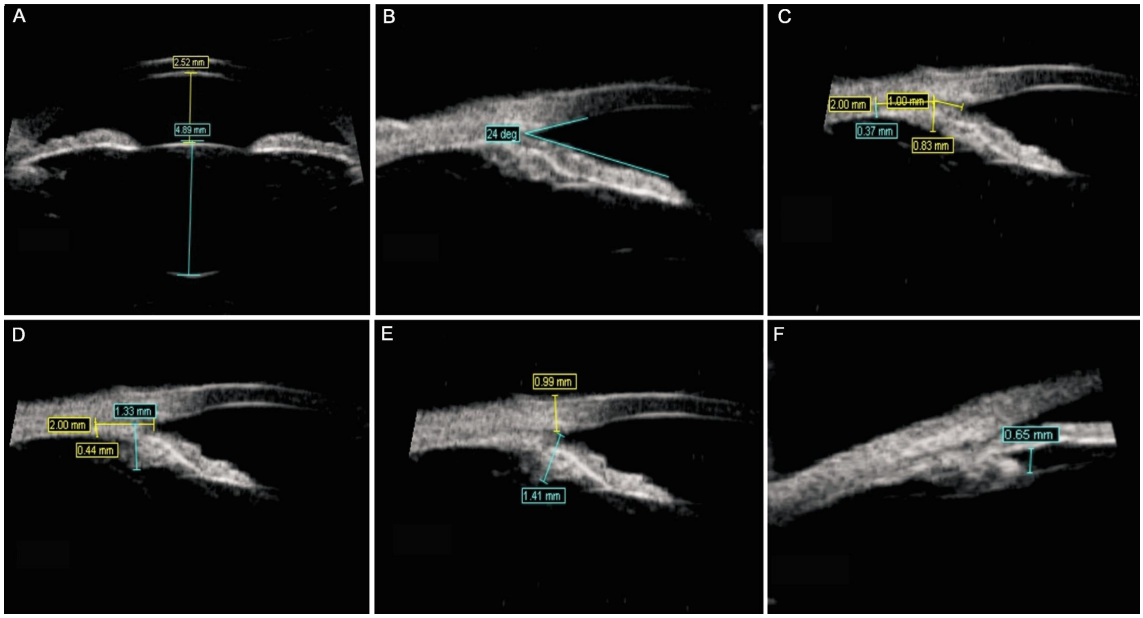


**Figure 1 Views of axial images of the anterior chamber and radial section of the angle images from the temporal quadrant** A: A UBM image of ACD and LT; B: A UBM image of the trabecular meshwork-iris angle (TIA); C: A UBM image of ciliary body thickness 1-3 (CBT 1-3); D: A UBM image of ciliary body thickness 2-Max (CBT 2-Max); E: A UBM image of scleral thickness (ST), trabecular meshwork-ciliary process distance (T-CPD); F: A UBM image of iris-ciliary process distance (I-CPD).

drive and used for the calculations. The values determined with dilatation and without dilatation were compared.

The normality of the distribution of each of the parameters was checked using the Kolmogorov-Smirnov test. Appropriate non-parametric tests were used to compare the values of both groups. *P* values of <0.05 were accepted as being statistically significant.

## RESULTS

Thirty patients with unilateral clinical XFS were included in the study; 14 were male (46.6%), 16 were female (53.3%) and the mean age was 66.6±7.46y (53-80). In terms of the eyes with XFS, 14 were right eyes (46.7%), and 16 (53.3%) were left eyes. The mean UBM measurement and statistical test results in eyes with unilateral clinical XFS without cyclopentolate and after cyclopentolate are given in Table 1. Without cyclopentolate and after cyclopentolate the mean LT in eyes with clinical XFS was found to be significantly thicker than in the eyes without clinical XFS (Table 1; Figure 2).

In the group with XFS, the average LT, before dilatation and after dilatation was found to be statistically unchanged (*P*= 0.062). In patients without XFS, the avarage LT before and after dilatation was found to be significantly lower (*P*= 0.001). The average ACD, in the group with clinical XFS, compared pre-dilatation to post dilatation was found to be statistically increased (*P*=0.014; Table 2). The average ACD of patients without XFS, comparing pre-dilatation to post dilatation was found to be statistically unchanged (*P*=0.450; Table 2).

## DISCUSSION

This study demonstrated that eyes with clinical XFS have

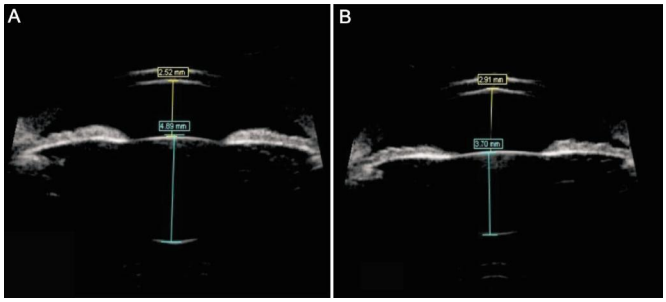


**Figure 2 AUBM image of anterior chamber depth (ACD) and lens thickness (LT) in an eye with (A) clinical pseudoexfoliation and (B) the fellow eye of the same subject without clinical pseudoexfoliation** Note that the crystalline lens is thicker in the eye with clinical pseudoexfoliation.

significantly thicker crystalline lenses compared to their fellow eyes without clinical XFS. Moreover, we were not able to find a significant difference in TIA and CBT between the eyes with clinical XFS and their fellow eyes without clinical XFS.

These results may indicate that eyes with clinical XFS might have thicker crystalline lenses and therefore be less responsive to cyclopentolate. According to the widely accepted Helmholtz Accommodation Theory, the zonules are relaxed during accommodation, which results in a thicker crystalline lens, and the opposite is true during disaccommodation [12]. Our results showed that iris, ciliary body, and angle configuration are not significantly different in eyes with clinical XFS and their fellow eye without clinical XFS. Therefore, the difference in lens thickness in eyes with and without clinical XFS cannot be explained by

**Table 1 The parameters of the anterior segment and the angle of the temporal quadrant of the eyes with XFS and no-XFS** $\bar{x} \pm s$ (range)

| Parameters | Without cyclopentolate distant fixation | | | | | After cyclopentolate | | | | |
|---|---|---|---|---|---|---|---|---|---|---|
| | XFS | Non-XFS | Mean difference | $P^1$ | $P^2$ | XFS | Non-XFS | Mean difference | $P^1$ | $P^2$ |
| ACD (mm) | 2.616±0.349 (2.18-3.27) | 2.680±0.360 (1.88-3.21) | 0.065±0.252 | 0.169 | 0.279 | 2.714±0.413 (1.9-3.46) | 2.720±0.500 (2.22-3.97) | 0.014±0.240 | 0.752 | 0.942 |
| LT (mm) | 4.350±0.531 (3.2-5.0) | 4.238±0.540 (3.27-4.96) | 0.112±0.182 | 0.002 | 0.001 | 4.310±0.500 (3.33-4.99) | 4.160±0.480 (3.42-4.74) | 0.147±0.177 | 0.000 | 0.001 |
| TIA (°) | 27.500±6.270 (20-41) | 27.400±5.360 (22-41) | 0.100±5.371 | 0.919 | 0.763 | 27.200±7.300 (19-41) | 27.700±6.120 (19-36) | 0.500±6.055 | 0.654 | 0.772 |
| CBT 1 (mm) | 1.354±0.100 (1.23-1.52) | 1.338±0.080 (1.22-1.48) | 0.016±0.079 | 0.267 | 0.190 | 1.327±0.130 (1.06-1.51) | 1.319±0.100 (1.07-1.42) | 0.008±0.078 | 0.579 | 0.861 |
| CBT 2 (mm) | 0.876±0.140 (0.81-1.09) | 0.882±0.120 (0.83-1.03) | 0.006±0.067 | 0.612 | 0.703 | 0.832±0.15 (0.64-1.13) | 0.872±0.120 (0.67-1.21) | 0.040±0.094 | 0.282 | 0.097 |
| CBT 3 (mm) | 0.477±0.110 (0.3-0.78) | 0.478±0.090 (0.34-0.75) | 0.001±0.077 | 0.944 | 0.845 | 0.468±0.110 (0.33-0.81) | 0.477±0.080 (0.39-0.79) | 0.009±0.064 | 0.434 | 0.471 |
| CBT Max (mm) | 1.448±0.150 (1.33-1.79) | 1.425±0.120 (1.29-1.67) | 0.023±0.086 | 0.157 | 0.091 | 1.428±0.090 (1.23-1.55) | 1.409±0.090 (1.21-1.58) | 0.019±0.108 | 0.345 | 0.665 |
| ST (mm) | 0.893±0.0700 (0.81-1.03) | 0.896±0.060 (0.74-1.01) | 0.003±0.064 | 0.779 | 0.765 | 0.912±0.070 (0.71-1.00) | 0.915±0.060 (0.79-1.03) | 0.003±0.057 | 0.778 | 0.673 |
| T-CPD (mm) | 1.415±0.120 (1.29-1.67) | 1.396±0.110 (1.24-1.59) | 0.018±0.101 | 0.331 | 0.318 | 1.379±0.250 (1.12-1.8) | 1.391±0.140 (1.14-1.75) | 0.012±0.207 | 0.175 | 0.174 |
| I-CPD (mm) | 1.129±0.110 (0.97-1.29) | 1.102±0.100 (0.91-1.21) | 0.027±0.101 | 0.152 | 0.132 | 1.115±0.140 (0.82-1.32) | 1.131±0.110 (0.93-1.32) | 0.016±0.099 | 0.386 | 0.343 |

ACD: Anterior chamber depth; LT: Lens thickness; TIA: Trabeculer meshwork-iris angle; CBT 1, 2, 3: Ciliary body thickness of 1, 2 and 3 mm; CBT Max: Maximum ciliary body thickness; ST: Scleral thickness; T-CPD: Trabecular meshwork-ciliary process distance; I-CPD: Iris-ciliary process distance. [1]Student's *t*-test. [2]Wilcoxon signed rank test. $P<0.05$ indicates statistical significance.

**Table 2 The comparison of anterior segment and temporal quadrant angles parameters before and after dilatation in eyes with XFS and no XFS** $\bar{x} \pm s$ (range)

| Parameters | XFS | | | | | Non-XFS | | | | |
|---|---|---|---|---|---|---|---|---|---|---|
| | Before dilatation | After dilatation | Mean difference | $P^1$ | $P^2$ | Before dilatation | After dilatation | Mean difference | $P^1$ | $P^2$ |
| ACD (mm) | 2.616±0.349 (2.18-3.27) | 2.714±0.413 (1.9-3.46) | 0.098±0.205 | 0.014 | 0.017 | 2.680±0.360 (1.88-3.21) | 2.72±0.500 (2.22-3.97) | 0.047±0.335 | 0.450 | 0.829 |
| LT (mm) | 4.350±0.531 (3.2-5.0) | 4.310±0.500 (3.33-4.99) | 0.037±0.104 | 0.062 | 0.086 | 4.238±0.540 (3.27-4.96) | 4.160±0.480 (3.42-4.74) | 0.072±0.106 | 0.001 | 0.002 |

ACD:Anterior chamber depth; LT: Lens thickness. [1]Student's *t*-test. [2]Wilcoxon signed rank test. $P<0.05$ indicates statistical significance.

the difference in the configuration of the angle, iris, and ciliary body. Previous studies clearly showed that zonules are weakened in eyes with XFS. The thicker crystalline lenses in eyes with clinical XFS in our study may be explained by weaker zonules that exert less tension on the crystalline lens and capsule compared to zonules in their fellow eyes without clinical XFS. In this study, we also found that the crystalline lens thickness was decreased in all eyes after dilatation with cyclopentolate. However, the magnitude of decrease in crystalline lens thickness was less in eyes with clinical XFS than in their fellow eyes with no clinical XFS. This may indicate that the response of zonules to increased tension during ciliary muscle relaxation after cylopentolate was less in eyes with clinical XFS.

Pavlin *et al*[13] also showed that lenticular sphericity increases at the site of zonular abnormalities in a study using UBM. In addition, several other studies showed that cataract formation and zonular weakness can be seen earlier in eyes with pseudoexfoliation [14]. There are studies indicating that UBM determines the involvement of zonules in patients with XFS before cataract operations [15,16]. Using UBM, Gohdo *et al*[17] showed that zonules coated with pseudoexfoliative materials are thicker and more well defined in patients with XFS and angle-closure glaucoma. It has been evaluated that there is an increase in the spherical shape and the axial thickness of the lens, probably due to the loss of zonular fibers. An increase in the IOP is described due to the forward movement of the anterior pole of the lens causing pupillary block. As a result, in this case, anterior camera shallowing or angle-closure glaucoma can be seen in patients with XFS. In these cases, laser iridotomy should be performed without the instillation of they drops because pilocarpine they may increase pupillary block.

Guo *et al* [18] evaluated the characteristics of eyes with XFS, the thickness of the anterior lens capsule, and zonules using UBM in their study. In eyes with XFS, anterior and peripheral lens capsules and zonular fibers were found to be thicker than in the control group. It was shown that there were deposits in the zonular fibers. Earlier, it was found that the risk of operative complications and XFS can be determined using UBM. Gohdo *et al* [17] evaluated ocular parameters in the eyes with XFS and those without XFS in patients with unilateral XFS. The lens thickness (4.8 mm) in the eyes with XFS is significantly thicker than in the eyes without XFS (4.7 mm). In our study, LT (4.35 mm) was found to be significantly thicker in the eyes with XFS than in

the eyes without XFS (4.23 mm). In addition, LT thickness is thinner than in the study by Omura *et al*[19] This is thought to be a result of the younger population of our study group (66.6y) compared to the age in the study by Omura *et al*[19] (75.1y).

The research by Esaki *et al*[20] in regard to patients with XFS was related to ACD and postural with UBM; ACD significantly decreased statistically from the supine to the prone position. To the best of our knowledge, we are not aware of any study of TIA, CBT, T-CPD, or I-CPD using UBM in eyes with XFS in the literature.

There are several limitations of our study. Besides the quality of the image acquisition and the analysis differences, UBM evaluation of the anterior chamber angle may also be affected by physiological variables. Room illumination, fixation and accommodative efforts are factors that affect the anterior segment anatomy. Therefore, especially when retrieving quantitative measurements, these factors should remain constant. We also provided measurements within the framework of a protocol using a standard environment and conditions. Previous studies clearly showed that individual variability and age may affect UBM measurements particularly lens thickness measurements. To overcome the possible influences of individual variability and age on the UBM measurements in our study, we compared the eyes with pseudoexfoliation with their fellow eyes of the same age and genetic background[5].

In conclusion, our study showed that eyes with clinical XFS may have thicker crystalline lenses and be less responsive to cyclopentolate than those of their fellow eyes without clinical XFS. On the other hand, we were not able to find a significant difference in TIA and CBT between the eyes with clinical pseudoexfoliaton and their fellow eyes without clinical pseudoexfoliation. Prospective studies are needed to determine what types of changes will occur in the anterior segment structures in the non XFS eyes of the patients with unilateral XFS. Longitudinal studies, possibly with the evaluation of the zonules and changes in refraction are needed to elucidate the changes in anterior segment and particularly the crystalline lens, zonules, and ciliary body in eyes with clinical XFS.

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