ORIGINAL ARTICLE

Measurements of central corneal thickness using two immersion ultrasound techniques and optical technique

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Abstract

Objective: To compare the accuracy of central corneal thickness measurements using ultrasound biomicroscopy, Orbscan II tomography and an Artemis-2 very high frequency ultrasound scanner.

Methods: The prospective study was conducted at Eye World Centre, Riyadh, Saudi Arabia, from September to November 2012. One eye from each of 60 normal subjects was analysed. The central corneal thickness was measured using ultrasound biomicroscopy, Orbscan II tomography and the Artemis-2 very high frequency ultrasound scanner. Results were compared using analysis of variance, repeated-measures analysis of variance and limits of agreement.

Results: The mean central corneal thickness was 530.30±30.75μm, 548.95±30.33μm and 554.73±31.97μm for biomicroscopy, tomography and the scanner respectively. The intraobserver repeatability analyses of variance were not significant for the three procedures (p=0.19, 0.23 and 0.41, respectively). A significant difference was noted among the three different methods (p=0.0001). However, comparison among instruments revealed no significant difference between tomography and the scanner (p>0.05), yet significant differences were noted in biomicroscopy vs. tomography, and biomicroscopy vs. the scanner (p<0.01 and P < 0.001, respectively). The mean differences (and upper/lower limits of agreement) for central corneal thickness measurements were 18.92±40.71 (60.90/-98.70); 24.7±13.13 (1.00/-50.40), and -5.80±38.61 (69.90/-81.40) for biomicroscopy vs. tomography, biomicroscopy vs. scanner, and tomography vs. scanner respectively.

Conclusions: The central corneal thickenss measurements obtained using Orbscan II tomography and the Artemis-2 very high frequency ultrasound scanner can be used interchangeably. However, Orbscan II tomography and the Artemis-2 scanner measurements cannot be used interchangeably with ultrasound biomicroscopy.

Keywords: Central corneal thickness, Ultrasound biomicroscopy, Orbscan II, Artemis-2 VHFUS, Normal eyes. (JPMA 64: 266; 2014)

Introduction

Precise quantitative measurement of the central corneal thickness (CCT) is clinically crucial. For instance, variation in CCT affects applanation tonometry accuracy, because a 10% change in CCT may result in an approximately 3.4 mmHg change in intraocular pressure (IOP).[1,2] The popularity of refractive surgery has increased, and consequently the precise preoperative assessment with CCT measurements is vital to determine eligibility for refractive surgery since underestimation can lead to patient exclusion. However, overestimation may cause over-ablation, which may increase the risk of iatrogenic keratectasia.[3] Therefore, studies evaluating CCT measurements using various instruments are essential and have significant clinical relevance.[4,5]

Currently, popular approaches to measure the CCT are either ultrasound or optical techniques. The ultrasound technique can be either contact ultrasound, such as ultrasound pachymetry (USP),[6] or immersion ultrasound, such as ultrasound biomicroscopy (UBM)[7,8] and Artemis-2 very high frequency ultrasound scanner (VHFUS) measurements.[9,10] Optical techniques include Orbscan II tomography,[6] confocal microscopy[11] and visante anterior segment optical coherence tomography.[6,10]

USP is the gold standard for CCT measurements. However, it has several disadvantages: physical contact with the cornea; use of topical anaesthesia is required; accuracy is dependent on the perpendicularity of the probe's application to the cornea; and reproducibility relies on precise probe placement on the corneal centre.[4,10] UBM involves immersion in high frequency ultrasound using broad-band 50 MHz. The precision of various measurements has been verified as high, especially for clearly-defined structures such as the cornea.[12] However, the disadvantages are: penetration of only 5-6 mm, the image is influenced by the plane of section, distance to the anterior chamber, orientation of the probe, room

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illumination, fixation, and accommodative effort.[8]

The Artemis-2 VHFUS is a very high frequency (VHF) digital ultrasound device. Its immersion technique uses a broad-band 50 MHz VHF ultrasound transducer (bandwidth approximately 10 to 60 MHz). The Artemis-2 VHFUS is an arc-scanner tool capable of imaging and measuring the whole anterior segment, or the whole cornea, in one scan sweep. The measurement zone for CCT is a 3-mm diameter of the cornea. The cornea is swept by a reverse arc high-precision mechanism to acquire B-scans as arcs that follow the surface contour of the anterior or posterior segment structures of interest. Ultrasound data is first digitised and then stored. Subsequently, the digitised ultrasound data is transformed using Cornell digital signal processing technology, which statistically significantly reduces noise and enhances the signal-to-noise ratio.[13]

Orbscan II tomography is an optical noninvasive technique used to determine the corneal thickness at the centre and periphery. However, several studies have reported that Orbscan II tomography yields overestimated measurements with a mean overestimation of 30µm. To compensate for this difference, the manufacturer suggests applying a correction (acoustic) factor of 0.92.[14,15] Earlier studies have reported agreements between CCT measurements obtained with UMB vs. Artemis-2 VHFUS,[16] and Orbsacn II vs. Artemis-2 VHFUS.[9] However, to the best of our knowledge, this is the first study to compare measurements obtained with Orbscan II tomography and UBM in normal eyes.

The aim of this study was to compare CCT using UBM, Orbscan II tomography and the Artemis-2 VHFUS exclusively on normal subjects.

Subjects and Methods

The prospective study was conducted at Eye World Centre, Riyadh, Saudi Arabia, from September to November 2012 during which 60 eyes of 29 female healthy subjects were evaluated. Comprehensive anterior segment examinations of all subjects were performed using a slit lamp. The exclusion criteria comprised systemic diseases such as diabetes mellitus (DM), pregnant women, IOP not more than 20 mmHg and high refractive error or high astigmatism $\geq\pm4.00$ DS or ≥-3.00 DC, respectively. All measurements of CCT were conducted by a single investigator. In this study, corneal curvature was determined using an auto-refractometre (Auto Kerato-Refracto-Tonometer TRK-1P; Topcon Corporation, Tokyo, Japan). One eye was randomly selected for each subject using a table of random numbers generated using Microsoft Excel (Microsoft Corporation, Redmond, WA, USA). The CCT has been shown to increase overnight and return to baseline within 3 hours of awakening.[17] Thus, all CCT measurements were collected during the period from 12:00 noon to 3:00 pm. The first CCT measurements were taken with the Orbscan II and then all measurements were subsequently obtained using the Artemis-2 VHFUS. After an hour of rest, measurement was made using the UBM to prevent inadvertent corneal indentation caused by UBM.[18] Three consecutive measurements were performed using each method for each subject. All of the measurements were conducted at the same clinic.

The Orbscan II scanning slit tomography system (Bausch & Lomb, Rochester, NY, USA) is a noncontact computerised slit scanning tomography system. The subject was seated comfortably and positioned properly, and was instructed to focus on the red blinking light in front of him or her. The slits were then adjusted and a measurement was made. During acquisition, 40 slits were projected and scanned over the cornea, each providing 240 data points from the anterior and posterior corneal surfaces. The corneal thickness was computed for every corneal point from the elevation difference between the two surfaces. The acoustic equivalent correction factor (0.92) was used to achieve equivalence with the ultrasonic evaluation as recommended by the manufacturer.[19]

For the Artemis-2 VHFUS (Scott Phillips Engineering, Victoria, Canada) measurements, the patient sat and positioned his or her face on a three-point forehead and chin rest while placing the eye into a soft-rimmed eye-cup akin to a swimming goggle. The sterile coupling fluid filled the compartment in front of the eye and the scanning was performed via an ultrasonically transparent (sterile) membrane without the need for a speculum. As such, there was no contact of the scanner probe with the eye. Performing a 3-D scan set with the Artemis-2 VHFUS required 2 to 3 minutes for each eye. The CCT values were obtained from the pachymetry map, which was derived from the four-scan set. Three readings were obtained for each eye and the average was calculated.

For the VuMAX™ USB (Sonomed Inc. New York, USA) measurements, the subject was asked to look at a fixated target on the ceiling. One drop of topical anaesthesia (benoxinate hydrochloride 0.4%) was instilled. The cup was disinfected with an alcohol swab. The transducer head was immersed in methylcellulose 1% within an eye-cup, which was placed on the sclera. Centrality was ensured by acquiring an image in which the pupil diameter was the greatest. Perpendicularity was ensured

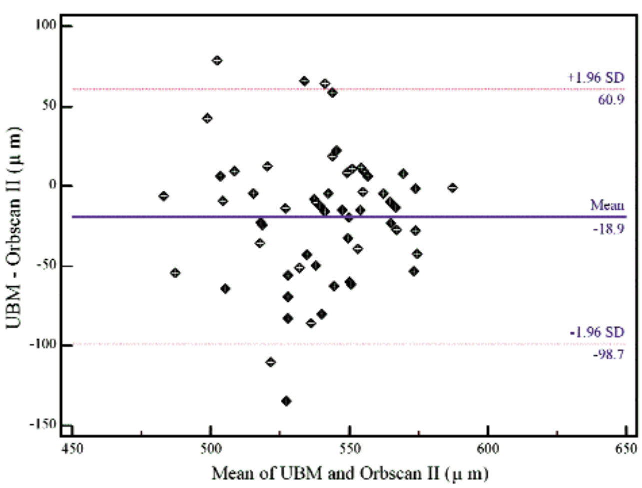
by adjusting the transducer head until the brightest reflection lines from the various corneal layers were observed in real time. Three separate images of each eye meeting the above criteria were captured and stored on the instrument system.

Before the initiation of any procedures the purpose of the study was explained to all subjects and informed consent was obtained from each subject before the examination. The study was conducted in conformity with the ethical considerations laid out in the 2008 Declaration of Helsinki, and the study protocol was approved by the institutional ethics review board.

The demographic data of all subjects was analysed using Microsoft Excel 2007. A repeated measurements Bland-Altman analysis was performed to determine the repeatability of measurements for the three instruments, and a repeated measure analysis of variance (ANOVA) was conducted. ANOVA test and paired t-test were performed using Medcalc software version 11.4.4.0.

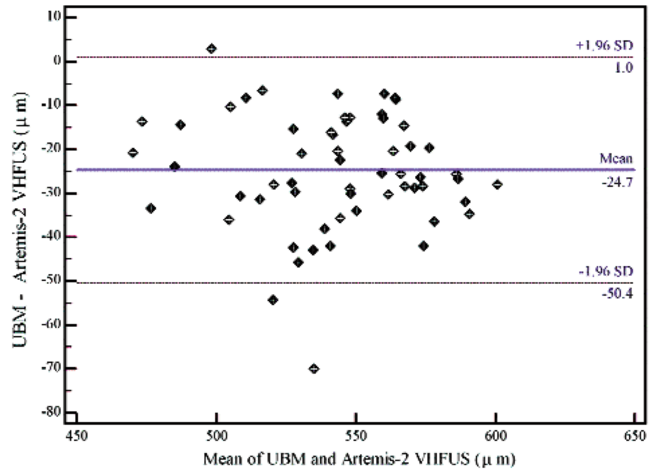
Results

The study analysed 60 normal eyes of 29 healthy female subjects whose mean age was 22±2.30 years, ranging from 19 to 30 years. Of the 60 eyes evaluated, 27 (45%) were right eyes and 33 (55%) were left eyes. Two (6.8%) subjects dropped out of the study as they were apprehensive about being examined with UBM. All their associated was excluded from analysis. The mean intraocular pressure was 14.00±1.50 mmHg. The mean spherical equivalent of refractive error was -0.75±1DS.



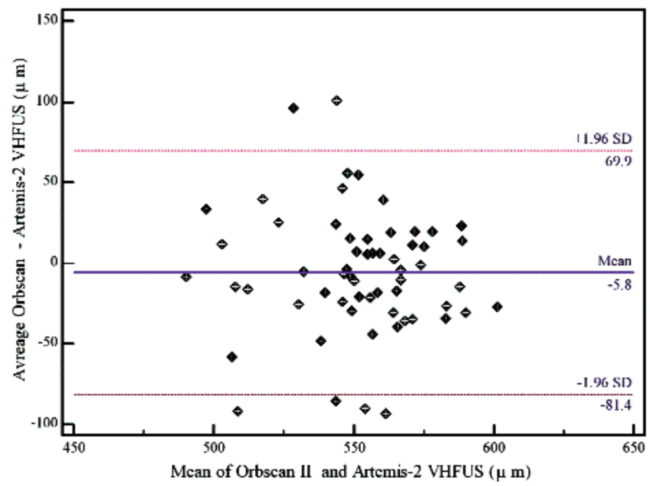
CCT: Central corneal thickness. UBM: Ultrasoud biomicroscopy.

Figure-1: Bland-Altman plot for comparison of the CCT measurement UBM vs. Orbscan II tomography.



CCT: Central corneal thickness. UBM: Ultrasound biomicroscopy. VHFUS: Very high frequency ultrasound scanner.

Figure-2: Bland-Altman plot for comparison of the CCT measurements UBM vs. Artemis-2 VHFUS.



CCT: Central corneal thickness. VHFUS: Very high frequency ultrasound scanner.

Figure-3: Bland-Altman plot for comparison of the CCT measurements Orbscan II tomography vs. Artemis-2 VHFUS.

Table: Instrument comparison.

	Mean CCT ± SD* (μm)	LOA** (μm)	P value***
UBM vs. Orbscan II	-18.92 ± 40.71	60.90 to - 98.70	< 0.01
UBM vs. Artemis-2 VHFUS	-24.70 ± 13.13	1.00 to - 50.40	< 0.001
Orbscan II vs. Artemis-2 VHFUS	-5.80 ± 38.61	69.90 to - 81.40	> 0.05

*SD: Standard Deviation. **LOA: Limits Of Agreement. ***Paired t-test.
UBM: Ultrasound biomicroscopy. VHFUS: Very high frequency ultrasound scanner.

The means of the CCT for UBM, Orbscan II tomography, and the Artemis-2 VHFUS were 530.03±30.75µm, 548.95±30.33µm, and 554.73±31.97µm, respectively. The P values of the repeated measures ANOVA for UBM, Orbscan II tomography and the Artemis-2 VHFUS were 0.19, 0.23, and 0.41, respectively. ANOVA test showed that there was a significant difference between the three instruments (p<0.0001). The mean difference ± standard deviation, limits of agreement and the paired t-test pvalues of comparison for UBM vs. Orbscan II tomography, UBM vs. the Artemis-2 VHFUS and Orbscan II tomography vs. the Artemis-2 VHFUS were noted separately (Table). Bland-Altman plots for comparison of the CCT measurements among UBM, Orbscan II tomography and the Artemis-2 VHFUS were also conducted (Figure 1, 2, and 3).

Discussion

Anterior segment imaging has recently been developed with highly advanced technology in the field of ophthalmology. The new imaging modalities employ either immersion ultrasound, such as UBM and the Artemis-2 VHFUS, which allow measurement of the CCT in a 3mm diametre of the cornea, or optical techniques, such as Orbscan II scanning slit tomography, rotating Scheimpflug imaging (Pentacam-Scheimpflug) and anterior segment optical coherence tomography (Visante OCT). These modalities provide quantitative information and qualitative imaging of the cornea and anterior segment.

In this study, the CCT values with the Artemis-2 VHFUS were greater than those with Orbscan II tomography and UBM. The mean difference was the greatest between UBM and the Artemis-2 VHFUS, and was the least between Orbscan II tomography and the Artemis-2 VHFUS. The intraobserver repeatability of the CCT measurements demonstrated high repeatability using UBM, Orbscan II tomography and the Artemis-2 VHFUS. ANOVA revealed a significant difference between UBM, Orbscan II tomography and the Artemis-2 VHFUS in CCT measurements (p=0.0001). The pvalues of the paired comparisons for UBM vs. Orbscan II tomography, UBM vs. the Artemis-2 VHFUS, and Orbscan II tomography vs. the Artemis-2 VHFUS were 0.01, 0.001, and 0.05, respectively. These results demonstrated that the mean difference in the CCT measurements was statistically significant between UBM and Orbscan II tomography, and Orbscan II tomography and the Artemis-2 VHFUS. These instruments, therefore, cannot be used interchangeably. However, the mean difference in CCT measurements showed no statistically significant difference between Orbscan II tomography and the Artemis-2 VHFUS. Therefore, these instruments can be used interchangeably. The Bland-Altman analysis of CCT measurements revealed a high level of agreement between Orbscan II tomography and the Artemis-2 VHFUS with a mean difference of 5.80µm. However, there was a poor level of agreement between the UBM versus Orbscan II tomography and the Artemis-2 VHFUS.

Prior studies reported high intraobserver repeatability in the CCT measurements using UBM,[8,18,20] Orbscan II tomography[14] and the Artemis-2 VHFUS[6,9,10,16] with normal eyes. Our findings demonstrated that intraobserver repeatability was high for CCT measurements using UBM, Orbscan II tomography and the Artemis-2 VHFUS.

Several studies reported that the earlier versions of the Orbscan overestimated CCT measurements compared with ultrasound pachymetry (USP). Their results showed that Orbscan overestimated CCT measurements by 23µm to 28µm when compared with USP, indicating that this difference could be caused by the absence of tear film after the application of the probe during USP[8,21] Because of this, the acoustic equivalent correction factor was introduced and the value recommended by the manufacturer was 0.92 with Orbscan II tomography. However, consecutive studies reported underestimations of CCT measurements with Orbscan II tomography when the correction factor was used.[8,22] Our results showed underestimation of CCT measurements with Orbscan II tomography compared with the Artemis-2 VHFUS by 5.80µm. This result is in agreement with a previous study that reported that Orbscan II resulted in a mean CCT of 7.5±15.7µm thinner than Artemis 2 values.[9] Our difference was slightly less because of the sample size and subject criteria, such as age and refractive error, which were not stated in the other study.[23]

Our findings showed that UBM underestimations of CCT measurements, when compared with Orbscan II tomography and the Artemis-2 VHFUS, were 18.92µm and 24.70µm, respectively. In the case of Orbscan II tomography, this could be because the tear film of 7µm[24] was included in the measurement of CCT by optical pachymetry, but not in the UBM measurement due to the use of a coupling medium. Neither were the Descemet's layer or the endothelium layer of 15µm[24] included in the UBM measurements of CCT as the reflection from the interface of the stroma and Descemet's layer, the endothelium layer, and endothelium layer aqueous humor could not be separated from one another. The first reflection was regarded as the interface between the cornea and aqueous humor, giving a lower ultrasonic measuring distance.[20] In case of Artemis-2 VHFUS, the UBM required a supine position, a transducer, immersion

in transduction fluid, and no contact with the cornea. Thus, the level of perturbation of the pre-corneal tear film and epithelium was different from the Artemis-2 VHFUS measurements. The examiner must manually adjust the transducer head to maximise centrality and perpendicularity of the image, which requires more time to perform. Analogue-based UBM does not allow imaging of the interface consistently because analogue processing does not produce a high enough signal-to-noise ratio between the interface echo complex and the surrounding tissue.[7,16]

There is an abundance of published data regarding CCT measurements using different techniques. The data from these studies show great variation in CCT, which may be because the instrument methodology and subject criteria, such as age and refractive state, had a significant impact on CCT measurements.[7-10,16,23,25]

Conclusion

CCT measurements obtained using Orbscan II tomography and the Artemis-2 VHFUS can be used interchangeably. However, Orbscan II tomography and the Artemis-2 VHFUS CCT measurements cannot be used interchangeably with UBM.

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