

Comparison of central corneal thickness: ultrasound pachymetry versus slit-lamp optical coherence tomography, specular microscopy, and Orbscan

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Background: Central corneal thickness (CCT) can be measured by using contact and non-contact methods. Ultrasound pachymetry (US pachymetry) is a contact method for measuring CCT and is perhaps the most commonly used method. However, non-contact methods like scanning slit topography (Orbscan II), slit-lamp optical coherence tomography (SL-OCT), and specular microscopy are also used. Not many studies have correlated the measurement of CCT with all four modalities. The purpose of this study was to compare and correlate the CCT measurements obtained by US pachymetry with SL-OCT, specular microscopy, and Orbscan.

Method: This is a prospective, comparative study done in an institutional setting. Thirty-two eyes of 32 subjects with no known ocular disease and best-corrected visual acuity of 20/20 were enrolled. CCT measurements were obtained using SL-OCT, specular microscopy, scanning slit topography (Orbscan), and US pachymetry. Three measurements were made with each instrument by the same operator. Mean, standard deviation, and coefficient of variation were calculated for CCT measurements acquired by the four measurement devices. Bland–Altman plot was constructed to determine the agreements between the CCT measurements obtained by different equipment.

Results: The mean CCT was $548.16 \pm 48.68 \mu\text{m}$ by US pachymetry. In comparison, CCT averaged $546.36 \pm 44.17 \mu\text{m}$ by SL-OCT, $557.61 \pm 49.92 \mu\text{m}$ by specular microscopy, and $551.03 \pm 48.96 \mu\text{m}$ by Orbscan for all subjects. Measurements by the various modalities were strongly correlated. Correlations (r^2) of CCT, as measured by US pachymetry compared with other modalities, were: SL-OCT ($r^2=0.98$, $P<0.0001$), specular microscopy ($r^2=0.98$, $P<0.0001$), and Orbscan ($r^2=0.96$, $P<0.0001$). All modalities had a linear correlation with US pachymetry measurements.

Conclusion: In subjects with healthy corneas, SL-OCT, specular microscopy, and Orbscan (with correction factor) can be used interchangeably with US pachymetry in certain clinical settings. The four modalities showed significant linear correlations with one another.

Keywords: central corneal thickness, pachymetry, slit-lamp optical coherence tomography, specular microscopy, Orbscan

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Background

Central corneal thickness (CCT) is an important biometric measurement in several ocular conditions such as corneal edema, corneal dystrophies, and corneal endothelial diseases. CCT is even preferred in patients whose corneas are otherwise healthy, eg, in those undergoing LASIK procedure. It has become an important measurement to establish accurate intraocular pressure (IOP) readings. Ultrasound pachymetry (US pachymetry)

is the most common method used for CCT measurements.¹ This is performed by direct apposition of an ultrasound probe to the anterior corneal surface.² However, limitations of this method include contact with the corneal surface, misalignment of ultrasound probe perpendicularly to corneal surface, and insufficient tear film displacement after probe compression.

Non-contact techniques such as Orbscan (Bausch & Lomb Incorporated, Bridgewater, NJ, USA),³ specular microscopy, and optical coherence tomography (OCT)⁴ have been used to measure CCT with varying success. Orbscan II² uses a scanning-slit principle in order to measure the corneal thickness. Specular microscopy uses reflections of light from the anterior and posterior corneal surface as a means to distinguish corneal layers and measure corneal thickness.⁵ The slit-lamp OCT (SL-OCT) combines slit-lamp biomicroscopy⁶ and imaging technology of OCT and it can also be used to measure the corneal thickness. There have been several studies done in the past comparing two or more of these modalities for the measurement of CCT.¹⁻¹⁰ However, very few studies have compared all four modalities. In this prospective study, we measured corneal thickness with non-contact Orbscan II, specular microscopy, and SL-OCT, and compared these modalities to US pachymetry in subjects with no ocular disease.

Materials and methods

Subjects

In this comparative, prospective study, 32 individuals were recruited from the Department of Ophthalmology at the University of Florida at Jacksonville. The inclusion criteria were: best-corrected visual acuity (BCVA) of 20/20 or better, absence of ocular pathology by history and undilated eye exam, and IOP of less than 21 mmHg. If the subject was a contact lens wearer (n=2), then measurements were taken at least 24 hours after being off the contact lens. Exclusion criteria included history of any ocular surgery or anterior segment pathology and refractive error more than or equal to ± 6 diopters. Written informed consent was obtained from all the subjects after the protocol and possible risks were explained; the consent form was approved by the Institutional Review Board at the University of Florida. All participants were subjected to comprehensive eye examinations which included BCVA, pupil examination, IOP measurements, slit-lamp biomicroscopy, and undilated fundus examination. Individuals enrolled were from different races, and subset analysis comparing CCT among races was not performed due to small sample size.

Devices

Kerasonix KSX-1000 ultrasound pachymeter (DGH Technology, Exton, PA, USA) utilizes ultrasound energy to measure

CCT. When ultrasound energy is emitted from the probe tip, some of the energy is reflected back in the form of an echo. Based on velocity and time for the energy to travel back to the receiver, the measurements are obtained. Measurements were made with the ultrasound velocity (acoustic index) set to 1,640 m/s.

The SL-OCT (Heidelberg Engineering, Heidelberg, Germany) employs an internal, short coherent, infrared light source (super-luminescent light emitting diode) with a central wavelength approximately 1,310 nm. The SL-OCT is capable of 15 mm scan sizes with a scan depth of 7 mm. The lateral optical resolution capacity is less than 100 μm and the lateral digitalized resolution capacity is 75 μm . The axial resolution capacity is less than 25 μm for optical resolution and 10 μm for digitalized resolution. The slit-beam produces a reflex that appears on both the outer and inner corneal surface as well as a sharp reflex beam through the anterior chamber. Scans were saved and analyzed for CCT via the Heidelberg Eye Explorer (HEYEX) SL-OCT (Heidelberg Engineering) viewing software.

The Konan Noncon Robo Pachy (Konan Medical Corporation, Fairlawn, NJ, USA) is comprised of a non-contact microscope and camera. This device obtains a specular image of the corneal endothelium and also measures the corneal thickness. Subjects were positioned to focus on fixation target, and the corneal image was captured using the Noncon Robo specular microscope. The KSS-300 Image Storage System was used to acquire and save the image and subsequently analyze the CCT.

Orbscan II (Bausch and Lomb, Rochester, NY, USA) analyzes reflected images from multiple concentric rings projected on the anterior surface of the cornea. A high-resolution video camera captures multiple light slits projected through the cornea similarly as seen during slit-lamp examination. The instrument's software analyzes multiple data points per slit and calculates the corneal thickness. The anterior and posterior corneal surfaces were automatically detected with the system software. Once the images were recorded, calculations of the CCT were performed. The final reading was automatically adjusted using an acoustic correction factor (AF) of 0.92, as recommended by the manufacturer.

Procedure

By default, data were obtained from the right eye in all the participants. The CCT was obtained using the four modalities and analyzed, as outlined below. CCT measurements were taken in triplicate for each study instrument by the same examiner during a single morning or afternoon visit. Triplicate measurements were taken to reduce intra-observer variability. The order of testing was randomized. For US

Table 1 Demographics of the subjects included in the study

Number of subjects	32
Number by race (%)	
Caucasian	19 (59%)
African	5 (16%)
Asian	7 (22%)
Hispanic	1 (3%)
Mean/median age (years)	31.2/32
Age range (years)	19–54
Sex ratio (male:female)	15:17
Mean/median refraction	−1.52/−2.00 diopter

pachymetry measurements after instillation of topical anesthetic (0.5% proparacaine), the probe tip was gently applied to the central cornea overlying the pupil. For the other three non-contact modalities guidelines were followed and images were analyzed with the respective software of the respective machines.

Statistical analysis

For statistical analysis the GraphPad InStat 3 (GraphPad Software, Inc., La Jolla, CA, USA) was used. Mean, standard deviation (SD), and coefficient of variation were calculated for CCT measurements acquired by the four measurement devices. Bland–Altman plot was constructed to determine the agreements between the CCT measurements acquired by different equipment and the *P*-value was obtained. Pearson's correlation coefficient (r^2) was also obtained for CCT, as measured by US pachymetry compared with other modalities. Intra-class correlations coefficient was also calculated to assess degree of relatedness between CCT measurements obtained between various apparatus.

Results

Thirty-two eyes of 32 normal subjects (15 men and 17 women) were included in this study. Their mean age was 31.2 years (range: 19–54 years) (Table 1). Although triplicate measurements were obtained on all subjects with Orbscan,

one data point each from two subjects were excluded due to poor scan quality.

The mean CCT measured by US pachymetry from the 32 subjects was $548.16 \pm 48.68 \mu\text{m}$. In comparison, the CCT averaged $546.36 \pm 44.17 \mu\text{m}$ by SL-OCT, $557.61 \pm 49.92 \mu\text{m}$ by specular microscopy, and $551.03 \pm 48.96 \mu\text{m}$ by Orbscan II (with AF of 0.92) for all the subjects (Table 2).

The Bland–Altman plot showed that the measurements acquired via US pachymetry were greater than those obtained by SL-OCT for mean CCT values from 475–550 μm (Figure 1). For CCT values beyond 550 μm SL-OCT measurements were higher than US pachymetry. The mean (\pm SD) CCT measurement difference between the two methods was $1.24 (\pm 4.51) \mu\text{m}$, and the 95% limits of agreement (LOA) were between -21.76 and $18.18 \mu\text{m}$. US pachymetry measurements when compared to specular microscopy, showed an overall decrease in measurement values for CCT when values ranged from 500 to 650 μm (Figure 2). In this case mean (\pm SD) difference was $8.69 (\pm 1.24) \mu\text{m}$ while the 95% LOA range was -8.82 to $27.4 \mu\text{m}$ (Figure 2). Bland–Altman plot comparison of CCT measurements obtained by US pachymetry vs Orbscan II (Figure 3) demonstrated that US pachymetry showed little relative difference in CCT measurements within the range of 500–650 μm as compared to Orbscan. Table 2 shows that the mean (\pm SD) difference between US pachymetry and Orbscan II was $2.8 (\pm 0.28) \mu\text{m}$ with a 95% LOA range between -30.15 and $24.40 \mu\text{m}$. Among the three methods for CCT measurement US pachymetry had the best agreement with the SL-OCT; the mean difference was the smallest (Table 2). Conversely, the comparison between US pachymetry and specular microscopy measurements had the least agreement; the mean difference was the largest (Table 2). Correlations (r^2) of CCT, as measured by US pachymetry compared with other modalities, were: SL-OCT ($r^2=0.98$, $P<0.0001$) (Figure 4), specular microscopy ($r^2=0.98$, $P<0.0001$) (Figure 5), and Orbscan ($r^2=0.96$, $P<0.0001$) (Figure 6). Measurements by the various modalities were strongly correlated. Intra-class

Table 2 Descriptive statistics for the central corneal thickness, as measured by the four different modalities

	US pachymetry	SL-OCT	Specular microscopy	Orbscan*
Mean CCT (μm)	548.16	546.36	557.61	551.03
Standard deviation (SD)	48.68	44.17	49.92	48.96
<i>P</i> -value (paired)	–	0.88	0.45	0.81
Mean (SD) CCT difference** (μm)	–	1.24 (± 4.51)	8.69 (± 1.24)	2.87 (± 0.28)
Minimum	471.00	469.00	453.00	460.00
Maximum	656.00	631.00	686.00	672.00
Median	543.00	546.5	550.00	549.5

Notes: *With acoustic correction factor of 0.92. **Mean CCT difference as compared to US pachymetry.

Abbreviations: US pachymetry, ultrasound pachymetry; SL-OCT, slit-lamp optical coherence tomography; CCT, central corneal thickness.

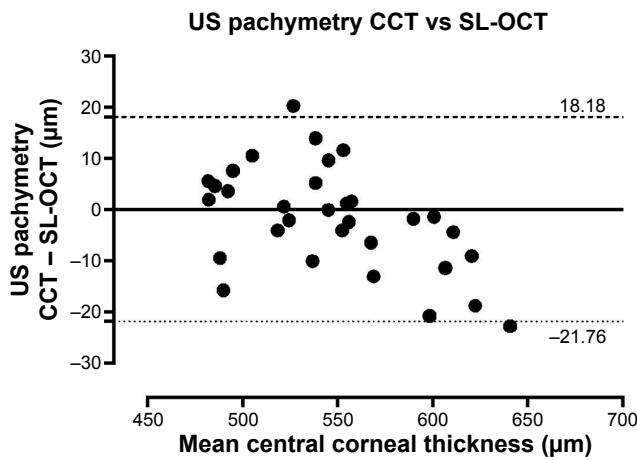


Figure 1 Bland–Altman plot with 95% limits of agreement (LOA) illustrates the difference in central corneal thickness measurements (y-axis) between values obtained by ultrasound pachymetry vs values obtained by slit-lamp optical coherence tomography (SL-OCT) against the average CCT measurements of the two methods (x-axis).

Abbreviations: US pachymetry, ultrasound pachymetry; CCT, central corneal thickness; vs, versus.

correlations of CCT, as measured by US pachymetry when compared with the other modalities, conveyed a strong and positive intra-class correlation coefficient (ICC =0.95).

Discussion

The mean CCT measured by the US pachymetry from the 32 subjects was $548.16 \pm 48.68 \mu\text{m}$, which is similar to previously published results in the literature. In studies by Al-Farhan and Al-Otaibi,¹ Williams et al,² and Christensen et al³ mean CCT was recorded as $530.1 \pm 30.5 \mu\text{m}$, $532.94 \pm 37.96 \mu\text{m}$, and $552.36 \pm 37.6 \mu\text{m}$, respectively.

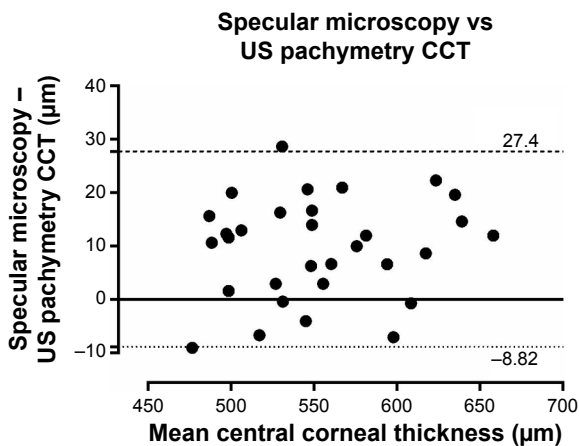


Figure 2 Bland–Altman plot with 95% limits of agreement (LOA) illustrates the difference in central corneal thickness measurements (y-axis) between values obtained by specular microscopy vs values obtained by ultrasound pachymetry against the average CCT measurements of the two methods (x-axis).

Abbreviations: US pachymetry, ultrasound pachymetry; CCT, central corneal thickness; vs, versus.

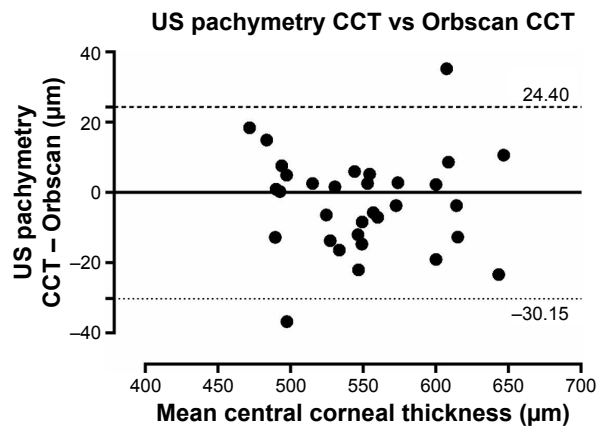


Figure 3 Bland–Altman plot with 95% limits of agreement (LOA) illustrates the difference in central corneal thickness measurements (y-axis) between values obtained by ultrasound pachymetry vs values obtained by Orbscan against the average CCT measurements of the two methods (x-axis).

Abbreviations: US pachymetry, ultrasound pachymetry; CCT, central corneal thickness; vs, versus; SL-OCT, slit-lamp optical coherence tomography.

In comparison to US pachymetry, the mean CCT measured by SL-OCT was $546.36 \pm 44.17 \mu\text{m}$ and it showed the best agreement compared to all other methods. Other studies by Li et al⁴ and Beutelspacher et al⁸ showed no significant difference between these two modalities. This high correlation of measurement values between the two modalities may be due to the similar mechanism of the two instruments – both use reflection of waves to determine the anterior and posterior boundaries of the cornea. It is possible that SL-OCT measures CCT from the same corneal surface or interface as US pachymetry.

The mean CCT, as obtained by specular microscopy, was $557.61 \pm 49.92 \mu\text{m}$ and was similar to mean CCT found in previous studies. A study by Wu et al⁵ found mean CCT

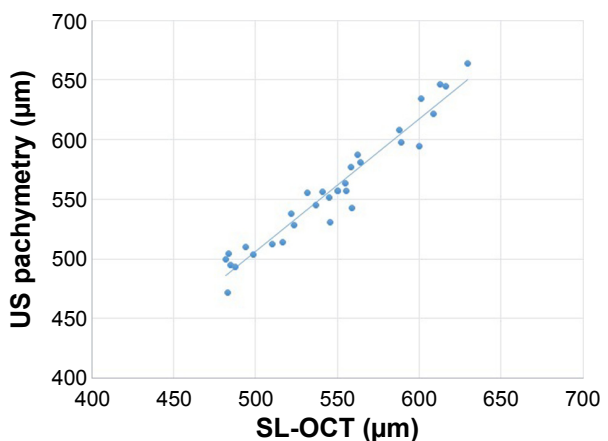


Figure 4 Scatter plot display of ultrasound pachymetry with SL-OCT measurement of CCT ($r^2=0.982$).

Abbreviations: US pachymetry, ultrasound pachymetry; CCT, central corneal thickness; SL-OCT, slit-lamp optical coherence tomography.

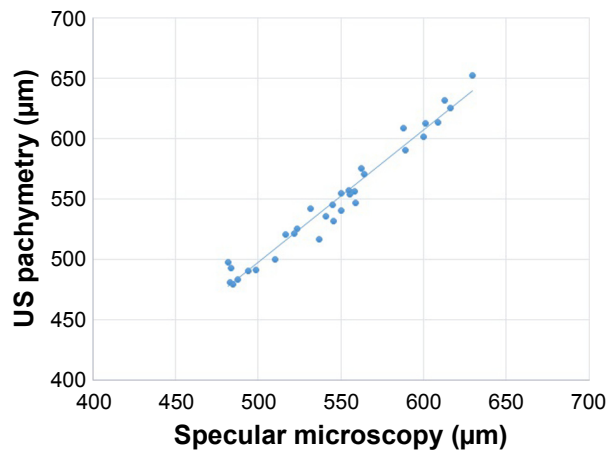


Figure 5 Scatter plot display of ultrasound pachymetry with specular microscopy measurement of CCT ($r^2=0.98$).

Abbreviations: US pachymetry, ultrasound pachymetry; CCT, central corneal thickness.

using Konan specular microscope to be $554.78 \pm 32.61 \mu\text{m}$. Doughty et al⁷ compared CCT using slit-lamp-based pachymetry which was 0.530 mm (median 0.525 mm) compared to ultrasound-based methods 0.544 mm (median 0.544 mm). Jonuscheit and Doughty⁸ have reported that the slit-scanning pachymeter can substantially overestimate more peripheral thickness measurements of the cornea than specular microscopy or US pachymetry, and therefore, cannot be used interchangeably. Similarly again a study by Jonuscheit and Doughty⁹ reports that Orbscan II provides the clinician with a repeatable noninvasive method of measuring corneal thickness that is not necessarily any better than US pachymetry, and should not be considered as interchangeable with ultrasound. However

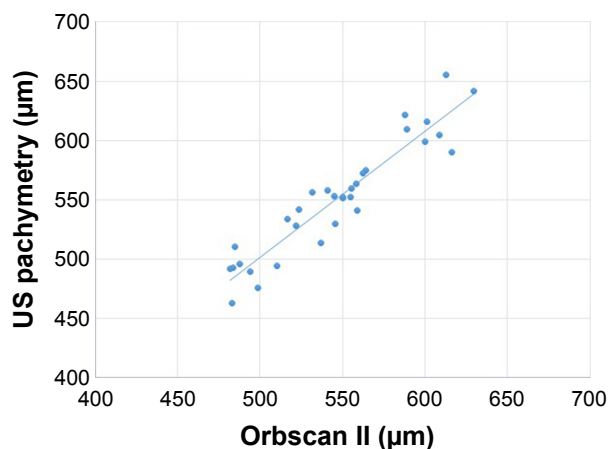


Figure 6 Scatter plot display of ultrasound pachymetry with Orbscan measurement of CCT ($r^2=0.96$).

Abbreviations: US pachymetry, ultrasound pachymetry; CCT, central corneal thickness.

there was no difference noted in our study which could be due to the ultrasound device used (Kerasonix KSX-1000). A study by Martin et al¹⁰ appreciated the repeatability of Orbscan pachymetry compared to ultrasound to measure corneas with and without corneal swelling and suggested that it could be useful to study central and peripheral corneal swelling variations in contact lens users. Módis et al¹¹ found mean CCT to be $549 \pm 33 \mu\text{m}$ with Tomey specular microscope. Our findings show that specular microscopy overestimated CCT by $8.69 \mu\text{m}$. Previous studies measuring CCT by US pachymetry vs specular microscopy have also shown a strong correlation and also demonstrated that CCT can be overestimated¹¹ or underestimated¹² by specular microscopy. However, different brands of specular microscopes were used in each of these studies and this variability in measurements may be inherent to the instrument. Different types of specular microscopes may record corneal parameters such as magnification, refractive index, and anterior corneal curvature, etc differently, which will affect the final specular image.

The mean CCT by Orbscan measured $551.03 \pm 48.96 \mu\text{m}$ in our study and showed good agreement with US pachymetry. Using the suggested correction factor of 0.92, Orbscan overestimated CCT by an average of $2.88 \mu\text{m}$ in our study in comparison to US pachymetry. Different studies have also shown an overestimation, underestimation, or even no difference between CCT measurements.^{13–16} Initial studies looking at the Orbscan found that it overestimated CCT when compared to US pachymetry.^{16,17} Hence, the development of an AF of 0.92. Doughty and Jonuscheit¹⁸ performed a meta-analysis of 46 studies evaluating Orbscan measurements with and without the correction factor; results showed that Orbscan may yield CCT measurement which is approximately 7% higher than US pachymetry. Some studies have suggested that universal use of correction factor of 0.92 may be inaccurate, and CCT measurements with Orbscan should be reported without any adjustment factor.^{13–15,18} This discrepancy between studies may be due to the fact that Orbscan measures thickness between air-tear interface and posterior corneal surface. The tear film surface can add 7–30 μm to the total CCT measurement.¹⁹ In addition, the exact posterior corneal reflection point for Orbscan is not known; it may be anywhere between Descemet's membrane and anterior chamber (3–10 μm).¹⁹

Although individuals enrolled in this study were different races, we did not perform a subset analysis comparing CCT among races due to small sample size. The comparison between our study and other studies reported

above has limitations too. Our study had a small sample size and measurements were randomly done, however non-contact methods should be performed before the contact methods. These studies have different population demographic profiles than ours. Future studies comparing CCT measurements among different ethnic origins could be more informative.

Conclusion

To our knowledge, this is one of the few studies comparing four common modalities for measuring CCT; we compared SL-OCT, specular microscopy, and Orbscan to the most commonly used modality, US pachymetry in individuals with healthy corneas. Since there was a strong correlation of these modalities with US pachymetry, any one can be used in a certain clinical setting.

Disclosure

All the authors declare that they have no competing interests. No financial support was received for this submission.

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