Central Corneal Thickness Measurements With Different Imaging Devices and Ultrasound Pachymetry

Lai-Yong Tai, MBBS,* Keat-Ween Khaw, FRCOphth,* Choung-Min Ng, PhD,‡ and Visvaraja Subrayan, FRCOphth* 

Purpose: The aim of this study was to compare 4 methods of central corneal thickness (CCT) measurements in terms of their agreement, repeatability, and measurement time.

Methods: CCT was measured in 184 eyes of 92 healthy subjects by the same examiner. The methods used were as follows: noncontact specular microscopy (SM; Topcon SP-3000P; Topcon Corporation, Tokyo, Japan), Pentacam rotating Scheimpflug photography system (Oculus Inc, Wetzlar, Germany), optical low-coherence reflectometry (OLCR; LenStar LS900; Haag-Streit AG, Koeniz, Switzerland), and ultrasound pachymetry (UP; PachPen; Accutome Inc, Malvern, PA). The duration for each examination was measured by an independent observer.

Results: The mean age (±SD) of the subjects was 54.3 (±15.3) years. The mean CCTs (±SD) for SM, Pentacam, OLCR, and UP were 507.8 (±30.2), 538.4 (±31.7), 531.8 (±31.4), and 528.3 (±32.9) μm, respectively. The Bland–Altman plots showed closest agreement for OLCR–UP, followed by OLCR–Pentacam and Pentacam–UP. SM had the poorest agreement with the other methods. CCTs measured by SM were on average 20 to 30 μm thinner than those of the other methods. The coefficient of repeatability for SM, Pentacam, OLCR, and UP were 3.14%, 4.23%, 1.51%, and 3.46%, respectively. The mean measurement times (±SD) were 13.5 (±5.7), 45.7 (±12.3), 18.5 (±7.1), and 5.6 (±1.0) seconds, respectively.

Conclusions: CCT measurements between OLCR–UP and OLCR–Pentacam are comparable and can be used interchangeably in clinical practice. However, SM underestimates CCT compared with the other methods, whereas Pentacam was found to be at least repeatable and took the longest time.

Key Words: central corneal thickness, Pentacam, LenStar LS900, noncontact specular microscopy, ultrasound pachymetry

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Central corneal thickness (CCT) measurement is clinically important in ophthalmology especially in the fields of cornea and refractive surgery and glaucoma. Corneal pachymetry is used to diagnose, monitor progression of various corneal pathologies, and aid in the preoperative evaluation for patients undergoing refractive surgery.1 Additionally, CCT affects intraocular pressure measurement by applanation tonometry and is an independent risk factor for the progression of ocular hypertension to primary open-angle glaucoma.2

An ideal corneal pachymeter should be one that not only gives precise and accurate measurements but is also quick and easy to operate, one that provides maximum patient comfort, is cost effective, and is incorporated into an instrument with multifunctionality. Currently, there are various technologies for CCT measurements, among which are videopachymetry, confocal microscopy, specular microscopy (SM), slit scanning, rotary scanning, Scheimpflug photography, partial coherence interferometry, optical coherence tomography and optical low-coherence reflectometry (OLCR), and ultrasound pachymetry (UP) and ultrasound biomicroscopy.3

Of these, UP is still regarded as the gold standard and it is widely used for its ease, portability, and quick measurement time. Newer generation ultrasound pachymeters like the PachPen (Accutome Inc, Malvern, PA), which uses a 10.5-MHz composite probe in a lithium battery–operated handheld device, has been shown to be comparable with other commercially available ultrasound pachymeters.4 However, this instrument has not been compared with other pachymetric technologies. One drawback of UP is that the accuracy of contact pachymetry may be affected by corneal indentation and misalignment of the probe. Furthermore, patient comfort is reduced by the need for topical anesthesia and the risk of epithelial abrasion and corneal infection.5 As such, noncontact measurements of CCT may be preferable so long as accurate measurements can be obtained.

Among these methods is the noncontact SM. Previous studies comparing SM with UP have found that CCT measurements produced by SM were significantly thinner,6–8 although one conflicting report showed that SM produced thicker CCT results.9 Two recent reports with Topcon SP-3000P (Topcon Corporation, Tokyo, Japan) found similar underestimation of CCT compared with UP.3,10

Another noncontact instrument is the Pentacam (Oculus Inc, Wetzlar, Germany), which uses single rotating Scheimpflug photography device to generate a cross-sectional reconstruction of the anterior segment. Each scan is said to take
only 2 seconds.\textsuperscript{11} This corneal tomography provides thickness of the entire cornea by measuring the front and back surfaces of the cornea. CCT measured on the Pentacam shows high intraobserver repeatability and interobserver reproducibility and is comparable with UP.\textsuperscript{11–13}

Recently, an alternative method of measuring CCT is by an OLCR ocular biometry device, the LenStar LS900 (Haag-Streit AG, Koeniz, Switzerland). Its CCT measurement has been shown to be comparable with that of UP\textsuperscript{13} and Pentacam\textsuperscript{14} and of other optical biometers.\textsuperscript{15,16} The manufacturer claims an accuracy and reproducibility of 1 \(\mu m\) for this instrument\textsuperscript{13} and that a single measurement can be performed in roughly 20 seconds.\textsuperscript{16}

Currently, there are no published data that have evaluated these newer devices collectively. Furthermore, data on measurement time is lacking. In a busy ophthalmology practice, we believe this factor to be important for clinicians when deciding on the instrument of choice to measure CCT. Therefore, we conducted this study with the aim of measuring agreement, repeatability, and measurement time of these 4 methods.

**MATERIALS AND METHODS**

This comparative case series adhered to the tenets of the Declaration of Helsinki. The institutional ethics committee approved this study. All subjects provided informed consent after receiving detailed information regarding the nature and purpose of this study. Before the investigations, all subjects underwent a complete ophthalmic examination including manifest refraction, slit-lamp microscopy, and indirect ophthalmoscopy. Exclusion criteria included history of contact lens wear, ocular surgery or injury, corrected distance visual acuity worse than 20/40, active ocular pathologies other than lens wear, ocular surgery or injury, corrected distance visual acuity worse than 20/40, active ocular pathologies other than cataract, and an inability to cooperate with the examination.

A total of 184 eyes of 92 healthy subjects were recruited from the University of Malaya Medical Center from December 2011 to February 2012. All measurements were performed by a single examiner (L.Y.T.) and were taken at the same time of day, between 10 AM and 4 PM. An independent observer (K.W.K.) timed each procedure using a stopwatch. Each subject underwent 4 different methods of measurements sequentially using the following instruments: Topcon SP-3000P (Topcon Corporation), Pentacam (Oculus Inc), LenStar LS900 (Haag-Streit AG), and PachPen (Accutome Inc). For examination with SM, Pentacam, and OLCR, 5 consecutive measurements were performed. Nine consecutive measurements were taken for UP as per the factory settings of the device.

Noncontact pachymetry examinations were performed as described in the literature.\textsuperscript{7,14,17} Subjects were positioned on the headrest and instructed to look straight ahead into the built-in fixation targets within each device. After proper alignment, they were asked to blink just before each measurement was taken. Following each acquisition, subjects were then instructed to take their head off the chin rest, blink, and return to the examination position. The device was moved backward and realigned for the next scan.

After completing the noncontact examination, UP was performed. The cornea was first anesthetized with 1 drop of 0.5% topical proparacaine hydrochloride (Alcaine; Alcon, Belgium). The subject was asked to look straight ahead to a fixation target, and the probe was applied perpendicularly to the central corneal surface. After a measurement was taken, the subject was instructed to blink and a repeated measurement was obtained. The ultrasound probe was sterilized with alcohol after each subject.

**Statistical Analysis**

Statistical analysis was performed using the R software (version 2.14.0). The Bland–Altman plot was produced to assess the agreement of measurements between pairs of SM, Pentacam, OLCR, and UP procedures. For a single patient, the 5 consecutive measurements for each noncontact procedure and the 9 consecutive measurements for UP were averaged. Then, the difference of these averaged values for a pair of methods was obtained for the eye. Because 4 methods were considered, there were 6 pairs of mean differences. For each pair of methods, the overall mean of the mean differences and the SD of the mean differences for the 184 eyes were calculated. From these values, the 95% limits of agreement (LoA) were derived. The SD was not corrected, although it has been obtained for averaged values because it is the norm to report averaged CCT measurements clinically.\textsuperscript{18} Two methods were said to be in good agreement when the 95% LoA were within allowable clinical margins.

The coefficient of repeatability\textsuperscript{19} was used as a measure of within-subject variation for a unit of the mean, which enabled fair comparison of variations between different methods that yield different means. A smaller variation indicated that the measurements taken were closer to each other.

For each patient, the total time for the 5 consecutive measurements was recorded for SM, Pentacam, and OLCR, whereas the total time for the 9 measurements was recorded for UP. For comparison, average time per measurement was obtained for each method. Hence, the total time recorded was divided by 5 for SM, Pentacam, and OLCR, whereas it was divided by 9 for UP. Then, the mean and median of the averaged times from all the patients for each device were obtained. The significance of the differences between the median times of the 4 devices was assessed using Kruskal–Wallis test with multiple comparisons. A significance level of \(\alpha = 0.05\) was used for all statistical inferences. All CCT measurements have been checked to satisfy the condition of normality.

**RESULTS**

The mean age (±SD) of the subjects was 54.3 (±15.3) years (range: 16 to 80 years). About 56% of subjects were women. The mean CCT (±SD) for SM, Pentacam, OLCR, and UP were 507.8 (±30.2), 538.4 (±31.7), 531.8 (±31.4), and 528.3 (±32.9) \(\mu m\) respectively. It is found that the differences between pairs of mean CCT for the methods are statistically significant except for the pairs of OLCR–UP and OLCR–Pentacam, as shown in Table 1.
Agreement Analysis

The overall mean differences along with the corresponding 95% LoA and correlation for the 6 pairs of methods are given in Table 1. The scatter plots to compare the means for pairs of methods for the 184 eyes are given in Figure 1. These plots show high correlation between the methods used. The dotted lines are the line of equality for the corresponding 2 methods. Only 3 pairs of devices show close agreement, namely OLCR–Pentacam, OLCR–UP, and Pentacam–UP, as judged by the proximity of the solid regression line to the dotted equality line. The agreement between pairs of methods will be examined further using the Bland–Altman plots. Based on the values in Table 1, 6 Bland–Altman plots have been produced in Figure 2 to examine the agreement between the 4 methods. Clearly, OLCR and UP have the closest agreement, followed by OLCR and Pentacam. Thus, Pentacam also agrees satisfactorily with UP, as confirmed by the Bland–Altman plot. SM was found to have the poorest agreement with the other 3 methods. Measurements with SM were thinner than those of Pentacam, OLCR, and UP by 30, 24, and 20 μm, respectively.

Repeatability Study

The coefficients of repeatability for SM, Pentacam, OLCR, and UP were 3.14%, 4.23%, 1.51%, and 3.46%, respectively.

Measurement Time

The mean measurement times per measurement (±SD) for SM, Pentacam, OLCR, and UP are 13.5 (±5.7), 45.7 (±12.3), 18.5 (±7.1), and 5.6 (±1.0) seconds. The spread of the times taken per measurement for all methods is as

TABLE 1. Mean Difference (SD), 95% LoA, and Pearson Correlation Between the Pairs of Methods

<table>
<thead>
<tr>
<th>Comparisons</th>
<th>Mean Difference (SD)</th>
<th>95% LoA</th>
<th>Significance of Difference (P*)</th>
<th>Correlation</th>
</tr>
</thead>
<tbody>
<tr>
<td>OLCR–SM</td>
<td>24.03 (5.97)</td>
<td>12.32 to 35.75</td>
<td>&lt;0.001</td>
<td>0.98</td>
</tr>
<tr>
<td>Pentacam–UP</td>
<td>10.08 (10.96)</td>
<td>−11.40 to 31.56</td>
<td>0.012</td>
<td>0.94</td>
</tr>
<tr>
<td>OLCR–UP</td>
<td>3.54 (6.94)</td>
<td>−10.06 to 17.14</td>
<td>0.704</td>
<td>0.98</td>
</tr>
<tr>
<td>OLCR–Pentacam</td>
<td>−6.54 (9.40)</td>
<td>−24.96 to 11.88</td>
<td>0.194</td>
<td>0.96</td>
</tr>
<tr>
<td>SM–UP</td>
<td>−20.49 (8.91)</td>
<td>−37.95 to −3.04</td>
<td>&lt;0.001</td>
<td>0.96</td>
</tr>
<tr>
<td>SM–Pentacam</td>
<td>−30.57 (10.26)</td>
<td>−50.69 to −10.45</td>
<td>&lt;0.001</td>
<td>0.95</td>
</tr>
</tbody>
</table>

Values are in micrometers except for correlation.

*P* values are obtained from Tukey test for multiple comparisons.
shown in Figure 3. There are a number of outlying values in the figure. Because the value of the mean is affected by outliers, the median times for each device are as follows: 12.4, 42.4, 17.0, and 5.6 seconds for SM, Pentacam, OLCR, and UP, respectively. These median times per measurement are found to be significantly different from each other (Kruskal–Wallis $P$ value <0.001 for all pairs).

**DISCUSSION**

Accurate CCT measurement is clinically important because diagnostic and therapeutic decisions are made based on this. There are various available methods to measure CCT, each with its own merits and limitations. In this study, we compared agreement, repeatability, and measurement time of 4 different methods, namely SM, Pentacam, OLCR, and UP.

We found that OLCR–UP showed the closest agreement, followed by OLCR–Pentacam and Pentacam–UP. This concurs with previous published data in the literature. Beutelspacher et al.\(^\text{20}\) who compared CCT using optical coherence tomography, UP, OLCR, and Pentacam, noted that the closest agreement was also between OLCR and UP. Based on the Bland–Altman plots, Huang et al.\(^\text{14}\) showed that the mean differences between the OLCR and Pentacam CCTs were not significantly different from zero. Furthermore, they found a narrow 95% LoA of $-8.2$ to $15.7 \text{ µm}$ for CCT measurement between the 2 devices suggesting good agreement. Sedaghat et al.\(^\text{5}\) in a study of 157 eyes, also found close agreement between Pentacam and UP. O’Donnell and Maldonado-Codina\(^\text{21}\) reported good agreement and repeatability between Pentacam and UP. However they found a small underestimation of CCT with Pentacam compared with UP, a finding not replicated in our study. Our study showed that the mean CCT by Pentacam was on average $10 \text{ µm}$ higher than that of UP. This could be because of the fact that optical modalities such as Pentacam pachymeter may include the precorneal tear film in the measurement of corneal thickness, whereas the ultrasound probe may displace the precorneal tear film and compress the epithelium.\(^\text{13}\)

SM, in contrast, was found to agree poorly with the other methods because it consistently underestimated CCT measurements. We found that the CCT measurement by SM was $20 \text{ µm}$ thinner than that of UP. This is consistent with previous studies using Topcon SP-3000P. Almubrad et al.\(^\text{10}\) found in their study that the CCTs measured were $28$ and $33 \text{ µm}$ thinner than those of UP in sessions 1 and 2, respectively. Similarly, Gonzalez-Perez et al.\(^\text{3}\) also reported that the CCTs were $25 \text{ µm}$ thinner than that of UP and $23 \text{ µm}$ thinner than that of Pentacam.
The exact reason for this difference is unclear, although most authors attribute it to the different operating principles of the devices. UP has been said to be less accurate because of the effect of corneal indentation and topical anesthesia, displacement of the precorneal tear film, and a variable posterior reflection point between the Descemet membrane and anterior chamber.9 Despite these, results from various studies including ours seem to indicate otherwise: that the CCT measurement with UP has good agreement with other noncontact optical pachymetry devices like Pentacam and OLCR and that SM, although precise, appears to be less accurate. Módis et al22 explain that this may be because noncontact specular images are affected by the anterior corneal refractive power and the variation in air–corneal refractive indices.

Whereas agreement analysis studies the similarity of measurements between devices, repeatability measures the precision of a device. In our study, all 4 methods produced good intraobserver repeatability, with OLCR showing the greatest repeatability and Pentacam showing the poorest. This is consistent with other studies. Barkana et al13 demonstrated the coefficient of repeatability in the order similar to ours: highest with OLCR, followed by UP and Pentacam. The repeatability of measurements in UP mainly depend on examiner expertise. However, in Pentacam, the alignment of the measurement is not affected by the examiner. The repeatability mainly depends on the fixation of the examinee in this method. These differences might also be affected by the number of sampling points, variations in corneal curvature along the meridian, eye microsaccade, and the uneven distribution of the precorneal tear film. Almubrad et al10 also found that SM had better repeatability compared with UP. Among patients with keratoconus, de Sanctis et al23 showed that Pentacam yielded better repeatability compared with UP. Table 2 summarizes the studies that reported their coefficient of repeatability of the various pachymeters. For comparison, we have recalculated the values of their given repeatability coefficients based on the repeatability coefficient formula used in this article.

Besides reliability studies, measurement time is an important factor to consider when choosing an appropriate pachymetric device. Quicker measurement time would translate to better patient comfort and reduce consultation time. From our study, we found that the duration per measurement was fastest with UP, followed by SM, OLCR, and Pentacam. This finding has not been reported in similar studies previously. We believe measurement time is clinically relevant and future studies can be conducted to confirm the findings of our study.

Ultrasonic pachymeters are popular because, besides other advantages, they give quick measurement. However, as the factory setting of our current UP model requires 9 measurements, this makes the total time taken longer than a single reading by the other devices. In contrast, this setting reduces systematic errors by requiring repeated measurements, which can be seen as an advantage. Furthermore, based on Figure 3, there are noticeably more outliers for the noncontact SM, Pentacam, and OLCR methods. Thus, measurement time with handheld UP is more consistent.

In our study, we found Pentacam to be the slowest because of the time taken for proper alignment. It requires the subject to fixate for 1.0 to 2.0 seconds. Suboptimal scans from blinking or eye movements were discarded and repeated. Furthermore, our study subjects were older compared with the other studies, and hence, they may have more difficulty completing the examination. Our experience with both SM and OLCR showed easier and quicker time for proper alignment. Additionally, the finer alignment and image capture for SM are automated, thereby reducing the overall measurement time.

In conclusion, with the many different technologies to choose from, the pachymeter of choice would be one that is accurate, precise, and quick. From the 4 devices that were studied, we found that CCT measurements between OLCR–UP and OLCR–Pentacam are comparable and can be used interchangeably in clinical practice. SM, however, underestimates CCT values by 20 to 30 μm compared with the other methods. OLCR was noted to give the highest repeatability and was relatively quick, whereas Pentacam had the lowest repeatability and took the longest time to measure.

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