Comparison of Central corneal thickness by ultrasound pachymetry, oculus pentacam and specular microscope in normal cornea

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Abstract

Background: Precision of central corneal thickness measurement is important because many diagnostic and therapeutic decisions based on it. There are various methods for central corneal thickness measurement, which differ in their operating principles and technology beside the difference in their advantages and limitation.

Purpose: To compare three methods of central corneal thickness (CCT) measurements namely, OCULUS Pentacam, non-contact specular microscope (Topcon SP-3000P) and ultrasound pachymetry (Tomey SP-3000) in terms of their agreement, correlation and interchangeability.

Methods: Central corneal thickness (CCT) was measured in 400 eyes of 200 healthy subjects by different examiners. The methods used were as follow: Pentacam rotating Scheimpflug photography system (Oculus Inc, Wetzlar, Germany), non-contact specular microscopy (NCSM; Topcon SP-3000P; Topcon Corporation, Tokyo, Japan), and Ultrasonic Pachymetry (USP; SP-3000 Tomey Corporation, Nagoya, Japan).

Results: The mean age (±SD) of the subjects was 35.2 (±9.5) years. The mean CCTs (±SD) for ultrasound pachymetry, Pentacam and non-contact specular microscope were 544.4 (±23.7), 548.6 (±24.4) and 509.8 (±27.4) µm, respectively. Correlation was highest for ultrasound pachymetry-Pentacam, followed by ultrasound pachymetry-non-contact specular microscope and Pentacam-non-contact specular microscope. The Bland-Altman plots showed closest agreement for ultrasound pachymetry-Pentacam while non-contact specular microscope had the poorest agreement with the other two methods. Central corneal thickness measured by non-contact specular microscope was about 34 and 38 µm thinner than ultrasound pachymetry and Pentacam respectively.

Conclusions: Central corneal thickness measurements between ultrasound pachymetry-Pentacam were comparable but cannot be used interchangeably in clinical practice. While, non-contact specular microscope underestimates central corneal thickness compared with the other two methods.

Key words: central corneal thickness, ultrasound pachymetry, pentacam, specular microscopy

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Introduction

The cornea is a transparent avascular tissue with a smooth, convex surface and concave inner surface. The cornea must be transparent, refract light, contain the intraocular pressure and provide a protective interface with the environment. It is an excellent example of the structural characteristics that a tissue needs to fulfill its dual role of transparency and mechanical support.¹,²,³,⁴ The cornea consists of Epithelium, Bowman's layer, Stroma, Descemet’s membrane, and Endothelium. Pachymetry is term used for the measurement of corneal thickness.¹ A large meta-analysis of 230 data sets found the normal CCT to be 536 µm (SD 31 µm). A meta-analysis of all cross-sectional and Annals of Tropical Medicine & Public Health http://doi.org/10.36295/ASRO.2020.231021
longitudinal corneal thickness studies over a 30-year time period showed that no significant age-related change in central corneal thickness occurred beyond the infant years. It has become a routine and is increasingly important in ophthalmic practice. Refractive surgeons invariably use central corneal thickness (CCT) in planning surgery, as adequate thickness is key in reducing the risk of developing post-refractive ectasia. Among patients with the condition termed ocular hypertension, which is elevated IOP in the absence of identifiable optic nerve damage or visual field loss, lower CCT has been found to be an important risk factor for progression to glaucoma. Similarly, among patients with open angle glaucoma (OAG) with higher baseline IOPs, lower CCT is a risk factor for disease progression. This increased risk for progression can be explained, in part, by the fact that the true IOP in eyes with lower CCT is higher than that measured by Goldmann tonometry. However, low CCT may be a biomarker for disease susceptibility.

Pachymetry can also be used to assess corneal hydration and the function of the corneal endothelium in its dual role as a barrier to aqueous humor and as a metabolic pump. Corneal pachymetry is useful in monitoring the functional health of the corneal endothelium in corneal transplants when performed serially. Corneal pachymetry is valuable in determining and monitoring abnormalities in corneal structure and/or function, including disorders characterized by corneal thinning such as keratoconus and pellucid marginal corneal degeneration, and by corneal thickening including endothelial dysfunction due to Fuchs endothelial corneal dystrophy and herpetic disciform keratitis. In contact lens wear, pachymetry can be used to assess corneal edema. Corneal edema and hypoxia can develop in daily wear, extended wear and therapeutic lens patients. Although absolute pachymetry measurements are difficult to interpret given the wide range of normal values in the general population, serial pachymetry measurements are an excellent measure of corneal endothelial cell layer function.

There are two types of pachymetric techniques:

**A. Spot measurements:** These technologies include traditional optical pachymetry, specular, confocal microscopy, ultrasound pachymetry, and optical low-coherence reflectometry.

**B. Wide area mapping:** These provide the capability to map a wide area of the cornea. Pachymetric mapping technologies include slit scanning optical pachymetry, pentacam and very high-frequency ultrasound imaging. Pachymetric mapping provides several advantages over spot measurements. Mapping can reveal abnormal patterns such as keratoconus and pellucid marginal degeneration. It also allows preoperative planning for surgeries that primarily do not concern just the center of the cornea, such as astigmatic keratotomy.

The aim of the study is to compare and analyze agreement and interchangeability between three different instruments (ultrasound pachymetry, Pentacam, non-contact specular microscope) each based on a different technique for central corneal thickness (CCT) measurement.

**Subjects and methods**

In this prospective comparative study, 400 eyes of 200 healthy subjects were enrolled, including staff members volunteers, candidates for refractive surgery and attendants for routine ophthalmological examination. Study was carried out during the period from May 2016 till the first of March 2017 at Ibn Al-Haitham Eye Teaching Hospital in Baghdad. The inclusion criteria were: best-corrected visual acuity (BCVA) of 6/6 or better with Snellen chart, clear cornea and absence of corneal pathology by history and undilated eye exam. Exclusion criteria included history of any ocular surgery or anterior segment pathology, current topical medication and any external eye infection. Verbal informed consent was obtained from all the subjects after explanation of the study protocol and possible risks. All participants were subjected to comprehensive eye examinations which included: BCVA, pupil examination, IOP measurements, slit-lamp biomicroscopy, and undilated fundus examination.

**Devices used in this study**

A. Ultrasonic Pachymetry (USP) S P-3000 (Tomey Corporation, Nagoya, Japan)

This is one of the most commonly used method nowadays and is regarded as the gold standard. It utilizes ultrasound energy to measure CCT. Ultrasound Frequency 20MH.

B. (NB. Non-contact specular microscope (NCSM) Topcon SP-3000P (Topcon Corporation, Tokyo, Japan)

The newer non-contact machines are better as they do not touch the cornea. Being quick and easy, they are also equipped with auto-focus and image analysis program, captures an image of the corneal endothelium and assesses corneal thickness simultaneously.

C. Pentacam (Oculus Inc, Wetzlar, Germany)

The Pentacam instrument uses a rotating Scheimpflug camera system and provides three dimensional scanning of the whole anterior segment of the eye. Pentacam can provide information regarding corneal pachymetry, anterior and
posterior corneal topography, anterior chamber (depth, volume, and angle) and lens density. The non-contact measuring process with the Pentacam system takes two seconds.

All measurements were done at the same time of the day, between 10:00 am and 2:00 pm, within 45 minutes. Measurements started with Pentacam, then NCSM, and lastly with USP by masked multiple examiners.

For Pentacam, subjects look at fixation target, then asked to blink before measurement, the measurement automatically started whenever correct alignment with the corneal apex and focus was achieved. CCT was taken if the quality specification record OK.

For NCSM, subjects were positioned on the headrest and instructed to look straight ahead into the built-in fixation targets within the device. CCT values were accepted if the endothelial cells were in clear focus.

After completing the non-contact examination, USP was used. The cornea was first anesthetized with one drop of 0.5% topical proparacaine hydrochloride (Alcaine; Alcon, Belgium). The subject was seated on the chair, asked to look straight ahead, 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 measurements were obtained, the mean of the three measurements was taken. The ultrasound probe was sterilized with alcohol before each individual.

**Statistical Analysis**

1. Statistical analysis was performed using the SPSS software (version 22).
2. The descriptive statistics were presented as mean ± standard deviation (SD).
3. The correlation between the measurements using three instruments was calculated and expressed as (Pearson correlation coefficients) indicates the degree to which measurements in the different devices resemble each other.
4. The Bland-Altman plot is a graphical method used to assess the agreement of measurements between pairs of (USP-Pentacam; USP-NCSM; Pentacam-NCSM).
5. paired t-test analysis was performed to assess difference between pairs (USP-Pentacam; USP-NCSM; Pentacam-NCSM).

*P*-value of ≤ 0.05 was considered as significant.

**Results**

The study included 400 eyes of 200 volunteers. The mean age of the subjects (±SD) was 35.2 (±9.5) years (range: 18–58 years). 45% of the participants were female while 55% were male. Results of CCT for USP, Pentacam and NCSM were shown in table-1.

**Table-1: mean and standard deviation of CCT for each method**

<table>
<thead>
<tr>
<th>Method of measurement</th>
<th>Mean</th>
<th>Standard deviation</th>
</tr>
</thead>
<tbody>
<tr>
<td>USP</td>
<td>544.40</td>
<td>23.78</td>
</tr>
<tr>
<td>Pentacam</td>
<td>548.65</td>
<td>24.45</td>
</tr>
<tr>
<td>NCSM</td>
<td>509.85</td>
<td>27.48</td>
</tr>
</tbody>
</table>

Pearson’s correlation coefficient test showed correlation between each pair of instruments; USP and Pentacam, USP and NCSM, and Pentacam and NCSM were shown in Table 2.

**Table-2: Mean Difference (SD), 95% LoA, and Pearson Correlation Between the Pairs of Methods**

<table>
<thead>
<tr>
<th>Comparisons Pairs</th>
<th>Mean Difference (SD)</th>
<th>95% LoA Difference (P*)</th>
<th>Significance</th>
<th>Correlation</th>
</tr>
</thead>
</table>

The agreement between pairs of methods was examined using the Bland-Altman plots, based on the values in Table-2. Bland-Altman plots have been produced in Figure 2,3,4 to analyze the agreement between the three methods.
Figure 2: Bland-Altman plot comparing mean CCT and CCT difference (USP vs. Pentacam)

Figure 3: Bland-Altman plot comparing mean CCT and CCT difference (USP vs. NCSM)
Precision of CCT measurement is important clinically because many diagnostic and therapeutic decisions based on it. There are various methods for central corneal thickness measurement, each with its advantages and limitations. In this study, we compared agreement and interchangeability of three different methods: USP, Pentacam and NCSM.

Mean CCT measurements using three different methods showed approximately normal distribution as shown on histogram figure-1. We found that USP-Pentacam showed the highest correlation followed by USP-NCSM and Pentacam-NCSM.

Clearly, USP-Pentacam had the closest agreement, followed by NCSM-Pentacam, and lastly USP-NCSM showed least agreement, as confirmed by the Bland-Altman plot. NCSM found to have the poorest agreement with the other two methods. Measurements with NCSM were thinner than those of USP and Pentacam respectively. Figure (2, 3, 4).

Mean CCT value in this study was 544.40 ± 23.78μm using ultrasonic pachymeter, this result comparable to CCT values in two studies [17, 18].

The comparison of USP with Pentacam has been studied by many authors; Farhood et.al. compared ultrasound pachymetry and Pentacam for the measurement of CCT in normal eyes as control group in their study [17]. Tai et.al. compared three different devices for measuring CCT with USP and regarding USP-Pentacam found narrow limit of agreement and high correlation [19]. Mohamed et.al. concluded that with respect to the two standard methods of CCT measurements, the USP and Pentacam, the difference was about 10μm in the normal eyes group with USP was thinner [20].

Other few studies show different results. Amed [21] claimed that USP significantly overestimates the corneal thickness and eyes, have higher Pentacam CCT values than ultrasonic values, but the differences were not statistically significant. This might be due to small sample size.

Although USP-Pentacam mean difference was significant in our study, which could be due to sample size, but we found good agreement and high correlation between the two methods.

Discussion

Figure 4: Bland-Altman plot comparing mean CCT and CCT difference (Pentacam vs. NCSM)

Thinner CCT reading with USP in comparison with Pentacam that seen in many studies, including this study, may be attributed to that USP causes tear film dislocation and epithelium compression, resulting in CCT measurements that are lower, while Pentacam measure tear film regarding it as a part of CCT.

The results for comparing USP-NCSM showed that mean difference was 34.54µm with \( p\)-value < 0.05, Pearson correlation coefficient \( (r = 0.81) \) and 95% LoA (1.30 to 67.78), these results mean that NCSM underestimated CCT, USP-NCSM correlation lower than USP-Pentacam and limit of agreement also better for USP-Pentacam.

Our results are comparable with Almubrad \textit{et.al}. study which included repeatability and reproducibility and revealed that NCSM gave CCT reading thinner by (28.17µm and 32.81µm) for Session 1,2 respectively \cite{15}. They concluded that both of these devices are useful for assessing CCT.

Study by Calvo-Sanz \textit{et.al}. also comparable with our study and they concluded that CCT measurement obtained by NCSM reveals a very poor concordance versus the gold standard technique (USP), making the technique more suited to longitudinal follow-up of corneal pathology patients \cite{22}. Tai \textit{et.al}. compared CCT reading by (USP, Pentacam, OLCR and NCSM) concluded that "NCSM, is poorly agree with the other methods because it consistently underestimated CCT measurements\cite{19}.

On the other hand, few studies showed different results, Chalam. K \textit{et.al}. used different brands of specular microscopes and found that specular microscopy overestimates CCT by 8.69µm \cite{23}. The exact reason for this difference between (USP-NCSM) was unclear, although most authors attributed it to the different operating principles of the devices. This consistent difference is explained by the different operating principles of each device: NCSM uses light reflection and USP uses ultrasound reflection at each interphase. The posterior limit of the ultrasound reflection located in the space between Descemet’s membrane and the anterior chamber whereas NCSM considers the posterior limit in the endothelial cells layer \cite{15}.

In this study, we thought that the exact point of light reflection in NCSM located in space anterior to Descemet's membrane, that is why NCSM always underestimated CCT by a value more than the thickness of endothelium and Descemet’s membrane.

The present study showed that NCSM underestimates CCT by 38.80µm in comparison with Pentacam \( (r = 0.79) \) and 95% LoA (7.60 to 69.9) which mean that there is correlation but NCSM constantly underestimates CCT by variable value. These results were comparable with Tai \textit{et.al}. who revealed that NCSM underestimates CCT by 30.57µm in comparison with Pentacam \cite{19}. Saleh \textit{et.al}. mentioned that NCSM underestimates CCT in normal and post-LASIK patients by about 40µm and 33µm respectively and the two methods were not interchangeable \cite{24}.

Bernardo \textit{et.al}. \cite{25} compared CCT measured by Pentacam with NCSM, and gave more detail regarding CCT measured with Pentacam as (corneal apex, pupil center, thinnest location). They found that NCSM underestimates CCT by a value around 34µm, these results were comparable with our results.

\textbf{Conclusion:} There are many devices for CCT measurement, operating principle and technology vary between these devices. The device of choice would be one that is accurate, safe, precise, quick with minimum disturbance for the patient.

This study which included three different methods of CCT measurement, revealed that USP-Pentacam were comparable regarding correlation and agreement in spite of the overestimation of CCT reading by Pentacam which should be kept in mind.

For this reason we concluded USP-Pentacam were comparable but not interchangeable and we recommend USP for more precise measurement.

NCSM, underestimated CCT in comparison with USP and Pentacam by 34µm, 38µm respectively beside that it showed wider limit of agreement in comparison with the other two devices, for these reasons we found that NCSM not recommended for precise CCT measurement.
References


