Comparison of Central Corneal Thickness Measurements by Ultrasound Pachymetry and Non-Contact Specular Microscopy in Normal Eyes

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Abstract
Central corneal thickness measurement plays a crucial role in the assessment and treatment of glaucoma and several corneal diseases in addition to its importance in refractive surgery management. 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. This study aims to compare central corneal thickness (CCT) values of healthy eyes measured by two common devices: ultrasound pachymetry (UP) and non-contact specular microscopy (NCSM) and to determine the average difference between the two measurements. The study was conducted in the ophthalmology outpatient clinic in Imam Al-Sadiq Hospital- Hilla city and included 99 healthy individuals (198 eyes) of both genders. Results indicated that NCSM tends to give thinner CCT values compared to UP while providing quicker, safer and more comfortable evaluation for corneal thickness in addition to corneal endothelial cell density.

1. Introduction
The cornea serves as the gateway for light beams. When passing through the cornea and lens, the light beams bend (refraction). As the beams strike the retina, they are converted into electrical and chemical energy, and the resulting signals are transmitted via the optic nerve to the brain, where they are analyzed and processed as an image. The cornea is approximately 0.5 mm thick, and the thickness increases gradually toward the periphery (0.7 to 0.9 mm). The cornea is composed of six layers: the epithelium and its basement membrane, Bowman layer, the stroma, Dua’s layer, Descemet membrane, and the endothelium. Besides three main cell types, epithelial cells, stromal keratocytes, and endothelial cells, the cornea is endowed with a heterogeneous population of accessory cells involved in its homeostasis [1, 2]. Central corneal thickness (CCT) measurement plays a major role in diagnostic and therapeutic approaches to corneal pathology and has an important impact on intraocular pressure readings. Precise measurements of corneal thickness are also important to evaluate the outcome of laser refractive surgical procedures, especially when considering enhancement surgery. Underestimation of corneal pachymetry may lead to exclusion of some of these
patients and, in general, to an overly conservative treatment plan. Conversely, overestimation may increase the risk of corneal ectasia in ineligible patients[3]. Pachymetry is a term used for the measurement of corneal thickness. 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. An ideal method of CCT measurement should be accurate, repeatable, reproducible, and safe, as well as easy and quick to perform [4]. Ultrasound pachymetry (UP) is considered as the gold standard technique for measuring CCT. It involves direct placement of ultrasound probe on the anterior corneal surface. Ultrasound waves are transmitted to the eye and then reflected back to the transducer from tissue interfaces which have different acoustic impedances, enabling the distance from the ultrasound probe at the anterior epithelial interface to determine the distance between itself and the endothelium–aqueous interface. The transducer determines the time difference between the pulse signals obtained at the two interfaces and computes the corneal thickness based on this time delay and the velocity of sound in corneal tissue, which is approximately 1580 m/s at body temperature. A direct measurement of corneal thickness is then displayed on a digital readout. Prior to undertaking ultrasonic pachymetry, the cornea is anaesthetized and the patient is slightly reclined [5].

Despite the many advantages, there are a few drawbacks to this method. First, the direct contact of the ultrasound probe with the patient’s cornea which cause discomfort to the patient and increase the possibility of infection risk. In addition, the probe must be placed perpendicularly to the corneal surface in order to secure an accurate reading. On the other hand, non-contact specular microscopy (NCSM) uses reflections of light from the anterior and posterior corneal surface as a means to distinguish corneal layers and measure central corneal thickness. Besides being quick and easy instrument to use, it is also equipped with auto-focus and image analysis program. In addition, NCSM reported to has more consistent reading from one operator to another [6, 7].

The aim of this study is to compare central corneal thickness (CCT) measurements taken with ultrasound pachymetry (US) and noncontact specular microscope (NCSM) and in normal eyes and to assess the agreement between the two devices.

2. Patients and methods
2.1 Subjects
In the present study, CCT measurements were taken, by both devices, from 99 individuals (198 eyes) who were attending Imam Sadiq hospital in Hilla city. The subjects included in the study consisted of 87 males (88%) and 12 females (12%) with age range between 15 and 57 years and mean age of 31.54 ± 9.89 years.

All subjects had a negative history of corneal diseases (such as trauma, keratoconus, etc.). Exclusion criteria were as follows: subjects who are uncooperative in the measurement of CCT by either devices, history of any ocular surgery or anterior segment pathology, current topical medication and any external eye infection.

2.2 Techniques and instrumentation
In all subjects, measurements started with non-contact specular microscopy (NCSM) (CEM-530, NIDEK Co., Ltd. Japan), and then followed with ultrasound pachymetry (UP) (US-4000, NIDEK Co., Ltd. Japan) since contact ultrasound pachymetry can affect the corneal structure. All measurements were performed by a single operator in order to avoid interobserver variations.

For NCSM, the subject was positioned with his or her chin on the chinrest and forehead against a headband. Automated mode low flash intensity pictures from the center of the cornea were taken while the subject focused on a fixation target. After the proper position of the alignment dot, circle, and bar on the screen, the picture was captured and printed out with numerical data, including corneal thickness.

For UP, the cornea was anaesthetized with Tetracaine Hydrochloride 1% w/v eye drops applied 2-3 minutes prior to measurement. The subject was seated on the chair and asked to look straight ahead while the measurements were taken by touching the pachymeter probe gently to the center of the cornea. The test was performed three times to each eye and the mean of the measurements was used as CCT.
2.3 Classification of Data

The difference in readings between the two devices were first calculated for all subjects regardless their age or sex. Then, the data collected were classified into five age groups and the reading differences between the two devices was calculated for each age group. Age groups were classified as follows (Table 1): 11–20 years, 21–30 years, 31–40 years, 41–50 years and 51–60 years.

3. Results and Discussion

The mean CCT measured with ultrasound pachymetry from the 99 subjects was 552.92 ± 21.91μm. In comparison, the mean CCT measured by non-contact specular microscopy was 549.59±21.437 μm (Table 1). The mean result for all subjects was approximately 3.3 μm thinner with NCSM than UP and this difference was statistically significant (p < 0.01) (Figure 1).

Table 1 Descriptive statistics for the central corneal thickness, as measured by the two different modalities

<table>
<thead>
<tr>
<th>Age Groups</th>
<th>No. of subjects</th>
<th>Mean CCT + SD (μm)</th>
<th>P value</th>
</tr>
</thead>
<tbody>
<tr>
<td></td>
<td></td>
<td>UP</td>
<td>NCSM</td>
</tr>
<tr>
<td>Total</td>
<td>99</td>
<td>552.92±21.91</td>
<td>549.59±21.437</td>
</tr>
<tr>
<td>11-20</td>
<td>15</td>
<td>552.6±23.99</td>
<td>548.93±21.31</td>
</tr>
<tr>
<td>21-30</td>
<td>35</td>
<td>552.65±21.196</td>
<td>547.84±22.76</td>
</tr>
<tr>
<td>31-40</td>
<td>28</td>
<td>554.16±21.143</td>
<td>548.66±18.249</td>
</tr>
<tr>
<td>41-50</td>
<td>18</td>
<td>550±22.95</td>
<td>552.36±24.454</td>
</tr>
<tr>
<td>51-60</td>
<td>3</td>
<td>564.17±23.18</td>
<td>565.33±8.115</td>
</tr>
</tbody>
</table>

Figure 1 CCT measurements by UP and NCSM (** = p <0.01)

The current study also demonstrated that there were significant differences in the CCT measured with US and NCSM in age groups 21-30 and 31-40 while other age groups showed no significant difference in CCT measurements between UP and NCSM (p >0.05) (Figure 2).
Figure 2 Differences in CCT measurements by UP and NCSM in different age groups (* = p <0.05)

The correlation ($r^2$) of CCT measurements obtained via UP and NCSM (Figure 3) was 0.479 which suggests weak agreement between the CCT measurements acquired through these two techniques.

Figure 3 Scatter plot display of UP with NCSM measurement of CCT

Accurate measurements of corneal thickness are essential for evaluating the outcome of laser refractive surgical procedures, especially when considering enhancement surgery. Underestimation of corneal pachymetry may lead to exclusion of some of these patients and, in general, to an overly conservative treatment plan. Conversely, overestimation may increase the risk of corneal ectasia in ineligible patients [3]. In this study, the measurements with UP were generally thicker than NCSM and these results agree with the findings of previous studies [3, 7–10]. These differences can be attributed to the different operating principles of the two devices. NCSM depend on the reflection of light, and the UP depend on the reflection of ultrasound from the anterior and posterior corneal surfaces. In UP, the exact posterior reflection point is not known; it may be located between Descemet’s membrane and the anterior chamber. If the reflection point is located at the anterior chamber, this will cause overestimation of the corneal thickness [7, 11].

Finally, the results indicated weak correlation ($r^2$) of CCT measurements obtained via UP and NCSM ($r^2= 0.479$). This result is inconsistent with the findings of Módis et al. [12] and Babbar et al. [8] which found strong correlation of CCT measurements between the two modalities ($r^2= 0.91$ and 0.88, respectively). As mentioned earlier, since UP is an operator depended device, errors in measurements could occur due to multiple reasons such as incorrect probe placement, differences in pressure applied during measurement and lack of a fixation light for gaze control which might affect the resulted measurements.

4. Conclusions
This study compared two commonly used devices for measuring central corneal thickness, the
ultrasound pachymetry and non-contact specular microscopy. While NCSM offers some distinct advantages over the UP (the gold standard for measuring corneal thickness) such as the opportunity to dispense the topical anaesthetic drops and measuring CCT without touching the corneal surface which means that the patient will be examined more safely and comfortably, it gave significantly lower CCT readings compared to UP in total subjects and in most of age groups, except for 41-50 and 51-60 groups where it gave slightly higher CCT readings than UP with no significance between the results. In addition, results have also shown weak correlation between the two modalities, thus these two devices cannot be used interchangeably in healthy patients.

Conflict of Interest
The authors declare that they have no conflict of interest.

References