Repeatability and Reproducibility of Central Corneal Thickness Measurement With Pentacam, Orbscan, and Ultrasound

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ABSTRACT: Purpose. The purpose of this study was to compare central corneal thickness (CCT) measurements obtained with a novel rotating Scheimpflug camera (Pentacam; Oculus) with scanning slit topography (Orbscan; Bausch & Lomb), and with ultrasound pachymetry (SP-2000; Tomey). Methods. CCT in 30 healthy eyes was measured twice with each modality by 2 independent observers in random order. The results from scanning slit topography are given both with and without multiplication with the “acoustic correction factor” of 0.92. In addition, the displayed images from the rotating Scheimpflug camera and scanning slit topography were used to calculate the signal difference-to-noise ratios (SD/N) between cornea and background signal. Results. The mean CCT values as determined with the different modalities (± standard deviation) were: 542 ± 29 μm, 576 ± 37 μm, 530 ± 34 μm, and 552 ± 32 μm for rotating Scheimpflug imaging, for uncorrected and for corrected scanning slit pachymetry, and for ultrasound, respectively. The differences between modalities (± 95% limits of agreement) were −9.8 ± 31 μm between rotating Scheimpflug and ultrasound, 24 ± 31.2 μm between scanning slit and ultrasound, and 33 ± 27 μm between scanning slit and rotating Scheimpflug imaging. The limits of agreement for within and between observer effects were within 4.2% of the absolute CCT values for scanning slit and ultrasound and within 2.2% for the rotating Scheimpflug imaging. The rotating Scheimpflug camera showed similar SD/N ratios but steeper edges of the corneal surfaces in the intensity profile plots. Conclusion. In the assessment of normal corneas, the Pentacam measured CCT values closer to ultrasound pachymetry and with less variability compared with Orbscan. The (interobserver) reproducibility with the Pentacam was highest of all 3 modalities. (Optom Vis Sci 2005;82:892–899)

Key Words: central corneal thickness, method comparison, optometry, Scheimpflug imaging, ultrasound pachymetry

High accuracy in the assessment of central corneal thickness (CCT) is primarily desirable in 3 circumstances: First, it is an integral part in planning keratorefractive procedures to avoid complications such as corneal ectasia. Second, CCT can be regarded as a correlate of the physiological condition of the corneal endothelium and used in the diagnosis of certain corneal diseases such as keratoconus and Fuchs dystrophy. Finally, the connection between decreased CCT and apparently decreased intraocular pressure readings has stimulated recent debate about the role of CCT in the early diagnosis of glaucoma.

In the course of the development of a variety of modalities to measure CCT, the mean thickness reported by various authors, even in normal eyes, has not been consistent. Although handheld ultrasound-based systems offer the advantages of portability and relative ease of use, they experience relatively higher interobserver variability, possibly as a result of difficulties in centration and alignment.

The need for topical anesthesia and contact of the probe with the cornea has led to the search for noninvasive alternative solutions without the risk of epithelial lesions or transmission of infection. Optical methods such as optical coherence tomography or scanning slit topography were designed to acquire morphologic information about several structures in the anterior chamber simultaneously, often used in the preoperative assessment in refractive surgery. However, several investigations showed a consistent overestimation of corneal thickness with such systems compared with ultrasound measurements, which led to the introduction of an acoustic correction factor to numerically reduce the measured values on such devices.

A novel apparatus capable of modeling the anterior chamber is the Pentacam (Oculus, Wetzlar, Germany). The system is based on...
a rotating Scheimpflug camera, which scans and measures the complete cornea and anterior chamber in approximately 2 seconds. Its reproducibility and accuracy in assessing CCT compared with traditional modalities have as yet not been established.

The purpose of the present study was to compare CCT measurements obtained with the rotating Scheimpflug camera with scanning slit topography and with ultrasound pachymetry to provide estimates for the error between measurements with the different modalities and of the reproducibility of measurements within and between observers.

METHODS

Thirty healthy volunteers (16 women and 14 men with a mean age of 31.5 years [standard deviation 3.8 years]) were recruited for the study. The study was performed in compliance with institutional and legal requirements. Informed consent was obtained in writing from all participants. All subjects had normal eyes without corneal abnormalities as verified by slit lamp examination. Soft contact lens wearers were included but were required not to wear contact lenses within 24 hours before the investigations.15,17 The refractive error was measured with an autorefractometer (model 597; Humphrey Systems, Dublin, CA). The mean spherical equivalent was \(-1.44 \pm 1.95 \) D. All measurements were taken on one randomly chosen eye per subject and at least 3 hours after awakening.6

Central corneal thickness was determined with 3 different modalities: (1) with a novel rotating Scheimpflug camera (Pentacam 70,700; Oculus, Wetzlar, Germany), (2) with scanning slit topography (Orbscan, version 4.00; Bausch & Lomb, Rochester, NY), and (3) with ultrasound pachymetry (Pachymeter SP-2000; Tomey, Erlangen, Germany). Each modality was carried out by 2 independent observers (BL, GS) blinded to all previous measurements of the study, who acquired 2 measurements on each eye with each of the modalities, respectively. The order of the examiners and of the modalities was randomly assigned to each eye; however, ultrasound pachymetry measurements were always scheduled last to avoid influence on the other modalities as a result of corneal flattening.

Rotating Scheimpflug Imaging

Rotating Scheimpflug imaging was performed with the patient seated using a chinrest and forehead strap. The patient was asked to keep both eyes open and to fixate on a blinking fixation target. The system uses a rotating Scheimpflug camera and a monochromatic slit light source (blue LED at 475 nm) that rotate together around the optical axis of the eye. Within 2 seconds, the system rotates 180° and acquires 25 images that contain 500 measurement points on the front and back corneal surfaces to draw a true elevation map. The software acquires the images as volume data, thus multiplanar reprojections allow the creation of axial and tangential maps. The thinnest value of corneal thickness was recorded as CCT.

Scanning Slit Topography

Scanning slit topography measured CCT by a noncontact pachymeter (Orbscan; Bausch & Lomb) operating under software version 4.00. Subjects were seated in typical position using the chinrest; the instrument was aligned and scanned the cornea. The
system software automatically detects the corneal anterior and posterior surface on the acquired images, compensates for differences in refraction from the corneal anterior surface using a ray trace algorithm, and calculates the corneal diameter over the whole surface. From these measurements, the thinnest value is automatically selected as CCT. Thickness measurements were recorded both with and without multiplication with an “acoustic factor” equal to 0.92, which had been proposed by the manufacturer and used in previous publications to compensate for the known offset of the Orbscan measurements compared with ultrasound measurements.

In both optical modalities, patient eye movement was constantly monitored and recorded by the respective system, and only measurements with <0.6 mm decentration between the optical axes of the eye and the instrument were included. Furthermore, it was ascertained that no eye in the series showed a corneal apex farther than 0.6 mm away from the optical axis of the eye.

### Ultrasound Pachymetry

CCT was measured using a handheld ultrasound pachymeter (SP-2000; Tomey, Nagoya, Japan) calibrated by the manufacturer. The instrument used an ultrasound velocity (acoustic index) of 1640 m/second. The cornea was anesthetized with topical 1% oxybuprocaine. The patient was brought into a faceup position on the examination chair and asked to fixate a target on the ceiling. The pachymeter probe was brought in light contact with the cornea centrally and perpendicularly. CCT was recorded as the thinnest value is automatically selected as CCT. Thickness measurements were recorded both with and without multiplication with the “acoustic correction factor” of 0.92 as suggested by the manufacturer.

### Image Analysis

In a subset of eyes, the displayed images from the scanning slit topography system and the rotating Scheimpflug camera (Fig. 1A, B) were analyzed on a standard personal computer in an 8-bit noncompressed format. Using public domain software (ImageJ 1.32; National Institutes of Health, Bethesda, MD), a line was drawn perpendicular to the corneal vertex, and intensity profiles along the line were recorded. To create a mean intensity profile throughout the cornea, the individual intensity profiles obtained with either modality were then numerically overlaid with their peaks aligned, and the mean intensity profiles for each modality was plotted (Fig. 1C, D). Furthermore, circular regions of interest (ROIs) measuring 500 μm in diameter were drawn in the cornea and in the adjacent background. For each ROI, mean pixel intensity and standard deviation was calculated by the software. Signal difference-to-noise ratios were determined by dividing the difference between cornea and background intensity (signal) by the standard deviation of the background intensity (noise).

### Statistical Analysis

Central corneal thickness was measured (1) with different measurements, (2) by different observers, and (3) with different modalities. Thus, the variance of CCT consists of (1) the variance of the CCT itself (i.e., the difference between the mean of all measurements and the mean of all measurements of that individual eye), (2) the variance of the extra error in CCT resulting from the observer, and (3) the variance of the error in individual measurements in a single observer.

Variances between the measurements and between the observers were examined using 2-factor analysis of variance (ANOVA) with repeated measurements (RM). One factor was the number of the measurement, the other factor the observer. Variances resulting from the different modalities were calculated using one-factor ANOVA with repeated measurements; the factor was the modality. For the between-modalities comparison, the mean value from all measurements of both observers in the respective modality was used.

To visualize the correlation between the difference between methods and the absolute values of CCT, data were presented graphically with Bland-Altman plots, in which for each pair of measurements obtained with 2 modalities, the difference of the values is plotted over the mean of the values. To compensate for correlation between CCT difference and average, the plots were logarithmically transformed so that CCT ratios were plotted over average CCT. Limits of agreement between modalities were calculated as mean difference of the log CCT values ± 1.96 standard deviations and backconversion using the exponential function.

The signal difference-to-noise measurements from the digitized images of the scanning slit topography system and the rotating Scheimpflug camera were compared with the paired t test at a level of significance of 0.05 (all calculations: SPSS 10.0; SPSS Inc., Chicago, IL).

### RESULTS

#### Device Effects

The mean values of CCT measurements and their standard deviations are shown in Table 1. The differences between the modalities and their confidence intervals are shown in Table 2. Uncorrected scanning slit topography measured the largest mean...
CCT, while rotating Scheimpflug imaging and ultrasound measured 6% (34 µm) and 4.3% (24 µm) shorter, respectively. The standard deviations of the respective modalities were similar. The scanning slit topography data are given as uncorrected data and after multiplication with the "acoustic correction factor" of 0.92.

The application of the "acoustic correction factor" to scanning slit topography data led to more conservative (thinner) measurements for CCT than with all other modalities (22 µm thinner than the values acquired with ultrasound pachymetry). The correlation between scanning slit topography and ultrasound decreased with the application of the correction factor. The signal difference-to-noise ratios as a measure for overall image quality did not differ significantly (mean Orbscan: 31.1, mean Pentacam: 29.7, 95% confidence interval [CI] of the difference: −9.3–12.1; p = 0.738, paired t test). In contrast, the intensity profiles through the corneal vertex obtained from the Pentacam images showed steeper edges, especially on the anterior corneal surface, than the Orbscan images. Rotating Scheimpflug imaging compared with ultrasound (Fig. 3D) showed both the smallest mean difference as well as the narrowest 95% limits of agreement. The Bland-Altman plots in the method comparisons (Fig. 3) showed a significant correlation between average CCT and CCT difference and have thus been transformed to logarithmic scale to provide constant 95% limits of agreement. In the observer comparison plots, no such correlation was observed.

Variability In and Between Observers

Table 3 shows the mean difference and the variability, expressed as the standard deviation of the difference and the 95% CI of the differences within and between observers in the respective modalities. No significant influences of either number of measurement or observer were found on the CCT measurements. Although the 3 modalities showed similar intraobserver variabilities, rotating Scheimpflug imaging showed the lowest interobserver variability, and scanning slit topography and ultrasound considerably higher values (Fig. 2). However, the 95% confidence interval of all differences did not exceed 8.5 µm for either modality. This equals an observer-related reproducibility of CCT measurements within 1.6%.

**DISCUSSION**

The assessment of CCT with different modalities shows considerable differences between modalities. In the present collective of 60 eyes of healthy European volunteers, CCT determined with scanning slit topography (Orbscan) was on average 20 µm (3.6%) thicker than with ultrasound pachymetry, and CCT determined with rotating Scheimpflug imaging (Pentacam) was on average 13 µm (2.4%) thinner than with ultrasound pachymetry.

Regarding differences between modalities in CCT measurements, 2 most relevant questions need to be addressed: (1) how reliably can we predict the differences between CCT measurements obtained with the respective modalities; and (2) what amount of uncertainty in CCT measurement will be clinically acceptable?

**Pentacam**

The Pentacam yielded the best between observer reproducibility of all modalities (Fig. 2), and CCT values that were closer to

| TABLE 2. | Mean differences between the modalities used to determine central corneal thickness, their standard deviations, confidence intervals, and limits of agreement (all values in µm) a |
|---|---|---|---|---|---|
| | Mean difference | Standard deviation | 95% confidence interval | 95% limits of agreement | 99% limits of agreement |
| Scanning slit-US pachy | 23.5 | 15.9 | 18.0, 29.0 | −7.8, 55.0 | −18.0, 65.0 |
| Rotating Scheimpflug-US pachy | −9.8 | 8.1 | −13.0, −6.9 | −26.0, 6.1 | −31.0, 11.0 |
| Scanning slit–rotating Scheimpflug | 28.0 | 13.6 | 28.0, 38.0 | 6.6, 60.0 | −1.8, 68.0 |
| Corrected scanning slit–US pachy | −22.6 | 14.6 | −28.0, −17.0 | −51.0, 6.1 | −60.0, 15.0 |
| Corrected scanning slit–rotating Scheimpflug | −12.8 | 11.7 | −17.0, −8.6 | −36.0, 10.2 | −43.0, 17.5 |

a Note that the 95% confidence interval estimates in which the mean difference in a similar collective will be, whereas the limit of agreement estimates in which a single observation can be expected. US, ultrasound.

| TABLE 3. | Mean difference, standard deviation of the difference, and 95% limits of agreement between measurements and between observers (in µm) within the 3 modalities of central corneal thickness measurement |
|---|---|---|---|---|---|
| | Rotating Scheimpflug imaging | Scanning slit topography | Ultrasound pachymetry |
| Difference between measurements | 1.0 | 1.2 | 0.3 |
| SD of difference between measurements | 6.1 | 6.9 | 3.6 |
| 95% limits of agreement between measurements | −11.0, 13.0 | −12.0, 14.0 | −6.7, 7.3 |
| Difference between observers | 0.1 | 1.4 | 2.8 |
| SD of difference between observers | 3.0 | 11.9 | 9.9 |
| 95% limits of agreement between observers | −6.0, 5.8 | 122.0, 25.0 | −17.0, 22.0 |

SD, standard deviation.
ultrasound and differences showed less variability than those obtained with (corrected or uncorrected) Orbscan (Fig. 3). A potential explanation may be the different sampling modes of Orbscan and Pentacam. The Pentacam acquires images during a 180° rotation around the optical axis so that each section runs through the corneal vertex, whereas the Orbscan performs a translational movement from side to side of the cornea, covering the vertex in only a few sections.

In the assessment of image quality, the Pentacam and Orbscan images showed similar signal difference-to-noise ratios of cornea versus background. However, the intensity profiles showed steeper corneal edge depiction by the Pentacam, thereby potentially contributing to a decrease in detection errors as a result of less blurred images. This may further explain the fact that in the present study, the Pentacam tended to give the smallest CCT values of the 3 modalities. However, the exact image processing algorithms both within Orbscan and Pentacam are proprietary company information, and internal processing algorithms might be based on different (i.e., higher resolution or contrast) datasets.

Orbscan

The differences between CCT measurements determined with scanning slit pachymetry and ultrasound have been extensively discussed. There seems to be a trend to higher CCT values obtained with Orbscan, at least in the European and American population. Some investigators report values close to 30 μm higher; others found smaller differences below 10 μm. These differences are in part the result of the fact that the latter studies multiplied the Orbscan results with the “acoustic correction factor” of 0.92, as suggested by the manufacturer, to compensate for the systematic difference between Orbscan and ultrasound measurements. The results for corrected Orbscan values are close to CCT measurements obtained with a calibrated confocal microscope, in which mean CCT was 39 μm thinner than when measured with ultrasound. However, as stated subsequently, any general factor applied to all measurements on a given system will not necessarily decrease the amount of uncertainty between modalities. The results of the present investigation are therefore given with and without the acoustic correction factor. The uncorrected Orbscan data were 20 μm thicker than ultrasound, and the corrected Orbscan values were 26 μm thinner. These results are similar to a previous study comparing Orbscan and ultrasound.

Like other optical pachymetry devices, the Orbscan requires clear reflections on the epithelial and endothelial corneal surfaces and homogeneous composition of the diverse optical media to obtain precise measurements. As such, its use is limited to corneas that are free of sources of light scattering or distortion such as opacities, scarring, deposits, or edema. There is no satisfactory explanation why systematic measurement differences between ultrasound and slit scanning pachymetry exist, but it seems likely that they are the result of different locations of the respective reflective interfaces in the cornea.

Ultrasound

Some authors regard ultrasound pachymetry as a “gold standard” for CCT, mainly because of its superiority to older mechan-
ical pachymeters (e.g., the Haag-Streit pachymeter). Although ultrasound has been reported to have good intraobserver reproducibility, a higher degree of variation has been described between observers. In the present study, the difference between ultrasound and scanning slit topography was on the lower end of the range reported by previous studies (Gherghel, Chakrabarti, Rainer). The assessment of variability is complicated by the fact that some investigators report variability as the expected ranges of mean measurements of groups equal in size to the study collective rather than expected changes of individual measurements. Difficulties with centration of the handheld ultrasound probe on the thinnest part of the cornea may additionally contribute to a bias toward larger measurements for CCT compared with optical methods.

Reliability of the Differences

Traditionally, differences in CCT measurements between observers and modalities are given as mean difference ± 95% CI. It would, however, be incorrect to conclude that 95% of the actually measured CCT differences will be within this interval. A more adequate interpretation of the 95% CI is that the likelihood to receive the observed data is equal or higher than 95% if the difference between the modalities in the whole population lies within this interval. An estimate for the interval in which 95% of the actual differences will be is the “limit of agreement” (mean ± 1.96 * SD for normally distributed data). This interval is considerably broader than the 95% CI of the difference, and it is likely that one in 20 patients will still have larger differences in CCT measurements.

Even if the mean CCT differences between observers or modalities are small or zero, a high standard deviation will broaden the 95% limits of agreement, and might bring the borders close to or beyond clinically relevant levels. In such cases, it will probably be unacceptable to have 5% of the patients outside these intervals, and
99% (or higher) limits of agreement will be needed (Table 3). For these reasons, conversion equations, as suggested by some authors and manufacturers,7,31 must remain unsatisfactory. Even if the systematic component of the measurement differences between 2 methods is fully compensated by the application of a formula, a high intra- or interobserver variability can still impede their comparability.

Clinical Implications of Error Levels

Errors in determining CCT are most likely to be clinical relevant in 2 applications: First, accurate CCT measurements are of increasing importance in the diagnosis of glaucoma. It is known that intraocular pressure (IOP) measurements, especially when taken by with applanation tonometry, are influenced by CCT. A 10% increase in CCT can result in an apparent IOP increase of 3.4 mm Hg on average and up to 10 mm Hg in patients with acute-onset disease.8

Second, monitoring CCT in patients after refractive surgery is of importance because postoperative eye pressure readings by applanation tonometry are lower than the preoperative measurements solely as a result of a thinner postoperative cornea rather than a real decrease in eye pressure. False low eye pressure readings pose the risk of delaying the diagnosis of future glaucoma in patients who undergo refractive surgery. Importantly, ultrasound assessment of CCT in patients after refractive surgery might be additionally biased because of changes in corneal acoustic impedance resulting from differences in stromal extracellular matrix metabolism32 and carries the potential for complications in the vulnerable postoperative phase.35

Furthermore, CCT measurement is integral part of the preoperative assessment of patients undergoing refractive surgery. In treating patients with laser in situ keratomileusis (LASIK), it has been suggested that a minimum of 250 μm of tissue remain beneath the lamellar flap after stromal ablation to ensure maintenance of corneal structural integrity.21 Given the amount of uncertainty in determining CCT, considerably more tissue would have to be left unablated to ensure this condition. This would be an especially important issue when treating eyes with higher myopic refractive errors and proportionally larger ablation depths.

The results of the present study suggest that in healthy corneas, the corrected Orbscan and the Pentacam tend to give more conservative estimates than ultrasound pachymetry. Compared with ultrasound, the optical methods can be expected to err on the lower side of CCT only by 11 to 15 μm on a 99% limit of agreement basis, i.e., only one in 100 patients will have an optical CCT reading that is more than 11 to 15 μm lower than it would have been with ultrasound.

CONCLUSION

Of 3 investigated modalities, the Pentacam showed the lowest interobserver variability, suggesting a high degree of reproducibility. All 3 modalities yielded similar values of repeatability. It is not known which modality is closest to the “true” values, and all 3 modalities differ from each other with a systematic and a stochastic component. Although (uncorrected) Orbscan yielded larger CCT values than ultrasound in accordance with previous studies, the Pentacam measured CCT thinner than ultrasound. The Pentacam values for CCT were closer to the ultrasound values than the Orbscan values; thus, we conclude that Pentacam can be regarded as valid in determining CCT in eyes with normal cornea as the other modalities. The validity of Pentacam measurements of CCT in diseased corneas is currently under investigation.

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