Precision of High Definition Spectral-Domain Optical Coherence Tomography for Measuring Central Corneal Thickness

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PURPOSE. This study was intended to assess the reliability of central corneal thickness (CCT) measurements using Cirrus high-definition optical coherence tomography (HD-OCT) in healthy subjects and its accuracy compared with ultrasonic pachymetry.

METHODS. Seventy-seven consecutive subjects were recruited for evaluating repeatability, and agreement between two examiners. To analyze repeatability, one examiner measured 77 eyes four times in succession. To study agreement between two observers, a second independently trained examiner obtained another CCT measurement. We also measured eyes in a subgroup of 20 patients using standard ultrasonic pachymetry. Within-subject standard deviation (Sw), coefficient of variation (CV), limits of agreement (LoA), and intraclass correlation coefficient (ICC) data were obtained.

RESULTS. For repeatability, the Sw and precision (1.96 × Sw) were 4.86 and 9.52 μm, respectively. Intraobserver CV was 0.89% and the ICC was 0.98 (95% confidence interval [CI], 0.97–0.99). For agreement between two examiners, the Sw and precision were 7.58 and 14.85 μm, respectively; the CV was 1.40%. The mean difference between observers was −0.13 μm (95% CI, −1.85 to 1.58; P = 0.87). The width of the LoA was 29.64 μm. Median difference between Cirrus HD-OCT and ultrasound CCT measurements was −4.5 μm (interquartile range, −7.0–0.0; P = 0.04).

CONCLUSIONS. Cirrus HD-OCT provides repeatable CCT measurements, good agreement between two independently trained examiners, and its systematic bias compared to ultrasonic pachymetry is clinically negligible. Therefore, research laboratories and eye clinics using Cirrus HD-OCT as a diagnostic imaging method, can also benefit from a reliable noncontact pachymeter when counseling patients with glaucoma and those undergoing corneal and refractive surgeries. (Invest Ophtalmol Vis Sci. 2012;53:1752–1757) DOI:10.1167/iovs.11-9033

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Central corneal thickness (CCT) measurements are of paramount importance for diagnostic and therapeutic purposes. A reliable CCT measurement is required to monitor anterior segment anomalies, such as corneal ectasia2 and corneal edema,3 and for accurate diagnosis of ocular hypertension and glaucoma.4 Furthermore, the CCT measurement is critical when counseling candidates for primary excimer laser ablation5 and enhancement procedures and when planning phototherapeutic keratectomy procedures.6 Several techniques are available for measuring the CCT. The current gold standard is conventional ultrasonic pachymetry because of its established reliability and utility;7 however, this technique requires use of a probe contact, which has several shortcomings because of the contact between the probe and the eye: instillation of topical anesthesia, increased likelihood of patient discomfort, and risk of microbial contamination and epithelial alterations.7,8 In addition, measurement accuracy depends on the amount of epithelial indentation and the exact axial placement of the probe relative to the center of the corne.9,10 Therefore, noncontact methods are preferable for corneal biome, and alternative techniques such as scanning-slit technology,11 a rotating Scheimpflug camera,12 interferometry,13 corneal confocal microscopy, noncontact specular microscopy,14 and optical coherence tomography (OCT)15–19 are being used increasingly as diagnostic tools to measure the CCT.

OCT uses coherence interferometry and optical backscattered light to achieve high-resolution cross-sectional images of ocular structures in vivo.20 OCT currently is the most frequently used method for diagnosing retinal anomalies22,23; however, its use for assessing the anterior segment has increased during the last years.16,18,20,21 The latest generations of OCT (i.e., Fourier and spectral-domain (SD) OCT) allow acquisition of more data in a shorter time and provide three-dimensional image analysis with increased axial resolution.24 Cirrus HD-OCT (Carl Zeiss Meditec, Inc., Dublin, CA) is based on SD-OCT technology and has a scan speed of 27,000 A-scans per second and an axial resolution of 5 μm.25 Because of these features, it is currently used to diagnose several posterior segment anomalies such as age-related macular degeneration (AMD),22 diabetic retinopathy,26 central serous chorioretinopathy,27 epiretinal membranes,28 and glaucoma.29 Cirrus HD-OCT also can image structures within the anterior segment by changing the OCT beam focus30; thus, it may be advantageous for the posterior segment as well as the anterior segment.

The reliability of the measurements obtained by any ophthalmic instrument should be determined to avoid misdiagnosis or erroneous treatment based on the readings. The test–retest variability of Cirrus HD-OCT for measuring the macular and peripapillary retinal nerve fiber layer thickness in AMD and glaucomatous eyes, respectively, has been reported.22,23 Nevertheless, to the best of our knowledge, the...
reliability of Cirrus HD-OCT for measuring the CCT has not been investigated, and no published report of the ability of Cirrus HD-OCT to image the cornea has been published. Therefore, both researchers and clinicians using Cirrus HD-OCT as a diagnostic imaging method, can also benefit from a reliable noncontact pachymeter when assessing glaucoma or cornea patients, and in refractive surgery.

METHODS

All procedures were performed in accordance with the Declaration of Helsinki. All candidates received detailed information about the nature of the investigation and provided written informed consent. The institutional ethics committee approved this study.

Exclusion criteria included subjects with a history of corneal surgery, contact lens wear, suspected clinical and subclinical keratoc-tasia, active anterior segment disease, ocular pathology that might alter the optical quality or preclude proper viewing of the internal fixation target of the instrument, and a best-corrected visual acuity below 20/40. Before inclusion in the study, all eyes underwent a complete ophthalmic examination that included measurement of the manifest refraction, videokeratography, slit-lamp microscopy, applanation tonometry, and indirect ophthalmoscopy.

Optical Coherence Tomography Imaging

Cirrus HD-OCT is primarily used to image and measure structures in the posterior eye. By changing the focus of the OCT beam (840 nm), it also can image and measure the corneal thickness as the user manual indicates. Scanning with the Cirrus HD-OCT was performed using the five-line raster scan protocol that produces five horizontal scan lines 3 mm long separated by 250 μm; each scan line is comprised of 4096 A-scans. We selected this protocol because it provides higher resolution than the horizontal high-definition scan of the 512 × 128-cube scan protocol (1024 A-scans). Thus, it was easier for the practitioner to manually perform the CCT measurement because the corneal resolution is higher and the caliper tool can be placed more accurately.

After the patient was seated and properly aligned, he or she was instructed to stare at an internal fixation target during image acquisition. One eye of each subject was selected randomly for CCT measurement. Subjects were realigned after each OCT scan. Only images with signal strength equal to or higher than seven were evaluated. Examinations were carried out from 10:00 AM to 2:00 PM to minimize the effect of diurnal variations of the corneal thickness. The CCT was measured manually with the caliper tool in the cross-line scan; the vertical distance between the two indicators of the caliper tool was considered the CCT. The CCT measurements were always manually performed at the corneal apex (Fig. 1). Two different examiners (MECP and SMA) obtained and manually gauged CCT measurements to evaluate Cirrus HD-OCT intraobserver repeatability and agreement between two observers.

After the Cirrus HD-OCT CCT measurements were performed, the corneas of the first 20 consecutive subjects were anesthetized with one drop of 0.1% tetracaine combined with 0.4% oxybuprocaine (Alcon, Barcelona, Spain) before the ultrasonic CCT measurements were performed to evaluate the accuracy of the CCT measurement using...
Cirrus HD-OCT. A third experienced examiner (DIC) who was masked to the Cirrus HD-OCT CCT measurements placed manually the ultrasonic probe of the Corneogage Plus II (Sonogage Inc., Cleveland, OH) as perpendicularly as possible to the center of the cornea, and the subjects were instructed to stare at a distant target. Five consecutive CCT measurements were obtained and averaged for comparison with the Cirrus HD-OCT values.

**Statistical Analyses**

To investigate the intraobserver repeatability, the first examiner applied independent test results using the same method on the same subject and the same equipment with the shortest time possible between successive sets of readings. This first examiner performed four consecutive examinations in 77 eyes after ensuring proper focusing and alignment.

To calculate the intraobserver repeatability, the within-subject standard deviation ($S_w$) of four consecutive measurements was calculated by obtaining the square root of the variance, referred to as the residual mean square, in one-way analysis of variance. The precision, from a statistical standpoint, is the difference between a subject’s measurement and the true value (average value that would be calculated the intrasession coefficient of variation ($CV_w$)). The limits of agreement (LoA) were defined as the mean difference in the Cirrus HD-OCT values.

The intraobserver overall mean CCT measurement was $541.78 \pm 35.37 \mu m$ (range, 481–623 \mu m). The intraobserver $S_w$, precision, and reproducibility values were 4.86, 9.52, and 13.46 \mu m, respectively; the intraobserver $CV_w$ was 0.89%. The ICC for the repeatability was 0.98 (95% confidence interval [CI], 0.97–0.99).

The overall mean CCT measurement in the analysis of agreement between two observers was $541.71 \pm 35.35 \mu m$ (range, 480–619 \mu m). Their $S_w$, precision, and reproducibility values were 7.58, 14.89, and 20.99 \mu m, respectively; and their $CV_w$ was 1.4%. There was no statistical difference between the set of measurements obtained by each examiner ($P = 0.87$). The mean difference between observers was $-0.15 \mu m$ (95% CI, $-1.85$ to $1.58$).

A Bland-Altman plot created to assess the difference in individual measurement as a function of the mean of two measurements (Fig. 2) showed good agreement between the examiners; the width of the LoA was good. The upper limit of the LoA was 14.69 (95% CI, 11.74–17.63), the lower limit was $-14.95$ (95% CI, $-17.90$ to $-12.01$); thus, the width of the LoA was 29.64 \mu m.

Mean Cirrus HD-OCT and US CCT measurements in the subgroup of 20 subjects were $544.0 \pm 28.16$ and $547.7 \pm 29.03 \mu m$, respectively. The distribution of the differences between both devices was not normal (Shapiro-Wilk test, $P = 0.001$). The median value of the difference between devices was $-4.5$ \mu m (IR, $-7.0$ to $0.0$; range, $-2.00$ to $+18.00$), which was statistically significant ($P = 0.04$).

**Discussion**

CCT measurements have wide diagnostic applications. Regarding glaucoma diagnosis, it has been reported that thick or thin corneal pachymetry is clinically correlated with intraocular pressure (IOP) readings. In addition, Gordon et al. reported that each 40\mu m reduction in CCT is associated with a relative risk of 1.71 for development of primary open-angle
Reliability of Cirrus HD-OCT Pachymetry

Moreover, in the current study, we also evaluated the agreement between two independently trained examiners when measuring CCT. This analysis is extremely important because the same practitioners do not always perform the same diagnostic tests in the daily clinic. As expected, because of the inherent bias of the manual measurement method, the agreement outcomes were not as good as the repeatability outcomes; however, we did not find a significant difference between the practitioners. Moreover, the width of the LoA was acceptable considering that a 20-µm measurement error results in a clinically allowable error of 1 mm Hg in the Goldmann applanation tonometric IOP measurement.42 In addition, the scatterplot (Fig. 1) after Bland-Altman analysis did not show an association between the mean magnitudes and the differences in the CCT measurement between observers; thus, we did not detect any tendency with the CCT magnitude.

Other authors also have considered the importance of assessing the interobserver reliability of the OCT CCT measurements. Using the RTVue, Chen et al.44 reported an interobserver CV of only 0.45% and a narrow width of 95% LoA (10.2 µm). Mohamed et al.21 reported an interobserver CV of 0.1% when they studied the variability of CCT measurements within the 2-mm central area using Visante OCT. Our interobserver CV value (1.4%) reporting the agreement between two examiners was higher than those reported by Chen et al.44 and Mohamed et al.21 as might be expected, because Visante OCT and RTVue calculate the CCT measurements automatically instead of manually as the Cirrus HD-OCT does. Furthermore, RTVue and Visante OCT provide average central corneal values; thus, the variability should be lower than when measuring only one point (corneal apex) as in the current study.

The outcomes of the aforementioned studies have shown that SD-OCT devices provide better reliability values than TD-OCT values, as expected. First, the higher axial resolution of SD-OCT provides enhanced images because of higher reflectivity that improves edge detection; thus, either automatic or manual CCT measurements can be performed more accurately. Moreover, rapid acquisition scanning minimizes ocular movement artifacts and might make ocular movement negligible during measurement, which also accounts for lower variability.18 Therefore, SD-OCT devices might become the gold standard for measuring CCT because clinicians, researchers and patients demand noninvasive reliable procedures.

To establish the accuracy of Cirrus HD-OCT when measuring the central pachymetry, we also performed ultrasonic CCT gauging. Cirrus HD-OCT significantly (P = 0.04) underestimated the CCT measurements compared with ultrasonic pachymetry in a pilot study of 20 subjects. However, the median value (4.50 µm) of the difference between devices can be considered clinically irrelevant. Several authors have already reported discrepancies between SD-OCT and ultrasonic pachymetry. Ishihazawa et al.,7 who measured the CCT using SD-OCT and ultrasonic pachymetry in healthy corneas, found a mean underestimation of 14 ± 8 µm when using the RTVue. In contrast, Chen et al.44 using the same SD-OCT, reported an overestimation of 5.63 ± 10.75 µm using the RTVue. Nam et al.45 also found higher pachymetry values for the RTVue, 12.8 and 13.7 µm, depending on the centration of the CCT measurement, in the pupillary center and corneal vertex, respectively. These discrepancies between authors12,44 when comparing both methods are likely to arise because ultrasonic pachymetry is highly examiner dependent.45

The current study was the first to address Cirrus HD-OCT CCT measurement reliability; nonetheless, other authors have reported variability of other types of SD-OCT and time-domain (TD)-OCT devices when measuring pachymetry. Huang et al.18 studied the interobserver repeatability of an anterior segment TD-OCT (Visante OCT, Zeiss Meditec, Dublin, CA) and a SD-OCT (RTVue, Optovue, Inc., Fremont, CA) within the 2-mm central area and obtained a poorer CVw for the Visante OCT (1.02%) than our value for Cirrus HD-OCT (0.89%). However, the RTVue value (0.72%) was superior. Nevertheless, RTVue provides the average of the corneal thickness in the central zone instead of a single-point thickness.12 Nam et al.42 and Li et al.6 reported even better interobserver RTVue CVw values of 0.31% and 0.32%, respectively. Li et al.16 studied the measurement reliability of Visante OCT and a slit-lamp OCT (SL-OCT, Heidelberg Engineering, Dossenheim, Germany) for measuring the CCT automatically and manually. For Visante OCT, they reported CVw values of 0.9% and 1.2% for automatic and manual measurements, respectively; while for the SL-OCT, the CVw was exactly the same for both procedures (CVw = 1.0%). Thus, these authors showed that manual CCT measurement also can provide highly reliable results. Day-to-day variability has been also studied by Prakash et al.17 who reported excellent ICC values for Visante (0.962) and RTVue OCT (0.999), which are similar to our intraobserver ICC results (0.980).

In the current study, Doughty and Zaman36 published a meta-analysis study that found that a 10% difference in CCT results in a 3.4 mm Hg difference in IOP. Likewise, when assessing candidates for refractive surgery, whose CCT should be lower than 500 µm, error of 1 mm Hg in the Goldmann applanation tonometric IOP measurement.
The main limitation of the current study was that our results can be applied only when assessing normal corneas. Future studies are needed to assess variability in patients who have undergone excimer laser surgery or those with a corneal disease such as keratoconus. Another limitation is that we could have evaluated Cirrus HD-OCT interobserver reproducibility by using a higher number of examiners (more than two) to avoid statistical bias derived from measurement consistency between examiners. A higher measurement variability should be expected if a higher number of observers perform the CCT gauging because of the inherent subjective bias of any given manual procedure; it is also true that our two observers (MECP and SMA) were trained independently and carried out their routine examinations in an autonomous fashion, which makes it unlikely that both showed autocorrelation bias for the study and, conversely, may well reflect a good random combination representative of further independent examiners.

In conclusion, the current study showed for the first time that Cirrus HD-OCT provides reliable intraobserver CCT measurements and consistent agreement between two independently trained observers when gauging CCT in healthy corneas. In addition, its systematic difference with respect to the standard ultrasonic pachymetry technique can be considered minor, making it a clinically useful noncontact pachymeter. With the current model (4000) of the Cirrus HD-OCT, the corneal thickness can be measured only using the caliper tool. Cirrus HD-OCT does not have an automated corneal pachymetry analysis system as it does for retinal evaluations. Hence, although there are potential inherent errors in the manual measurements, the current data can alert researchers and clinicians to the expected low variability in values when performing this pachymetry technique. Despite the fact that Cirrus HD-OCT is used primarily for the posterior segment, investigators and clinicians can benefit from its ability to image the anterior segment structures, particularly to obtain valid noncontact pachymetry measurements. This expands the usefulness of Cirrus HD-OCT beyond the posterior segment and may help ophthalmologists conserve room space and costs in the research laboratory and in the clinic.

References


