·Clinical Research·

# Comparison of central corneal thickness measurements with three new optical devices and a standard ultrasonic pachymeter

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## Abstract

**• AIM: To compare the RTVue spectral optical coherence tomography (SD–OCT), Sirius Scheimpflug–Placido topographer, Lenstar optical low coherence reflectometry (OLCR) and ultrasound pachymetry (USP) devices in terms of their agreement and repeatability of measuring central corneal thickness (CCT).**

**• METHODS: In this prospective study, 50 eyes of 50 patients were included. Three repeated measures were obtained using SD–OCT, Scheimpflug–Placido topographer and USP and five measurements were determined with the OLCR. Bland–Altman plots were used to assess agreement among the instruments, and 95% limits of agreement (LoA) for each comparison were calculated. Intra–examiner repeatability was assessed using intraclass correlation coefficients (ICCs).**

**• RESULTS: The mean CCT by SD–OCT, Scheimpflug–Placido topographer, OLCR, and USP were 525.90 ± 34.08 μm, 525.92 ±34.10 μm, 530.30 ±35.62 μm, and 543.50 ±37.11 μm respectively. All 4 modalities of CCT measurements correlated closely with each other, with Pearson correlation coefficients ranging from 0.977 to 0.995. The mean differences (and upper/lower LoA) for CCT measurements were –0.05±6.77 μm (13.3/–13.3) between SD–OCT and Scheimpflug–Placido topographer, 4.38 ± 3.79 μm (11.8/–3.1) between OLCR and SD–OCT, 4.38± 6.03 μm (16.2/–7.5) between OLCR and Scheimpflug–Placido topographer, 13.20±6.46 μm (25.9/0.5) between USP and OLCR, 17.59±6.76 μm (30.8/4.3) between USP and SD–OCT, and 17.58±8.13 μm (33.5/1.6) between USP and Scheimpflug–Placido topographer. Intra–examiner repeatability was excellent for all devices with ICCs>0.98.**

**• CONCLUSION: For most practical purposes, CCT measurements with the RTVue, Sirius and Lenstar can be used interchangeably. Although highly correlated, CCT measurement differences between USP and these 3 optical instruments can be significant depending on the clinical situation.**

• **KEYWORDS:** central corneal thickness; optical low coherence reflectometry; spectral optical coherence tomography; Scheimpflug-Placido topographer

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## INTRODUCTION

Corneal pachymetry has an important role in both diagnosis and therapeutic decision of many diseases. Accurate determination of central corneal thickness (CCT) is necessary for assessing the function of endothelial cells, screening and planning refractive surgery, and obtaining true intraocular pressure measurements [1-4]. In refractive surgery, inaccurate measurements can cause excessive tissue removal in the stromal bed that could lead to iatrogenic keratectasia[3,5]. A meta-analysis by Doughty and Zaman[4] showed that a 10% change in CCT may result in an approximately 3.4 mm Hg change in intraocular pressure. Moreover, there is evidence supporting that CCT is an independent risk factor for the development and progression of glaucoma[6].

Corneal thickness measurements can be performed using ultrasonic based or optic based techniques. Various instruments are available for this purpose, of which applanation ultrasound pachymetry (USP) is the most common method. However, USP has several possible sources of error such as probe misplacement, lack of a fixation light for gaze control, oblique positioning of the probe in relation to the cornea, corneal compression during measurement and sound transmission variability due to dryness [7-10]. Also, the USP method has some disadvantages that are related to the device's contact with the cornea.

In recent years, a number of sophisticated imaging systems which allow assessment of CCT without contact has been introduced. The Lenstar LS 900 (Haag-Streit AG, Köniz, Switzerland) is a relatively new optical low coherence reflectometry (OLCR) instrument designed for cataract and refractive surgery procedures[11] and performs biometry of the entire eye including CCT measurement, as well as anterior chamber depth, lens thickness, axial length and retinal thickness data in around 20s per measurement.

The RTVue optical coherence tomography (OCT) system (RTVue-100; Optovue Inc, Fremont, CA, USA) based on spectral domain OCT (SD-OCT) technology, is another example of these optical techniques. It is capable of obtaining high definition cross-sectional images of the cornea by adjusting a corneal adaptor module; this provides both central and regional pachymetry.

The Sirius anterior segment analysis system (Costruzione Strumenti Oftalmici,Florence, Italy) is a new device using the combination of rotating Scheimpflug camera and a Placido-disk technology. It provides, in a single scan, anterior segment imaging and measurements, anterior and posterior corneal topography, wavefront analysis and complete corneal pachymetry. All 3 of these optical instruments have the advantage over ultrasound of providing CCT measurement without touching the eye.

The results of the studies available in the literature that compare CCT with various devices are contradictory, indicating that important discrepancies among instruments exist [12-15]. Thus, comparison of the new devices is important to evaluate the agreement. The aim of this observational study is to assess the level of agreement of CCT measurements using OLCR, SD-OCT, Scheimpflug-Placido topographer, and USP and intra-examiner repeatability of measurements. To our knowledge, current study is the first comparison of CCT using Sirius Scheimpflug-Placido topographer and higher axial resolution spectral OCT techniques. In addition, there is no study comparing the RTVue OCT device to the LenStar with regard to CCT measurements.

## SUBJECTS AND METHODS

This prospective study analyzed the CCT in young healthy adults. Patients with ocular or systemic disease or a history of having ocular surgery, and patients with refractive errors more than ±1.50 diopter spherical and/or cylindric values were excluded. All eyes had a corrected distance visual acuity of 20/20 or better. Fifty patients who met the inclusion criteria described were consecutively recruited.

The local ethics committee approved this observational cross sectional study, which followed the tenets of the Declaration of Helsinki. All patients provided written informed consent.

**Measurements** All measurements were taken at the same time of day (between 10:00 a.m. and 4:00 p.m.) and at least 2h after wakeup time to avoid the effects of diurnal variation in corneal thickness. Same examiner (Aslan Bayhan S) who was experienced in the use of all 4 measurement devices performed all measurements. The order of testing with the Scheimpflug-Placido topographer, OLCR, and SD-OCT was randomized for each patient. The ultrasound measurement required contact with the eye and thus was performed last. Only right eye of each patient was used for statistical analysis.

**Optical coherence tomography** The RTVue spectral OCT system (software version 6.1, Optovue, Inc) with a corneal adaptor module was used in this study. The system works at 830 nm wavelength and is capable of a scan speed of 26 000 axial scan per second. The depth resolution of the system is 5 μm (full-width, half-maximum) in tissue. The cornea anterior module produces telecentric scanning for anterior segment imaging using a wide-angle (long lens) or high magnification (short lens) adaptor lens. This study used the wide-angle lens, which provides a scan width of 6.0 mm and a transverse resolution (focused spot size) of 15 μm. Each eye was scanned 3 times during a single visit with the patient sitting. The patient's gaze was fixed with an internal fixating target. To center aiming circle on the pupil and maximize vertex reflection, the examiner used the real-time video image of the eye and the circular overlay. Patients were repositioned after each OCT scan.

**Optical low coherence reflectometry** The LenStar LS 900 (Haag-Streit AG, Köniz, Switzerland) uses the effect of time domain interferometric or coherent superposition of light waves to measure ocular distances in the eye. It uses an 820 μm superluminescent diode with a Gaussian-shaped spectrum. Its technical features provide higher spatial resolution than other reflectometry techniques. The reflections of the different structures within the human eye such as the cornea, lens, and retina are interferometrically superimposed on the reflections of the reference arms. An interference signal from a reflective interface is generated when the measurement beam is fixated by the patient and when it is perpendicular to the interface. The instrument takes 16 consecutive scans per measurement without the need for realignment. Patients were asked to perform a complete blink just before measurements were taken, and five measurements were taken to test intrasession repeatability.

**Scheimpflug –Placido topographer** The Sirius system (Costruzione Strumenti Oftalmici,Florence, Italy) is a new topography device that combines a monochromatic rotating Scheimpflug camera and a Placido disk to analyze the anterior segment by obtaining 25 radial sections of the cornea and anterior chamber. A 475 nm UV-free blue LED light is used to measure 35 632 points for the anterior corneal surface and 30 000 for the posterior cornea. Then, a pachymetric map is reconstructed using the point-by-point anterior and posterior corneal surface. Measurements with the Sirius system were performed while the device was brought into focus, and the patient's eye was aligned along the visual axis by a central fixation light. The patients were asked to sit back

**Table 1 Descriptive statistics for central corneal thickness (in μm) measurements**

| Methods | Mean±SD | Min | Max | 95% CI |
|---|---|---|---|---|
| OLCR | 530.30±35.62 | 451 | 607 | 520.17-540.42 |
| SD-OCT | 525.90±34.08 | 451 | 599 | 516.22-535.60 |
| Scheimpflug-Placido topographer | 525.92±34.10 | 453 | 595 | 516.22-535.61 |
| USP | 543.50±37.11 | 466 | 625 | 532.95-554.05 |

CI: Confidence interval; OLCR: Optical low coherence reflectometry; SD-OCT: Spectral-domain optical coherence tomography; USP: Ultrasound pachymetry.

**Table 2 Interdevice comparison of central corneal thickness measurements**

| Pairwise comparison | Mean paired difference | | 95% CI of mean difference (μm) | | Pearson correlation | |
|---|---|---|---|---|---|---|
| | [1]Mean±SD(μm) | [2]*P* | Lower | Upper | *R* | [3]*P* |
| OLCR and SD-OCT | 4.38±3.79 | <0.001 | 3.30 | 5.46 | 0.995 | <0.001 |
| OLCR and Scheimpflug-Placido topographer | 4.38±6.03 | <0.001 | 2.66 | 6.09 | 0.985 | <0.001 |
| USP and OLCR | 13.20±6.46 | <0.001 | 11.36 | 15.04 | 0.985 | <0.001 |
| SD-OCT and Scheimpflug-Placido topographer | -0.05±6.77 | 0.987 | -1.93 | 1.92 | 0.980 | <0.001 |
| USP and SD-OCT | 17.59±6.76 | <0.001 | 15.67 | 19.51 | 0.985 | <0.001 |
| USP and Scheimpflug-Placido topographer | 17.58±8.13 | <0.001 | 15.27 | 19.89 | 0.977 | <0.001 |

[1]Mean interdevice difference; OLCR: Optical low coherence reflectometry; SD-OCT: Spectral-domain optical coherence tomography; USP: Ultrasound pachymetry; [2]Repeated-measures ANOVA using Bonferroni adjustment for multiple comparisons; [3]Pearson correlation analysis.

after each measurement, and the device was realigned before the subsequent measurement. The patients were instructed to blink completely just before each measurement, and three measurements were carried out.

After the measurements with the non-contact devices, the cornea was anesthetized with topical proparacaine hydrochloride 0.50% and 80 seconds elapsed before the USP (Pacline, Optikon) measurement. The patient fixated on a distant target, and the calibrated ultrasound probe was placed manually on the center of cornea as precisely and perpendicularly as possible. Three consecutive measurements were taken.

The average of the consecutive measurements for each device was used to compare the CCT values between devices.

**Statistical Analysis** The descriptive statistics were presented as mean±standard deviation (SD). The association between the measurements using the various instruments was calculated and expressed as Pearson correlation coefficients.

The CCT measurements with the 4 methods were compared using repeated-measures analysis of variance (ANOVA), and pairwise comparisons were performed using the Bonferroni adjustment for multiple comparisons. Bland and Altman plots were used to assess agreement among the various methods, and the 95% limits of agreement (LoA) for each comparison (mean difference ±1.96×SD), which describe the range where 95% of all differences can be expected to be, were calculated. A $P$ value less than 0.05 was considered statistically significant. Repeatability was assessed using intraclass correlation coefficients (ICCs).

All data were analyzed using SPSS software (version 16.0 SPSS, Inc) and MedCalc (version 11.6.0.0, MedCalc Software bvba, Inc.).

**RESULTS**

Fifty eyes of 50 patients (23 men, 27 women) were included. The mean age was 29.78±4.95y (19-38y). Table 1 shows the mean CCT readings, 95% confidence intervals (CIs) and Table 2, the inter-device differences. There was a significant variation in the measurement results among the 4 methods ($P$<0.001, repeated-measures analysis of variance). The mean CCT values measured by SD-OCT and Scheimpflug-Placido topographer were similar ($P$=0.987, repeated-measures ANOVA using Bonferroni adjustment for multiple comparisons) whereas differences among the remaining 3 methods were significant (all; $P$<0.001; repeated-measures ANOVA using Bonferroni adjustment for multiple comparisons). The highest mean CCT (543.50±37.11 μm) was obtained from the USP, followed by OLCR (530.30±35.62 μm).

All 4 modalities of CCT measurements correlated closely with each other, with Pearson correlation coefficients ranging from 0.977 to 0.995 (Table 2). Bland-Altman plots of the paired CCT differences against the mean values and the 95% LoA are shown in the Figure 1. The 95% LoA were -7.5 to 16.2 μm between OLCR and Scheimpflug-Placido topographer, 0.5-25.9 μm between USP and OLCR, 4.3- 30.8 μm between USP and SD-OCT, -13.3 to 13.3 μm between SD-OCT and Scheimpflug-Placido topographer, 1.6-33.5 μm between USP and Scheimpflug-Placido topographer. The OLCR and SD-OCT measurement displayed the smallest range of LoA (14.9 μm).

Table 3 shows the results of the repeatability assessments

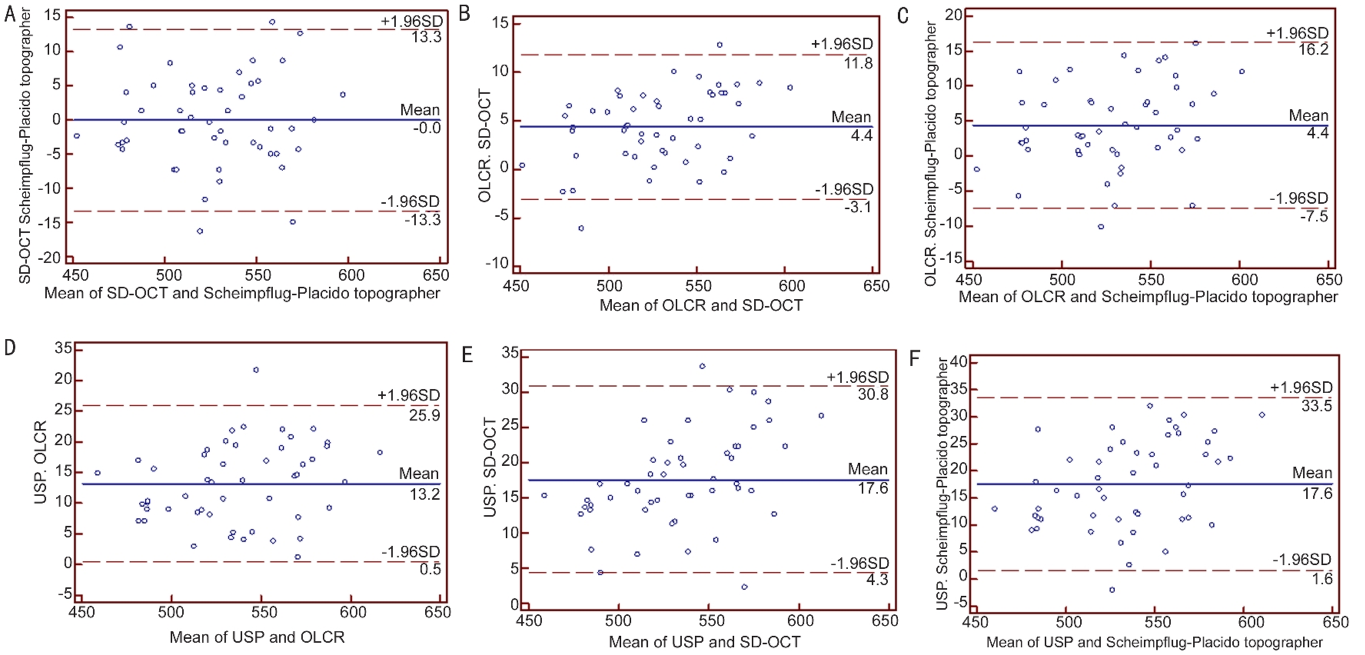


**Figure 1** Bland Altman plots comparing CCT between SD-OCT and Scheimpflug-Placido topographer (A), OLCR and SD-OCT (B), OLCR and Scheimpflug-Placido topographer (C), USP and OLCR (D), USP and SD-OCT (E), and USP and Scheimpflug-Placido topographer (F). The 95% limits of agreement are shown with dashed lines, and the solid line represents the difference between these measurements.

**Table 3 Intraexaminer repeatability of each method for CCT measurements**

| Methods | ICC | 95% CI |
|---|---|---|
| OLCR | 0.9892 | 0.9857-0.9933 |
| SD-OCT | 0.9979 | 0.9966-0.9987 |
| Scheimpflug-Placido topographer | 0.9884 | 0.9818-0.9931 |
| USP | 0.9882 | 0.9812-0.9929 |

ICC: Intraclass correlation coefficients; CI: Confidence interval; OLCR: Optical low coherence reflectometry; SD-OCT: Spectral optical coherence tomography; USP: Ultrasound pachymetry.

obtained with the devices. Agreement of successive measurements performed during the same visit was excellent for all devices (ICC 0.9892 for OLCR, 0.9979 for SD-OCT, 0.9884 for Scheimpflug-Placido topographer and 0.9882 for USP).

## DISCUSSION

Several technologies are available at this time to measure CCT. These include slit scan imaging, contact and noncontact specular microscopy, dual-beam partial coherence interferometry, OCT, confocal microscopy, USP, ultrasound biomicroscopy, Scheimpflug photography, and OLCR[7,11,15].In this study, we have compared USP and three different noncontact optical devices of measuring CCT. The USP is an already established method. The noncontact devices used in our study, the Sirius, Lenstar and RTVue, have been made commercially available only quite recently and have potential advantages. Although numerous studies have been performed to compare different pachymetry methods, to our knowledge, there is no study in the literature comparing the RTVue with Sirius and Lenstar. So, it is not clear whether the results of these systems match well and can be used interchangeably.

Repeatability and accuracy are very important for a device to be introduced into clinical practice. Repeatability, is the ability of an instrument or technique to give similar values on different occasions and accuracy describes how close the measurement is to the true value being measured. It has already been shown that Lenstar has a high repeatability that is better than the repeatability of Pentacam, specular microscopy, and USP, and has high interobserver reproducibility; that is comparable to USP[11,16-18]. RTVue also was shown to have a good intraexaminer repeatability data, comparable to Pentacam and USP and high interexaminer reproducibility [19,20]. Although always considered to be within acceptable limits, when compared with other devices, the repeatability data of USP is contradictory in previous studies [21-23]. The Sirius was also reported to provide repeatable pachymetric measurements especially for central and peripheral measurements at 2.5mm [24]. In our study, all devices demonstrated very high and comparable repeatability (with the ICCs more than 0.98 for all devices) in same young healthy adult population, though SD-OCT performed the best. One of the possible reasons for this excellent repeatability with RTVue is the precise delineation of the boundaries of the cornea because of high resolution. This may be similar to the better repeatability of SD-OCT over the time domain OCT [25,26]. Although SD-OCT has a manually centered system derived from the reference at the center of pupil, high speed scanning makes ocular movement negligible during measurement. As a result corneal center can be fixed and this -together with minimal corneal thickness variation along neighboring points-might also contribute to good repeatability.

Our study results showed a range of mean CCT from 525±34 μm to 543±37 μm, with the USP yielding the thickest CCT measurements. The mean CCT value measured by the USP in our study was similar to the overall mean CCT of 544±34 μm reported with ultrasound based studies in a meta-analysis[4].

To our knowledge, there is only one study comparing combined Scheimpflug-Placido disk system and USP, in which the devices provided high agreement [27]. Results of the studies comparing OLCR or OCT with USP are contradictory. Tai *et al* [17] and Beutelspacher *et al* [28] reported that OLCR and USP provide comparable results. Similar results between OCT and USP were also reported[20,29]. Despite that, it has also been reported that CCT measurements obtained by OCT, OLCR, partial coherence interferometry, spectral oscillation interferometry, specular microscope are lower than USP results [8,9,12,17-19,21,30,31]. Our results also showed that SD-OCT, OLCR and Scheimpflug-Placido topographer significantly underestimated the corneal thickness (by 17.59 μm, 13.2 μm and 17.58 μm, respectively) compared with USP measurements. There is no satisfactory explanation for differences in CCT measurements between USP and optical devices. Unlike USP, optical devices conceivably may include the tear film in the measurement of corneal thickness, as the anterior reflecting surface is the air-tear film interface. On USP side, the probe may disturb the precorneal tear film and even disrupt the epithelium which may lead to lower pachymetry values than those obtained by optical systems [8,21,32]. On the other hand, Gao *et al* [33] found that the use of eye drops significantly increases corneal thickness by more than 20 μm up to 63% of patients, so anesthetic drops used before USP could bias USP measurements toward higher values. In the current study, we tried to decrease the influence of anesthetic drops by waiting 80s before performing US measurements as Nam *et al* [34] suggests, thus we thought it had little influence on this measurement. Other theoretical explanations for the differences in CCT are uncertainty of the exact speed of sound in corneal tissue which can affect USP, small calibration errors in systems and a variable posterior reflection point between the Descemet membrane and anterior chamber with USP [35]. Actually it is unclear whether ultrasound, the current gold standard in normal eyes accurately shows the true corneal thickness, so it is important to note that we only evaluated the similarities and differences between the measurements, as the true CCT is not known.

Overall, pairwise comparisons of all devices showed significantly good correlations in our study. We found that the CCT measurement by Scheimpflug-Placido topographer was comparable to that by RTVue (with a mean difference of only 0.05 μm). The Bland Altman plots show that the 95% LoA between them ranged from -13.3 μm to 13.3 μm, meaning that RTVue measurements could be as much as -13.3 μm lower or 13.3 μm higher than the Scheimpflug-Placido topographer values. Milla *et al* [24] reported higher central pachymetry measurements with the same Scheimpflug-Placido topographer used in our study than those obtained by Visante time-domain OCT. The authors speculate that the tear film might have played a role in the discrepancies between Scheimpflug and OCT techniques. On the other hand, Prakash *et al* [36] showed that the CCT obtained by RTVue was also significantly more than that obtained by Visante OCT. It has been suggested previously that the automated algorithm of Visante delineates the anterior corneal boundary positioned slightly below the anterior corneal surface, therefore underestimating the corneal thickness [37]. Greater sensitivity and higher resolution of the SD-OCT system used in this study could lead to higher reflectivity from the outermost and the deepest layer of the cornea, hence improving the edge detection and overall width calculated, as Prakash *et al* [36] also suspected.

In this study, regarding the comparison between the CCT measurements using the OLCR and SD-OCT, the OLCR slightly overestimated CCT by an average of 4.38±3.79 μm. In contrast to us, López-Miguel *et al* [38] reported that OLCR significantly underestimates the CCT when compared with SD-OCT (Cirrus HD-OCT, mean difference 5.68±11.46 μm). But, since the SD-OCT used in their study does not have the capability to automatically measure pachymetry, the researchers measured the CCT manually. This manual measurement technique might have played a role in the difference between studies. Cruysberg *et al* [16] reported that CCT values were also higher with the OLCR than Visante OCT.

Although the difference in the mean CCT values between OLCR and SD-OCT was significant in our study, their measurements displayed the smallest range of LoA (14.9 μm) suggesting good agreement. In the Bland Altman plots, the values for the difference from the mean are mostly positively skewed in the plot comparing OLCR and SD-OCT. They are not as randomly distributed as the plot comparing SD-OCT measurements with the Scheimpflug-Placido topographer measurements. Similar distributions were also observed for the plots comparing USP with all optical devices. These plots suggest a relationship between CCT measurements by these devices.

In this study, we found a significant difference between CCT measurements obtained by OLCR and the Scheimpflug-Placido topographer. The devices use different technological methods. Lenstar biometer detects the anterior and posterior corneal peaks in the OLCR waveform, while Sirius reconstructs a pachymetric map using the point-by-point anterior and posterior corneal surface data. However, the absolute difference of -7.5 to 16.2 μm is within the range of ±18 μm reported for the diurnal variation in CCT [39]. The Bland Altman analysis showed good agreement between the devices. Chen *et al* [40] also reported good agreement between Scheimpflug-Placido topographer and OLCR biometer in CCT values, with narrow 95% LoA (range 6.85 to -15.43 μm).

In this study we measured only normal corneas of healthy subjects. Therefore, we do not have data concerning the agreement between the four methods when measuring corneas with pathological alterations, or postoperative corneas. The differences between the four systems might be larger in such cases.

In conclusion, how far apart measurements can be before they are considered significantly different must be determined by the clinician for each application. However it seems that for most practical purposes, measurements with the RTVue, Sirius and Lenstar can be used interchangeably. Although highly correlated, CCT measurement differences between USP and these 3 optical instruments can be significant depending on the clinical situation considered.

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