ORIGINAL ARTICLE

Accuracy of Cirrus HD-OCT and Topcon SP-3000P for measuring central corneal thickness

Jorge A. Calvo-Sanz a,*, Javier Ruiz-Alcocer b, Miguel A. Sánchez-Tena b

a Instituto de Ciencias Visuales, Madrid, Spain
b Universidad Europea, Madrid, Spain

Received 3 October 2016; accepted 23 December 2016
Available online 21 February 2017

KEYWORDS
Corneal pachymetry; Optical coherence tomography; Specular microscopy; Ultrasound pachymetry; Interchangeability

Abstract
Purpose: To compare and analyze the interchangeability of three measuring systems, each based on a different technique, for central corneal thickness (CCT) analysis.

Methods: CCT measurements were measured using optical coherence tomography (OCT), non-contact specular microscopy (NCSM), and ultrasonic pachymetry (USP) in 60 eyes of 60 healthy patients with a mean age of 66.5 ± 15.0 years and a mean spherical equivalent of 0.43 ± 1.14 D.

Analysis of variations in measurement concordance and correlation among the three different methods were performed. Comparison of CCT measurements were done using Bland–Altman plots (with bias and 95% confidence intervals), intra-class correlation coefficient (ICC), and paired t-student analysis.

Results: Mean CCT values were: 549.20 ± 26.91 μm for USP (range 503–618 μm), 514.20 ± 27.49 μm for NCSM (range 456–586 μm) and 542.80 ± 25.56 μm for OCT (range 486–605 μm). CCT values obtained with NCMS were significantly lower than those obtained with OCT and USP methods. NCMS CCT value was 36.08 ± 10.72 μm lower than USP value (p < 0.05), and NCMS CCT value was 7.88 ± 8.86 μm lower than OCT value (p < 0.05). ICC between USP–NCSM pair was 0.488 and 0.909 between USP–OCT pair.

Conclusion: OCT and UPS offered highly comparable results, whereas NCSM offered lower mean CCT values compared to the other two methods. Therefore, NCSM should not be considered a reliable method for measuring CCT and should rather be considered for assessing longitudinal changes in the same patient.

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* Corresponding author at: Department of Optometry, Instituto de Ciencias Visuales, INCIVI, Hospital La Zarzuela, C/ Ana Teresa, 24, 28023 Madrid, Spain.
E-mail address: jacalvosanz@gmail.com (J.A. Calvo-Sanz).

https://doi.org/10.1016/j.optom.2016.12.004
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Introduction

Central corneal thickness (CCT) measurement is required for several procedures in ophthalmology such as corneal dystrophy follow-up, contact lens wear complications, glaucoma and postoperative studies after corneal surgery.

Ultrasonic pachymetry (USP) instruments measure the CCT by, emitting short electrical pulses which are transformed into ultrasonic waves by a crystal probe at 20MHz frequency and 1640 m/s speed. The measurement is performed between the corneal epithelium and Descemet’s membrane. Due to the high reproducibility this technology is currently considered as the Gold Standard. However, CCT measurements with USP depend on a highly accurate location and positioning of the probe (orthogonal to the corneal surface). At the same time, USP requires local anaesthetic eye drop instillation as some corneal indentation occurs because of probe contact. Some authors suggest that CCT values may be altered by up to 10 µm because of corneal anaesthesia instillation.

Besides USP, other techniques offer the possibility of measuring CCT by direct methods. Among them, anterior segment optical coherence tomography (AS-OCT) offers fast and non-contact CCT measurement by analysing infrared interferometry. It uses a 1310 nm diode light with a rate of 4000 scans/s to scan captured images. The OCT device captures a corneal sectional image, which is then analyzed by software. In this case, the CCT value is calculated from tear film to corneal endothelium.

Non-contact specular microscopy (NCSM) is commonly used for studying the number, shape and size of endothelial cells, but can be used to measure CCT values. In NCSM technology, images and corneal thickness values, are obtained by photographic cell reflection acquisition, where each interface (tear film, corneal epithelium and aqueous humour) causes a light reflection due to a different refractive index. NCSM technology obtains CCT values by considering the space between the tear film and the corneal endothelium.

Both OCT and NCSM systems use optical technologies and do not require anaesthetic drop instillation. Therefore, the advantages of optical systems are a faster data acquisition and a fewer inherent complications related to corneal contact.

The existence of different CCT measurement methods makes it important to understand their strengths and weaknesses. In this respect, some studies have compared different methods for calculating CCT values, and substantial progress has been made in this field. One study has previously analyzed the inter-instrument reproducibility of CCT measurement using USP, slit-lamp optical coherence tomography and specular microscopy, but Cirrus HD-OCT has greater axial and transversal resolution. Furthermore, no statistical tests have been properly used to quantify the agreement among the three different instruments. Consequently, at present it is not easy to know if CCT values obtained with different instruments are comparable and equivalent.

Precisión de Cirrus HD-OCT y Topcon SP-3000P en la medición del espesor corneal central

**Resumen**

**Objetivo:** Comparar y analizar la intercambialidad de tres sistemas de medición, basado cada uno de ellos en una técnica diferente, para estudiar el espesor corneal central (ECC).

**Métodos:** Se realizaron mediciones del ECC utilizando tomografía de coherencia óptica (OCT), microscopía especular (NCSM), y paquimetría ultrasónica (USP) en 60 ojos de 60 pacientes sanos, con una edad media de 66,5 ± 15 años y un equivalente esférico medio de 0,43 ± 1,14 D. Se realizaron análisis de las variaciones de concordancia de las mediciones, y correlación entre los tres métodos diferentes. Se compararon las mediciones del EEC utilizando gráficos de Bland-Altman (con desviaciones, e intervalos de confianza del 95%), coeficiente de correlación intra-clase (ICC), y análisis de t para pareado de Student.

**Resultados:** Los valores medios de ECC fueron: 459,2 ± 26,91 µm para USP (rango 503-618 µm), 514,2 ± 27,49 µm para NCSM (rango 456-586 µm) y 542,8 ± 25,56 µm para OCT (rango 486-605 µm). Los valores de ECC obtenidos con NCMS fueron significativamente inferiores que los obtenidos con los métodos OCT y USP. El valor de ECC obtenido mediante NCMS fue inferior en 36,08 ± 10,72 µm al valor obtenido mediante USP (p < 0,05), y el valor de ECC obtenido mediante NCMS fue inferior en 7,88 ± 8,86 µm al obtenido mediante OCT (p < 0,05). El ICC entre el par USP-NCMS fue de 0,488, y de 0,909 entre el par USP-OCT.

**Conclusion:** Los métodos OCT y UPS aportaron resultados altamente comparables, mientras que NCMS aportó unos valores medios de ECC inferiores a los aportados por los otros dos métodos. Por tanto, NCMS no debería considerarse un método fiable en la medición del ECC, debiéndose utilizar en la valoración de los cambios longitudinal del mismo paciente.

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Therefore, in this study we have analyzed the agreement of 3 different CCT measurement systems.

Methods

This prospective study was carried out with a sample of 60 patients. Inclusion criteria were: age between 27 and 85 years, and spherical equivalent error between −1.50 and +4.50 D. Exclusion criteria included: ocular disease, history of ocular surgery or inflammation, and astigmatism >0.75D. An experienced clinician made three consecutive CCT measurements in selected eyes and the average value was considered for each case.

All subjects underwent a complete eye examination, which included refraction, screening for ocular and systemic diseases, slit-lamp biomicroscopy, and examination of the fundus. All subjects were free of any ocular pathology and had best-corrected monocular visual acuity of 20/20 (0 logMAR). All measurements were performed between 11 a.m. and 2 p.m. by only one observer.

Each device used in the study was correctly calibrated by technical staff before examinations. Subjects underwent CCT examinations with three different techniques. In each case the last measurement was always performed with the contact technique in order to avoid corneal impression. With non-contact techniques, subjects were asked to blink several times before measurements were taken in order to ensure a smooth tear film over the cornea’s anterior surface.

The study followed the tenets of the Declaration of Helsinki and was approved by the Institutional Review Board. Informed Consent was obtained from all patients after explaining the nature and possible consequences of the study.

Instruments used in the study

Optical coherence tomography

Cirrus HD-OCT S-5000 spectral optical coherence tomography (15) (Carl Zeiss Meditec AG – Germany) equipment was used for anterior segment analysis. It captures high resolution images of the cornea using non-contact OCT, and can also assess corneal thickness without direct contact. The captured image is aligned with the corneal apex area, looking for further corneal reflection. The system obtained 5 different images, separated by 0.25 mm with 5 μm of axial resolution and 15 μm of transversal resolution. Once the image is saved, the instrument’s calliper tool is used to identify the corneal limits (epithelium and endothelium) in order to obtain the CCT value in the different images.13,20 The mean value was taken as the CCT value.

Non-contact endothelial specular microscopy

Topcon SP3000P non-contact endothelial specular microscopy (NCSM) (Topcon Corporation, Tokyo, Japan) was used for endothelial and pachymetric analysis. This instrument obtains central corneal images through a central fixation spot. This system provides an auto alignment that simplifies the capturing procedure, making its automated measuring system very fast and simple.18 The software automatically displays the CCT measurement, and the captured image is analyzed by software, providing the endothelial cellular density, pachymetry, hexagonality and variation coefficient.18,21 Participant’s head movement was restricted with a chin-and-forehead rest and they were asked to look at the green fixation spot inside the apparatus. When the microscope obtained the endothelial focus by an automated process, it used a low-intensity flash to acquire the endothelial images. If the captured image was not perfectly clear and the endothelial cell outlines were not clearly visible, the image was eliminated and the process was repeated. Three consecutive measurements of each eye were taken, the mean value being used for this study.

Ultrasound pachymetry

Ultrasound corneal pachymetry was measured with a DGH Pachette3 USP (DGH Technology Inc. – Exton, PA – USA). Calibration was checked prior to each exam session and the velocity of ultrasound was set to 1640 m/s. Cornea was anesthetized with one topical drug (oxybuprocaine 0.4% and tetracaine 0.1%) that was instilled in each eye. Three minutes later the CCT measurement was made using Pachette3 contact ultrasonic corneal pachymeter. The system made 10 consecutive measurements and the mean value was taken as the CCT value. Each subject was seated on a chair and asked to fixate on the wall opposite. The pachymeter probe was sterilized and aligned perpendicularly to the central cornea within the pupil area.21

Statistical analysis

Statistical data was analyzed using SPSS 22.0 software (Inc, Chicago, IL – USA). Quantitative variables are given as a mean ± standard deviation (SD). In this study Bland-Altman concordance method with the 95% limits of agreement (LoA) and intraclass correlation coefficient (ICC) in groups (USP–NCMS and USP–OCT) were used. Sample size was calculated using G*Power software v7.12 (Institut Municipal d’Investigació Médica, Barcelona, Spain) according standard deviation observed in previous pilot study: the software indicated a minimum of 44 observations required for α = 0.05, risk β = 0.20 in bilateral contrast with a detectable minimum difference of 6 measurement units, which was less than the difference between OCT and USP.

These tests were used to achieve the goal of this study: paired t-student analysis was performed to assess the mean values between pairs (USP–NCMS; USP–OCT; NCSM–OCT); Bland–Altman is a graphical method used to analyze the agreement between two different variables,22 and ICC indicates the degree to which measurements in the different devices resemble each other.23 Only after a complete analysis of all the statistical results can we establish a relationship of equivalence among the data obtained with the three devices.

After normality and equality of variances were assessed (Kolmogorov–Smirnov (K–S) method), parametric tests were performed to assess the bias between instruments. Differences were considered to be statistically significant when the p value was <0.05 (i.e., at the 5% level). One-way ANOVA test was performed with Bonferroni correction factor.
Table 1  Intraclass correlation coefficient (ICC) between pairs of instruments.

<table>
<thead>
<tr>
<th>Instrument 1</th>
<th>Instrument 2</th>
<th>ICC</th>
<th>95% LoA</th>
<th>p-Value</th>
</tr>
</thead>
<tbody>
<tr>
<td>OCT-USP</td>
<td>OCT-USP</td>
<td>0.909</td>
<td>0.718 to 0.964</td>
<td>&lt;0.001</td>
</tr>
<tr>
<td>NSCM-USP</td>
<td>NSCM-USP</td>
<td>0.488</td>
<td>-0.047 to 0.830</td>
<td>&lt;0.001</td>
</tr>
<tr>
<td>NSCM-OCT</td>
<td>NSCM-OCT</td>
<td>0.576</td>
<td>-0.051 to 0.873</td>
<td>&lt;0.001</td>
</tr>
</tbody>
</table>

Results

This study included 60 eyes of 60 participants (28 men and 32 women) with a mean age of 66.5 ± 15.0 years (range: 27–85) and a mean spherical equivalent of 0.43 ± 1.14 D (range: 1.50 to 4.50).

The highest CCT value was obtained with the USP (mean value 549.20 ± 26.91 µm; range from 503 to 618 µm), followed by the OCT (mean value 542.80 ± 25.56 µm; range from 486 to 605 µm). Finally, the lowest value was obtained with the NCSM (mean value 514.20 ± 27.49 µm; range from 456 to 586 µm). The highest difference between pairs was found between NCSM and USP (−36.08 ± 10.72 µm; confidence interval −38.83 to −33.31 µm; p < 0.001), while the lowest difference was found between OCT and USP (−7.88 ± 8.86 µm; CI −10.17 to −5.59; p < 0.001). The difference between NCSM and OCT was close to the NCSM and USP pair (−28.20 ± 9.52 µm; CI −30.66 to −25.74 µm; p < 0.001). One-way ANOVA test showed statistically significant differences between groups (p < 0.001 in all cases). T Student analysis showed statistically significant differences between mean values from all paired instruments (p < 0.001 in all cases).

At the same time, the agreement between pairs of measurements was calculated using ICC values, and these values are shown in Table 1. The agreement between all pairs was significant (p < 0.001).

Finally, Figs. 1 and 2 shows the results obtained in the Bland–Altman analysis. The highest concordance was found between OCT and USP (Fig. 1), with differences between 9.47 and −25.24 µm (mean ± 1.96 SD) and a mean deviation of −7.88 ± 8.86 µm. Conversely, NCSM and USP (Fig. 2) showed the lowest concordance, with differences between −15.08 and −57.09 µm (mean ± 1.96 SD) and a mean deviation of −36.08 ± 10.72 µm. The limits of agreement 95% (LoA = mean of the difference ± 1.96 × SD of the differences) indicate that the values on the error between the pairs of measurement have exceeded the limits of concordance.

Discussion

This study shows that CCT measurement with OCT is equivalent for non contact corneal thickness measurement system compared to USP. Among the methods for CCT estimation, USP has been the most commonly used in the last decades, although the necessary instillation of oxybuprocaine 0.4% for the accomplishment of the CCT measurement with USP has been also described previously as inducing changes in pachymetry, it has been shown that the mean of the pre and post anaesthetic CCT measures are not significantly different and OCT returns to baseline within 80 s. On the other hand, today, however, many modern optically based pachymetric techniques are commercially available. The main advantage of the new measuring systems is that they avoid contact with the cornea, thus reducing the possibility of bacterial contamination, eye diseases infection, or epithelial damage.

For this reason, systems that provide rapid measurements, good portability and low costs should be taken into account due to being useful tools for screening data acquisition. At the same time, given the importance of this key parameter it is also important to assess the consistency and precision of CCT measurements with different devices. Previous studies have analyzed this relationship and the relationship between different SD-OCT devices from other manufacturers. In most of those papers difference between OCT and USP measurement was similar to the differences shown in this work. Similarly with measures obtained with different NCMS devices.
The fact that the differences results obtained between the
devices in our study were similar to those previously pub-
lished, gives consistency to our work, however not all of that
previous papers had analyzed and/or compared the differ-
ent devices under consideration by quantifying the degree of
concordance and interchangeability. Therefore, in this study
we have comprehensively analyzed the relationship among
the CCT values obtained using USP, SD-OCT and NCSM sys-
tems, and we have also quantified the agreement of CCT
values across these devices.

In relation to the average CCT values, the greatest
NCSM-USP difference and the smallest OCT-USP difference
obtained are similar to previous studies6,13 that showed
equivalent differences between CCT measurements with
NCSM and USP. The difference between values suggests a
strong correlation between OCT and the reference test,
that is, the USP. On the contrary, the largest difference
between measurements made with NCSM and USP would
indicate a worse relationship between them. As mentioned
previously, USP is currently the gold standard measure-
ment system; therefore, the smaller the difference with USP
measurements, the better the relationship between values,
especially in OCT.

Regarding these results, it should be noted that the
difference between CCT obtained with each device is
consistent regardless of the measurement obtained. This
consistent difference is explained by the different operat-
ing principles of each device: NCSM uses light reflection
and USP uses ultrasound reflection in each interphase. The
posterior limit of the cornea is located in the space between
Descemet’s membrane and the anterior chamber,14 whereas
NCSM considers the posterior limit in the endothelial cells
stratus.

On the other hand, spectral OCT systems take nearly
26,000 A-scans per second with 5 μm axial resolution. This
high-speed scanning makes ocular movements negligible
during measurements, giving a minimal corneal variation
in the exam results in a good repeatability.20 Moreover,
it is quite difficult to measure within the same central
corneal area. OCT and NCSM have macular fixation points,
but the USP is manipulated by the clinician who chooses
where to make the measurement. This might be considered
a measure bias in the study and explain the small differ-
ences between OCT and USP. Besides this consideration, all
the devices gave statistically significant different values.
These results suggest that the relationship among them is
not perfect. Therefore, in order to determine whether the
different methods are comparable and interchangeable, we
performed other statistical analyses.

In order to confirm the interchangeability of the mea-
surements between different techniques we determined the
ICC. The ICC analyses the correspondence between pairs
of measurement values of each system. It analyses the
average correlations between all possible orderings of the
pairs of data available, thereby avoiding the problem of
order dependence of the correlation coefficient.1 The rela-
tionship between values obtained by NCSM compared with
the USP ones has a low ICC (Table 1), while matching
values obtained with OCT and USP showed a significantly
higher ICC. If we follow the Landis–Koch classification15 we
can describe the relationship between NCSM and USP as
“Regular” (0.21–0.40), and the relationship between OCT
and USP as “Almost Perfect” (0.81–1.00). These relation-
ships, coupled with the differences, confirm that the CCT
measurements obtained by NCSM are neither comparable
nor interchangeable with those obtained by USP. On the con-
trary, the lower differences between OCT and USP and their
high ICC allow us to establish an agreement between these
two devices and the possibility of interchanging their values.
Therefore, according to the ICC values of each device, the
reliability of the measurements with respect to USP–NCSM
would be compromised, the measurement obtained by OCT
being more reliable.

Finally, we also calculated the difference between mea-
surement pairs USP–OCT by comparing the average value of
each pair. These results are presented in Bland–Altman dia-
grams. This analysis helped us to determine graphically the
relationship between value differences and how they relate
to the mean value in the whole measurement range.

In this case (Fig. 1) the dots are aligned with the mean
error line. It is important to note that vertical scale indi-
cates the difference between measurements, which means
that in the OCT–USP pair the measurement is more consis-
tent with the average difference with the values showed in
Bland–Altman diagram between NCSM and USP (Fig. 2).
These results confirm the contribution of the ICC value.

Conclusions

CCT measurement with OCT has a good agreement and
concordance with USP, and can be considered a reliable
noncontact corneal thickness measurement system. Fur-
thermore, is acceptable to interchange values between OCT
and USP. On the other hand, CCT measurement obtained
by NCSM reveals a very poor concordance versus the gold
standard technique, making the technique more suited to
longitudinal follow-up of corneal pathology patients.

Funding

No funding support was needed.

Conflicts of interest

The authors have no conflicts of interest to declare.

Acknowledgements

This research was made possible thanks to the technical
staff, equipment and the optometry department of the Insti-
tuto de Ciencias Visuales (INCIVI) – Hospital La Zarzuela.
Thanks to Professor M.A. Zato and the optometry depart-
ment staff for their scientific and personal support.

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