Repeatability and reproducibility of corneal thickness using SOCT Copernicus HR.

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PURPOSE. The aim of this study is to determine the reliability of corneal thickness measures derived from SOCT Copernicus HR (Fourier domain OCT).

METHODS. Thirty healthy eyes of 30 subjects were evaluated. Only one eye of each patient was chosen randomly. Images were obtained of the central (0-2 mm from the corneal apex) and paracentral (2-4 mm) cornea. We assessed the following variables: corneal thickness (central and paracentral) and epithelium thickness.The intraobserver repeatability data was analyzed using the intraclass correlation coefficient (ICC) for a range of 95% within-subject standard deviation (S_W) and the within-subject coefficient of variation (C_W). The level of agreement by Bland-Altman analysis was also represented for the study of the reproducibility between observers and agreement between methods of measurement (automatic vs. manual).

RESULTS. The mean value of the central corneal thickness (CCT) was 542,4 ± 30,1 µm (SD). There was a high intraobserver agreement, finding the best result in the central sector with an ICC of 0,99, 95% CI (0,989 to 0,997) and the worst, in the minimum corneal thickness, with an ICC of 0,672, 95% CI (0,417 to 0,829). Reproducibility between observers was very high. The best result was found in the central sector thickness obtained both manually and automatically with an ICC of 0,990 in both cases and the worst result in the maximum corneal thickness with an ICC of 0,827. The agreement between measurement methods was also very high with ICC > 0, 91. On the other hand the repeatability and reproducibility for epithelium measurements was poor.

CONCLUSION. Pachymetric mapping with SOCT Copernicus HR was found to be highly repeatable and reproducible. We found that the device lacks an appropriate ergonomic design since proper focusing of the laser beam onto the cornea for anterior segment scanning required that patients were positioned slightly farther away from the machine head-rest than in the setup for retinal imaging.

KEY WORDS: Corneal thickness, Fourier domain, Pachymetric, Optical coherence tomography

The measurement of central (CCT) and paracentral (PCT) corneal thickness has become a crucial test in ophthalmology practice. Preoperative planning corneal refractive surgery requires accurate estimation of the corneal thickness.[1-5] Likewise, assessing the risk of glaucoma also requires an accurate measurement of CCT.[1-7] Moreover, the analysis of corneal thickness (CT) in certain corneal diseases [4-5] in contact lens wearers is essential for monitoring any changes in the cornea.[2]

The most commonly used technique and current “gold standard” for CCT assessment is a spot measurement by ultrasound pachymetry (USP).[4-5, 8] Although USP has advantages such as low cost, simple use and portability, this method is quite operator-dependent. Corneal indentation, misalignment, and variations in placing the probe all influence the measurement accuracy. Furthermore, USP is a contact method which carries the risk for corneal epithelial damage and transmission of infections. [3]

Optical coherence tomography (OCT) is a noncontact imaging technique based on the principles of low-coherence interferometry.[1, 9] Although the technique was initially designed to study the posterior segment it can produce images of the anterior segment with some minor modifications in the system.[10-11] Recently, Fourier domain OCT (FD-OCT) has shown a higher speed, lower acquisition time and a higher signal to noise ratio compared to conventional time domain OCT (TD-OCT).[1, 8]

Several authors have performed agreement and precision studies of the optical coherence tomography with different devices used in clinical practice and the results show an excellent reliability on pachymetric measurements.[2-3, 8, 12-13]

The purpose of this study is then to evaluate the precision (repeatability and reproducibility) of SOCT Copernicus HR (Fourier-domain OCT) system of pachymetric mapping over 4mm diameter.

Since the OCT permits visualization of different layers in the cornea, in addition to analysis of total corneal thickness, we also decided to include in this study the reliability of corneal epithelial thickness measurements. Regarding this variable, we only found one paper in the literature about this issue[4] and the study shows poor repeatability. Therefore, we will try to confirm or discard this result here.

To the best of our knowledge, no study has performed the repeatability and reproducibility of this system on complete corneal thickness evaluation.

MATERIALS AND METHODS

The device used in this study was the SOCT Copernicus HR (Optopol SA, Poland), designed and built at the Physics Institute of University of Nicolaus

Copernicus in Torun.[14] It is a non-invasive tool that uses a Super Luminescent Diode (SLED), with a central wavelength of 855 nm. The generated interference signal is detected by a spectrometer that provides an axial resolution of 3 μm in tissue, with a scan speed of 52000 A-scans per second and a transversal resolution of 12-18 μm. The instrument has an A-Scan resolution of 1024 points and a B-Scan resolution of 20000 A-scans. The focus and alignment of the instrument's scanning head is adjusted with an automated, motorized system controlled from the computer screen.[15]

Subjects

A total of 30 patients participated in this study, 8 of them were men and 22 women. One eye of each patient was randomly selected. The subjects were volunteers from the student population at the University of Alicante. Excluded from the study were those who had a history of corneal refractive surgery, corneal abnormalities or at the time of exploration, were wearing their contact lenses. After being informed of their inclusion in the study, all patients signed an informed consent document in accordance with the Helsinki Declaration. All analysis was carried out without application of lubricating eye drops or pupil dilation.

Setup Analysis

Figure 1 shows the pachymetric map generated over a 4mm diameter circle by SOCT Copernicus HR. In it we can distinguish:

1. Preview of the eye examination, which selects the directional image where the corneal reflex appears brighter.

2. Pachymetric map of sectors, generated automatically and divided in two zones: central (0-2mm) and paracentral (2-4mm) which were subdivided in eight equally spaced radial sectors.

The pachymetric map appears doubled as shown in Figure 1. The one shown to the left of the output screen is overlaid with a pseudocolor map for faster interpretation.

Another application of interest to our study is the possibility of manual measurement of corneal thickness and corneal epithelial thickness on the tomographic image using the SOCT Copernicus HR instrument's software (see Figure 1).

<u>Procedure</u>

First, the patient's head was well positioned on the chin and forehead rest and the patient is asked to fixate on the central light. The anterior segment imaging attachment was used for the scans in order for the instrument to focus on the cornea effectively. To focus the laser beam onto the cornea, we found that patients had to be positioned slightly farther away from the machine head than in the setup for retinal imaging.

The instrument has two fixation modes, internal and external. Internal fixation is the most reproducible, and therefore is the method most used. External fixation is indicated when the visual acuity of the eye to be examined is too poor to provide stable fixation (for example, eccentric fixation). In the present study, all patients were examined with internal fixation. The anterior segment was scanned using the instrument's asterisk anterior scanning mode. The default pattern has 15 lines with a length of 7 mm each (Figure 2). The cross-sections were centered by the examiner to maximize the corneal vertex reflection. The corneal reflex aids in obtaining consistent alignment between scans.[1, 3, 8, 16] This position ensures that the scans are perpendicular to the corneal vertex and determine the tomographic section where layers are better defined.

We assessed central corneal thickness automatically using the pachymetric map. As we said before, the map is divided in a central area and eight paracentral sectors (see Figure 1). Corneal thickness for each sector were generated automatically by the instrument's software by interpolation, and presented values of maximum, minimum and average thickness.

Corneal thickness was also measured manually, by using the distance measurement tool on the scan section of the tomogram which includes the vertex reflection (see Figure 1). Epithelial corneal thickness was assessed solely in manual mode and also on this image.

To determine repeatability and reproducibility 3 scans were performed by examiner A and one further scan by examiner B at the same session.

Statistical analysis

All corneal thickness data were statistically analyzed using SPSS (version 18, SPSS Inc., Chicago, IL, USA) and Med Calc (version 11.6.1. MedCalc Software, Mariakerke, Belgium). The normality of all distributions of parametric data was confirmed with the Kolmogorov-Smirnov test. All values presented p-values> 0.05, indicating that data are normally distributed, and therefore, it is appropriate to use parametric statistical tests.

The first part of the study investigates the intraobserver reproducibility of CT measurements obtained with SOCT Copernicus HR. All tests were performed by the same examiner. Although three measurements of each subject were initially taken, only the first two were evaluated for the repeatability study, while the third was used for a later experiment. The mean ± standard deviation (SD), mean difference ± SD, within-subject SD (S_w) of two consecutive measurements, and within-subject coefficient of variation (CV_W) defined as 100 x S_w / overall mean, were obtained. We also examined the intraclass correlation coefficient (ICC) for a confidence interval (CI) of 95%, based on the analysis of the variance of a random effects model of two factors. The ICC will approach 1.0 when there is no variance within repeated measurements, indicating that the total variation in measurements is solely the result of the variability in the parameter being measured.[17] The maximum value of the ICC is 1 and the minimum value is 0 and according to the classification proposed by Fermanian, concordance is excellent for ICC>0.91, good for ICC range between 0.90-0.71, moderate for ICC range between 0.70-0.51 fair for ICC between 0.50-0.31 and bad for ICC<0.30.

In the second part of the study, we investigate inter-observer reproducibility- To this end, we used the first measurement of examiner A and the measurement made by examiner B. Mean ± standard deviation (SD), mean difference ± SD, within-subject SD (S_w), within-subject coefficient of variation (CV_W) and ICC were obtained . The differences between the two observers and limits of agreement were represented by the Bland-Altman method.

Finally, in the latter part of the study, to assess the correlation between different methods of measurement of the CCT in the central sector. We calculated the same statistical parameters in the cases of repeatability and reproducibility. This is the only parameter that has been measured both automatically and manually thus is the only one that we show in this analysis. We also represented the differences between the two measurement methods and limits of agreement by the Bland-Altman method.

RESULTS

CCT

The study evaluated 30 eyes of 30 patients. Eight men and twenty-two women participated in this study. The mean age of the male patients was 21.50 ± 2.07 years (SD) (range: 19 to 25 years); and the mean age of the female patients was 24.77 ± 5.27 years (SD) (range: 19 to 38 years). The mean age of the total 30 patients was 24.33 ± 5.46 years (SD) (range: 18 to 38 years). The mean refractive error (spherical equivalent) was -0.88 D ± 2.14 (SD) (range: -8.00 to +4.00 D). Of the 30 patients studied, 12 were emmetropes, 13 myopes (mean refractive error of -2.56 D ± 2.07 (SD), range: -8.00 to -0.50 D, and 12 hyperopes (mean refractive error of +1.40 D ± 1.52 (SD), range: +0.50 to +4.00 D.

For the 30 eyes, the mean CCT was 542.4 ± 30.1 μm.

The repeatability of the measurement of CT

Table 1 shows the statistical results obtained in the intraobserver repeatability of corneal thickness in the nine sectors as well as the CT measures of maximum, minimum, manual measurement in vertex and epithelial thickness. In all sectors, including manual measurements, within-observer concordance of the mean thickness, according to the classification proposed by Fermanian[18] was noted as very good (> 0,91). The concordance values for maximum and minimum thicknesses are significantly lower with ICC values of 0.672 and 0.715, respectively. On the other hand, these two variables also present higher values for S_w and CV_W indicating greater variability as reflected by the expansion of the confidence intervals for the ICC. Corneal epithelial thickness ICC was fair according the same criterium.

Table 2 tries to analyze whether, expanding the number of measurements to 3, consistent results for maximum and minimum thicknesses improve. It was found that there was little variation in the ICC and CI, but variability was increased when analyzing S_w and $CV_{W.}$

Reproducibility in the measurement of CT

Table 3 summarizes the results obtained in the evaluation of agreement between examiners. In all sectors we find a very good agreement (with ICC values>0.91). The best results are found in the central (automatic and manual) measurement. Although the results obtained in the maximum and minimum thicknesses are good, when analyzing the degree of agreement using the

Bland-Altman plots (Figure 3), we find that in both cases there is too much variability in practice. Although the measured differences between observers are not too large (5.2 μm and 1.6μm), when calculating the range of agreement, values of 38 and 53 μm are obtained, which are higher than 5% of the average pachymetry reading, thus indicating clinically relevant differences. Figure 4 shows Bland-Altman plot for epithelium. In this case, although absolute value of the mean difference is only 0.5 μm the range of agreement is by the order of 10% of the average epithelial thickness value which implies clinically relevant differences.

Agreement between methods of measurement of central corneal thickness.

Table 4 shows the results obtained by analyzing the agreement between methods of measurement (automatic vs. manual) obtaining a very good agreement with an ICC of 0.987 95% CI [0.972 0.994]. Bland- Altman plot (Figure 5) shows that good agreement between both methods is obtained. The automatic measurement underestimates central corneal thickness by 7.2 μm in regards to the value obtained with the manual method. It also gives a range of 9.3 μm agreement (2% average), indicating that there are not clinically relevant differences.

DISCUSSION

Any study should guarantee the quality of the measurements, not only because it largely determines the validity of their conclusions, but the importance of clinical decisions that are based on that research.[19] There are numerous studies in literature that evaluate the repeatability and reproducibility of OCT in the posterior segment and fewer in the anterior segment. To our knowledge, this is the first study that evaluates the repeatability and reproducibility of corneal thickness measurements with the Copernicus SOCT HR.

The central corneal thickness measured with OCT is comparable to results obtained with the ultrasound pachymetry, as shown by the study of Muscat et al.[2] They found that measurements obtained with OCT were lower than those obtained by USP (to a value of approximately 50 μm), but the ICC between the two methods was very high. Li et al.[20] in their study also compared the time domain Visante OCT (Carl Zeiss Meditec) with USP also getting an underestimation of the CCT value 14.6 μm. Muscat et al.[2], also analyzed the correlation in a group of patients with corneal edema, obtaining a high correlation by OCT (Humphrey Zeiss, time domain). On the other hand, Kim et al.[4] obtained a good reproducibility between the measurements obtained by the SL-OCT (Heidelberg Engineering, time domain) and ultrasound, but it is important to note that in clinical practice, the measurements captured by these two methods are not directly interchangeable. Huang et al.[8] compared the results obtained by a Scheimpflug imaging system (Pentacam) with the RTVue Fourier domain OCT (Optovue) showing that CCT measurements are reliable and interchangeable in corneas after LASIK, which is not the case with those obtained with USP. This implies that the OCT can be used immediately after corneal surgery and can be a useful tool for evaluating the surgery's success.

Fukuda et al.[16] also expanded their study to other anterior segment biometric measurements such as anterior chamber depth (ACD) or angle-angle distance (ATA), finding a good repeatability and reproducibility in them.

Sin et al.[13] in their study found a very good repeatability of the OCT (RTVue) in the measurement of CCT, but not so in the measurements of the epithelium, demonstrating the importance of optimizing each scan and the convenience of taking a high number of scans to maximize the consistency of the measurements. Mohamed et al.[12] finds that the pachymetric map obtained with the OCT (Visante) for the mean central and peripheral thickness are reproducible in both healthy subjects and those with keratoconus.

The comparison between the two OCT systems: FD -OCT and TD-OCT has also been studied by Prakash et al.[1] and Huang JY et al.[3] concluding that, although both OCT instruments showed good reliability, the FD-OCT was better. This may be due to a faster image capture, thus reducing testing time and therefore, decreasing the effect of eye movements.

In this study we obtained a good agreement between observer and intra-observer and between methods of measurement of CCT. We demonstrated that a reliable measurement of CCT can be obtained without many acquisitions as shown in Tables 1 and 2.

The results are better in terms of repeatability in the central area (both automatic and the manual measurements), with an ICC for both sectors higher than 0.91, indicating a very good match. These results are comparable to those obtained by Prakash et al.[1], Huang JY et al.[3] and Mohamed et al.[12] in their respective work. In our study, we found that the worst results of repeatability and reproducibility were obtained for the maximum and minimum corneal thickness map values with a ICC ranging from 0.805 and 0.854, corresponding to a good match. The exception is found in the repeatability of the minimum value with an ICC of 0.672 (moderate agreement). This result supports the results found by Prakash et al.[1] in which they find that the minimum corneal thickness repeatability was the worst parameter analyzed by the TD-OCT, but the best for the FD-OCT.

The reason for this difference in repeatability values may come from the data origin. While central (automatic) and vertex (manual) thicknesses come from an average calculation, the maximum and minimum values correspond to a single value obtained from the whole area. Also notice that, sampling becomes less dense as it goes further from the center. This may also increase the variability of the maximum and minimum thickness,provided that these points may be outside the central region.

Our average CCT was 542.4 ± 30.1 μm, which is comparable to the results obtained by different authors using FD-OCT and AS-OCT [1, 3, 11, 16, 20]

Table 5 summarizes the most relevant studies of repeatability and reproducibility of corneal thickness measured with OCT and its main results.

In their study Huang JY et al.[3] analyzed the central and paracentral cornea (2-5 mm) which is, in turn, subdivided into eight sectors, with two OCT devices from different domains. In both cases, the best repeatability results are in the central sector, as it happens in our study. However, we found a difference of opinion about which sectors are the least repeatable. Huang JY et al.[3] when used in their study the FD-OCT (RTVue), notice that the less repeatable are the superior temporal and inferior temporal sectors, whereas when using the AS-OCT (Visante) are superior nasal and superior temporal sectors which are the least repeatable. In our study (regardless of the values of maximum and minimum corneal thickness, which analyzed JY Huang et al.[3]) it follows that the least repeatable are nasal, inferior and superior temporal sectors, but no relationship between them was found.

When analyzing the intraobserver reproducibility we observed an overestimation of the first measurement with respect to the second, (as shown in Table 1). In the minimum and maximum sectors we made a comparative study between the first and second measurement and the average of the three measures taken by the examiner. This study aimed to demonstrate whether improved concordance is obtained for these variables based on three steps instead of two (Table 2). The results show that it is not necessary to take three steps to improve consistency.

Prakash et al.[1] and Huang JY et al.[3] found in different studies an overestimation of the corneal thickness measurement taken manually in reference to the automatic. Our study also reflected that overestimation.

In summary, although the results show good reproducibility, with ICC> 0.91 except for the minimum and maximum corneal thickness, the method Bland-Altman in these two sectors (Figure 3) shows limits of agreement (LoA) (um) 95% ranging from -33.2 to 43.7 µm for the minimum value and -54.5 to 51.2 µm for the maximum value, which makes us think there is too much variability in clinical measures.

Axial resolution of the OCT is in part responsible of the poor reliability obtained in corneal epithelial thickness measurements. The accuracy of 3 µm is above the 5% of total value of epithelium thickness (~50 µm). This limitation together with the experimental errors explain the poor results.

Our study has some limitations. First, all patients who participated in this study had healthy corneas. Additional studies are needed to see whether the results obtained in patients with normal corneas can be extended to patients with refractive surgery such as LASIK or showing corneal disorders such as keratoconus or corneal opacities. The changes of curvature of the cornea in these patients may make it difficult to find the apex corneal reflex as suggested by Huang JY et al.[3]

A second limitation is the difficulty in taking images because the SOCT Copernicus HR chinrest did not fit ergonomically to the facial features of patients. Also, for a correct approach to the cornea, the patient had to place the head slightly away from the machine than the configuration of the device for the retina scan. The study by Muscat et al.[2] also refers to this limitation.

The quality of a measuring instrument is reflected by the reliability and validity in their measurements. In this study we demonstrate the repeatability and reproducibility of the SOCT Copernicus HR. Therefore, it is left to be completed the analysis of its validity by comparing the results with those obtained using a reference test (gold standard) that is a valid and reliable measurement.

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TABLE 1. Summary of the results obtained by analyzing the intraobserver repeatability of corneal thickness measurement with SOCT Copernicus HR (n = 30) taking the first and second measurement obtained by the examiner.

	MEAN (µm) ± SD	MEAN DIFFERENCE (µm) ± SD	Sw (µm)	CV_w (%)	ICC (95 % CI)
SECTOR S	546,0 ± 31,4	3,3 ± 8,0	4,4	0,82	0,968 (0,934 - 0,985)
SECTOR ST	545,6 ± 31,3	1,8 ± 9,6	4,6	0,82	0,954 (0,905 - 0,978)
SECTOR T	541,1 ± 31,5	2,6 ± 8,3	4,3	0,80	0,966 (0,930 - 0,984)
SECTOR IT	538,9 ± 30,5	0,0 ± 6,7	3,4	0,62	0,976 (0,950 - 0,989)
SECTOR I	537,4 ± 30,6	0,6 ± 8,1	3,9	0,71	0,942 (0,882 - 0,972)
SECTOR IN	535,2 ± 30,7	1,1 ± 9,1	4,1	0,76	0,958 (0,914 – 0,980)
SECTOR N	536,9 ± 31,9	3,7 ± 12,2	4,1	0,77	0,929 (0,857 – 0,966)
SECTOR SN	541,7 ± 30,5	2,7 ± 8,8	4,1	0,75	0,959 (0,916 - 0,980)
CENTRAL	543,5 ± 29,9	0,5 ± 3,1	1,7	0,33	0,995 (0,989 - 0,997)
VERTEX MANUAL	550,5 ± 29,1	1,0 ± 4,7	2,7	0,49	0,973 (0,973 - 0,994)
MINIMUM	503,5 ± 28,0	6,6 ± 24,8	12,0	2,40	0,672 (0,417 - 0,829)
MAXIMUM	590,5 ± 41,5	4,3 ± 23,3	13,3	2,23	0,854 (0,715 - 0,928)
EPITHELIUM	50,0 ± 1,2	0,4 ± 1,6	0,8	1,65	0,379 (0,028 – 0,647)

S, superior; ST, superotemporal; T, temporal, IT inferotemporal; I, inferior; IN, inferonasal; N, nasal; SN, superonasal, Sw, within-subject SD; CV_w , within-subject coefficient of variation; ICC, intraclass correlation coefficient; IC, confidence interval

TABLE 2. Summary of the results obtained by analyzing the intraobserver repeatability of corneal thickness measurement with SOCT Copernicus HR (n = 30) taking the three measurements obtained by the examiner.

	MEAN (µm) ± SD	Sw (µm)	CV_w (%)	ICC (95 % CI)
MINIMUM	501,2 ± 31,1	16,4	3,34	0,600 (0,400 – 0,765)
MAXIMUM	590,1 ± 39,1	14,1	2,37	0,829 (0,713 – 0,908)

Sw, within-subject SD; CV_w , within-subject coefficient of variation; ICC, intraclass correlation coefficient; IC, confidence interval

TABLE 3. Summary of the results obtained by analyzing interobserver reproducibility in measuring corneal thickness with the SOCT Copernicus HR (n = 30).

	MEAN (μm) ± SD	MEAN DIFFERENCE (μm) ± SD	Sw (μm)	CV_w (%)	ICC (95 % CI)
SECTOR S	546,2 ± 31,7	2,9 ± 12,0	6,0	1,10	0,931 (0,860 - 0,967)
SECTOR ST	544,6 ± 31,3	3,8 ± 9,5	5,1	0,94	0,955 (0,907 - 0,978)
SECTOR T	539,9 ± 32,0	5,1 ± 6,9	4,6	0,86	0,977 (0,952 - 0,989)
SECTOR IT	537,5 ± 30,7	3,0 ±7,9	4,3	0,78	0,967 (0,932 - 0,984)
SECTOR I	536,6 ± 30,3	2,3 ± 9,2	4,7	0,87	0,955 (0,908 -0,978)
SECTOR IN	534,9 ± 31,3	1,6 ± 8,1	4,1	0,75	0,974 (0,945 - 0,987)
SECTOR N	536,6 ±33,1	4,3 ± 6,2	4,0	0,75	0,983 (0,964 - 0,992)
SECTOR SN	541,2 ± 31,2	3,7 ± 10,5	5,7	1,06	0,945 (0,887 - 0,973)
CENTRAL	542,7 ± 29,9	2,1 ± 4,3	2,7	0,50	0,990 (0,978 - 0,995)
VERTEX MANUAL	551,3 ± 29,9	-0,8 ± 4,3	2,7	0,49	0,990 (0,978 - 0,995)
MINIMUM	504,1 ± 31,8	5,2 ± 19,6	8,8	1,98	0,827 (0,667 - 0,914)
MAXIMUM	593,5 ± 41,0	-1,6 ± 27,0	15,0	2,52	0,805 (0,629 - 0,902)
EPITHELIUM	50,0 ± 1,7	0,5 ± 2,2	1,1	2,22	0,391 (0,042 – 0,655)

S, superior; ST, superotemporal; T, temporal, IT inferotemporal; I, inferior; IN, inferonasal; N, nasal; SN, superonasal, Sw, within-subject SD; CV_w , within-subject coefficient of variation; ICC, intraclass correlation coefficient; IC, confidence interval

TABLE 4. Summary of the results obtained by analyzing the agreement between methods of measurement (automatic vs. Manual) in corneal thickness measurements with the Copernicus SOCT HR (n = 30).

	MEAN (µm) ± SD	MEAN DIFFERENCE (µm) ± SD	Sw (µm)	CV_w (%)	ICC (95 % CI)
CENTRAL VERTEX MANUAL	547,3 ± 29,2	-7,2 ± 4,8	5,5	1,02	0,987 (0,972 - 0,994)

Sw, within-subject SD; CV_w, within-subject coefficient of variation; ICC, intraclass correlation coefficient; IC, confidence interval

TABLE 5**.** Summary of previous studies of repeatability and reproducibility in the measurement of corneal thickness and the main results obtained with different OCT devices.

References	Eyes (patients) [age range, years old]	Repeatability ICC (95 % CI)	Repeatability 95 % LoA (µm)	Reproducibility ICC (95 % CI)	Reproducibility 95 % LoA (µm)	Device used
Sin et al. (13)	32 (18) [15-53]	0,970[d] (-- [c]) 0,980[e] (-- [c])	-- [c]	-- [c]	-- [c]	Humphrey Zeiss OCT
Fukuda et al. (16)	85 (85) [22-89]	0,999 [a] 0,997 [b]	-12,0 a 10,1	0,998 [b]	-12,0 a 10,1	CAS-OCT (3D images, prototype)
		0,998 [a] 0,968 [b]	-12,0 a 10,1	0,987 [b]	-12,0 a 10,1	AS-OCT (Visante, Carl Zeiss Meditec)
Mohamed et al. (12)	27 (27) [18-71]	0,998 (0,995-0,999) [h] 0,996 (0,991-0,998) [i]	-- [c]	-- [c]	-- [c]	AS-OCT (Visante, Carl Zeiss Meditec)
		-- [c]	-- [c]	0,995 (0,988-0,998) 0,993 (0,984-0,997)	-- [c]	
Muscat et al. (2)	(14) [21-58]			0,998 [f] (-- [c]) 0,979 [g] (-- [c])	-3 a 4	Humphrey Zeiss OCT
Prakash et al. (1)	(100) [23,3 ± 2,4]	0,962 (0,945-0,975) [j] 0,949 (0,926-0,966) [k] 0,954 (0,948-0,960) [l]	-20,37 a 17,59 -20,55 a 18,11 -23,3 a 19,90	-- [c]	-- [c]	AS-OCT (Visante, Carl Zeiss Meditec)
		0,999 (0,998-0,999) [j] 0,999 (0,998-0,999) [k] 0,995 (0,994-0,996) [l]	-8,33 a 8,15 -3,33 a 3,66 -7,35 a 6,32	-- [c]	-- [c]	RTVue-OCT
Huang JY et al. (3)	72 (72) [44-86]	0,994 (0,991-0,996) [j]	-11,97 a 9,71	-- [c]	-- [c]	RTVue-OCT
		0,973 (0,958-0,983) [m] 0,978 (0,965-0,986) [n] 0,964 (0,943-0,977) [o] 0,978 (0,965-0,986) [p]	-30,86 a 20,88 -28,25 a 22,75 -20,17 a 20,33 -28,30 a 15,01	-- [c]	-- [c]	

		0,976 (0,963-0,985) [q]	-28,26 a 11,06			
		0,972 (0,956-0,983) [r]	-22,88 a 11,26			
		0,974 (0,959-0,984) [s]	-18,01 a 8,25			
		0,966 (0,947-0,979) [t]	-17,04 a 13,96			
		0,989 (0,982-0,993) [j]	-11,97 a 9,71	-- [c]	-- [c]	
		0,936 (0,899-0,959) [m]	-30,86 a 20,88			
		0,947 (0,917-0,967) [n]	-28,25 a 22,75			
		0,951 (0,922-0,969) [o]	-20,17 a 20,33			
		0,960 (0,936-0,974) [p]	-28,30 a 15,01	-- [c]	-- [c]	AS-OCT (Visante, Carl Zeiss Meditec)
		0,977 (0,964-0,986) [q]	-28,26 a 11,06			
		0,980 (0,968-0,988) [r]	-22,88 a 11,26			
		0,980 (0,968-0,987) [s]	-18,01 a 8,25			
		0,980 (0,968-0,987) [t]	-17,04 a 13,96			

[(a)] Repeatability of measurements on the same day and same observer (n = 10); [(b)] Repeatability of measurements different day and same observer (n = 30); [(c)] The information was not provided within the article; [(f)] Interobserver reproducibility ; [(g)] Intersession reproducibility; [(h)] Value obtained in $CCT_{0-2\ mm}$; [(i)] Value obtained in $CT_{2-5\ mm}$; [(j)] Value obtained in CCT; [(k)] Value obtained in $CT_{Minimum}$; [(l)] Value obtained in $CT_{Maximun}$; [(m)] Value obtained in $CT_{2-5\ mm\ Superonasal}$; [(n)] Value obtained in $CT_{2-5\ mm\ Superior}$; [(o)] Value obtained in $CT_{2-5\ mm\ Superotemporal}$; [(p)] Value obtained in $CT_{2-5\ mm\ Nasal}$; [(q)] Value obtained in $CT_{2-5\ mm\ Inferonasal}$; [(r)] Value obtained in $CT_{2-5\ mm\ Inferior}$; [(s)] Value obtained in $CT_{2-5\ mm\ Inferotemporal}$; [(t)] Value obtained in $CT_{2-5\ mm\ Temporal}$; 95 % LoA, 95 % limits of agreement defined as the mean ± 1.96 standard deviation (SD); ICC, intraclass correlation coefficient ; CI, confidence interval.

Vidal 12-048
RESEARCH PAPER
Repeatability and reproducibility of corneal thickness using SOCT Copernicus HR
Vidal, Viqueira, Mas & Domenech

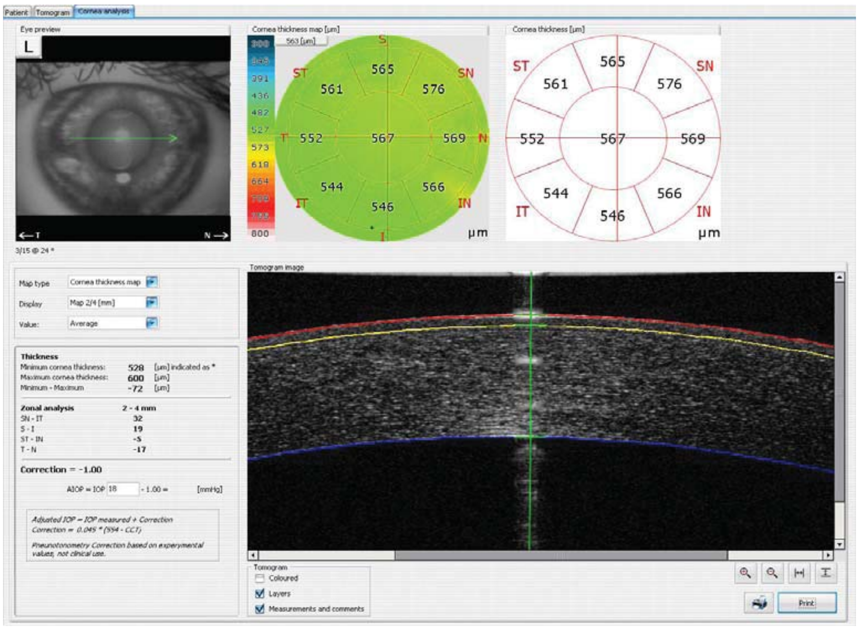

Figure 1. Detail of the output window of the corneal analysis software SOCT Copernicus HR. Tomographic image shows corneal layers (deriving corneal epithelial thickness and central corneal thickness) and vertex reflection

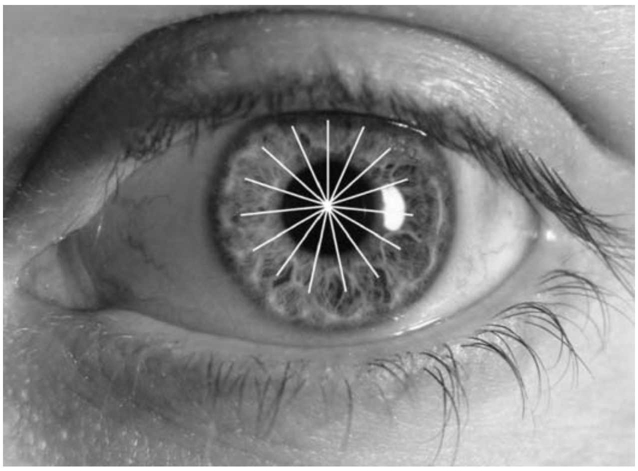

Figure 2. Simulation of the scan pattern of the mapping of the cornea

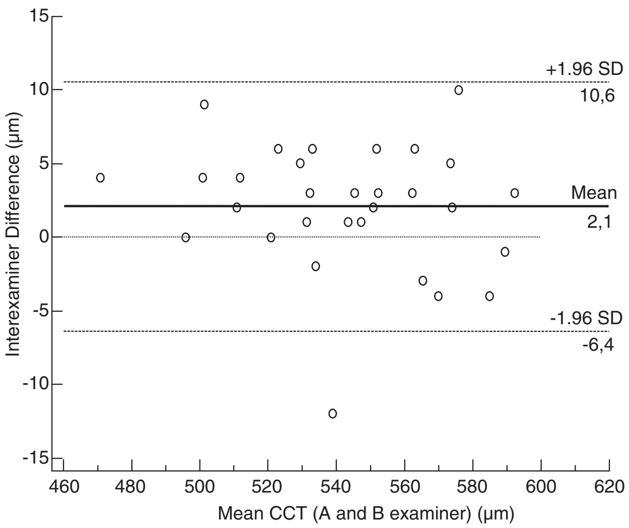

Figure 3. Bland–Altman charts for inter-observer repeatability of corneal thickness in the centre (CCT) and the manual, minimum and maximum. The limits of agreement (LoA) of 95% are shown with dashed lines and the solid line represents the mean of the differences between these measurements (n = 30).

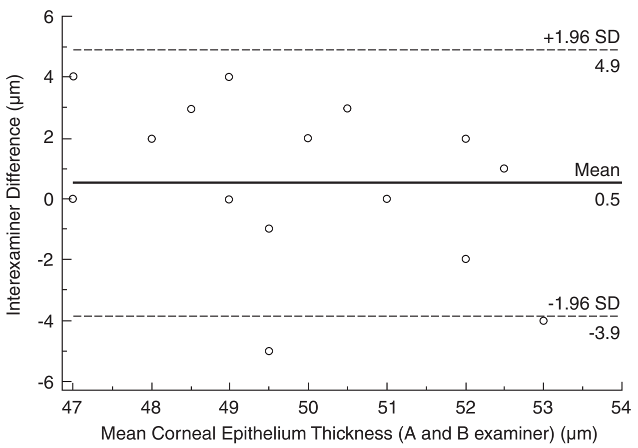

Figure 4. Bland–Altman charts for inter-observer repeatability of corneal epithelial thickness. The limits of agreement (LoA) of 95% are shown with dashed lines and the solid line represents the mean of the differences between these measurements (n = 30).

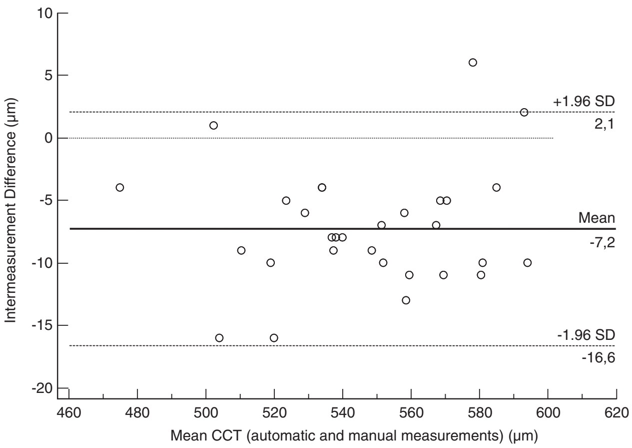

Figure 5. Bland–Altman chart agreement between measurement methods (manual versus Automatic). The limits of agreement of 95% are shown with dashed lines and the solid line represents the mean of the differences between these measurements (n = 30).