ORIGINAL ARTICLE

Eastern Journal of Medicine

East J Med 27(4): 634-640, 2022
DOI: 10.5505/ejm.2022.93763

A Comparison Study Between Four Different Pachymeters to Measure Corneal Thickness

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ABSTRACT

To compare the correlation and agreement between the central corneal thickness (CCT) measurements with ultrasound pachymeter and three different non-contact pachymeters and to analyze their influence on intraocular pressure (IOP) measurements.
This prospective study included 102 healthy adults. Optical biometer (OB), scheimpflug corneal topographer (TOPO), ultrasound pachymeter (UP), and non-contact pachytonometer (NCP) were carried out to measure the corneal thickness. Pearson and Spearman correlation and a 95% limit of agreement were calculated.
In this prospective study, the CCT of 102 right eyes of 102 healthy volunteers were analyzed. CCT measured with optic biometer, corneal topography, ultrasound pachymeter and non-contact pachytonometer were 534.7 (438-629), 544.8 (444-634), 553.1 (449-674) and 562.9 (464-665 µm), respectively. There were strong correlations between all pachymeters by Pearson correlation analysis. The correlation of Pearson between all measurement methods were over 0.950. When the CCT was divided into the three groups according to corneal thickness ranges, the correlation was higher than 0.7 in all groups (r=0.72-0.91 for <510 µm, r=0.85-0.95 for 510-580 µm, r=0.82-0.93 for >580 µm) by Spearman correlation analysis. A significant positive correlation was observed between the IOP values and CCT obtained by all pachymeters with a trend toward increasing the IOP with increasing corneal thickness.
The correlations between the pachymeters were high in normal corneal thickness, whereas it was slightly lower in the thick and thin cornea. A significant positive correlation was observed between IOP and CCT in all pachymeters.

Keywords: Central Corneal Thickness, AL-Scan Optic Biometer, Sirius Corneal Topographer, TRK-2P Non-Contact Pachytonometer, Ultrasound Pachymeter

Introduction

A correct measure of corneal central thickness is necessary for the diagnosis of various diseases of cornea and treatment applications such as monitoring corneal edema and endothelial disfunction, monitoring accurate intraocular pressure (IOP) in glaucoma, following corneal ectasias and planning correct refractive surgery procedures and monitoring postoperative period (1-2). Some methods based on either ultrasonic or optical principles can be used to measure the central corneal thickness (CCT).

Ultrasound pachymetry (UP) is the most known method and widely recognized as the benchmark of measuring corneal thickness. However, UP have several possible sources of error (3). It's accuracy depends on suitable central localization and perpendicularity of the probe on the cornea. Extreme pressure on the cornea and displacement of the tear film can lead to underestimation of actual thickness. Moreover, the need to make contact with the probe poses the risk of injury to the cornea or microbial contamination between individuals. In addition, the accuracy of measurement by the UP can be influenced by fluctuation of the ultrasonic wave speed in tissue of varying corneal hydration. Topical anesthesia is necessary to measure the corneal thickness with the UP. To overcome these disadvantages, a number of noncontact systems that provide fast, convenient, noncontact and objective measurements have been started to measure the CCT. Currently, there are various technologies including corneal topography with a rotating scheimpflug camera, optic coherence tomography, confocal and specular microscopy, optical low-coherence reflectometry, and non-contact pachytonometry (4).

The aim of the study was to compare the agreement between the CCT measurements with the optic biometer (OB), scheimpflug corneal topographer (TOPO), ultrasound pachymeter (UP), non-contact pachytonometer (NCP) and to analyze their influence on the IOP measurements.

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Received: 05.08.2022, **Accepted:** 04.10.2022

Materials and Methods

This study analyzed the CCT in 102 right eyes of 102 healthy adults. Informed consent was obtained from all patients in accordance with the Declaration of Helsinki before any intervention was performed. The study protocol was approved by the Clinical Research Ethics Committee of the Hitit University (397/Jan of 20, 2021).

A complete ophthalmic examination was performed. The exclusion criteria were prior to ocular surgery, anemnesis of contact lens wearing, existing corneal and/or significant systemic or ocular disease (e.g. cataract, corneal scarring, glaucoma, dry eye etc.). Patients with refractive errors of more than 3 diopters spherical and/or 2 diopter cylindrical values were also excluded.

All measurements were obtained between 10:00 am and 16:00 pm, to avoid the influence of diurnal variations of the CCT, with an interval of at least 5 minutes between consecutive measurements. The same experienced examiner (CC) obtained all measurements. For each subject, one randomly selected eye was used for statistical analysis. AL-Scan optic biometer (Nidek, Aichi, Japan), the Sirius corneal topography (Costruzione Strumenti Oftalmici, Florence, Italy), and TRK-2P non-contact autokeratorefractopachytonometer (Topcon, Tokyo, Japan) were performed on each patient, respectively. As a contact test, the UP (Micropach 200P, Sonomedescalon™, New York, USA) was last to be performed in all cases. Subjects were positioned in the chin and head rest, and asked to open both eyes and fixate straight ahead on the center target of the camera for the first three devices. After the measurements with non-contact devices, topical proparacaine hydrochloride 0.5% (Alcaine; Alcon Laboratories, Fort Worth, TX, USA) was dropped to anesthetize the cornea before the UP measurement. The patient fixated on a distant target, and the calibrated ultrasound probe was placed perpendicularly on the center of the cornea. Three consecutive measurements were carried out for each device. The average of the consecutive measurements for each device was used to compare the CCT values between devices. The IOP was determined by a non-contact pachytonometer.

The data was analyzed using SPSS (version 22.0; SPSS Inc., Chicago, IL, USA). Normality of data was confirmed using the Kolmogorov–Smirnov test. The data was described as average, SD, minimum-maximum and 95% confidence interval for the mean. A p-value <0.05 was considered statistically significant. Corneal thickness obtained with four different pachymeters were compared in each corneal thickness group using the repeated measures ANOVA and Bonferroni correction was performed for pairwise comparisons. The Pearson correlation and its 95% confidence interval (CI) were utilized to quantify the correlation between the methods of measurement. Spearman rank correlation coefficient (r) was calculated for the purposes of establishing association between the pachymeters evaluations in each thickness groups (<510 μm, 510-580 μm, >580 μm).

Bland–Altman plots and the 95% limits of agreement (LoA) (95% LoA = mean difference ± 1.96 SD) were applied to find the agreement between each pair of pachymeters. The difference between measurements using different methods is plotted against their average in a Bland-Altman graphic. The 95% limits of agreement (LoA) (mean difference ± 1.96 standard deviation) gave the distance between the measurements by the methods with 95% confidence. The influence of NCP, OB, TOPO, UP on IOP was established through four univariate linear regression models, IOP being the dependent variable in all of them, and each of the four pachymetric measurements the predictive variable in each model.

Results

In this prospective study, the CCT of 102 right eyes of 102 healthy volunteers with a mean age of 39,43±13,83 years of age (range, 20 to 66 years) was determined. Sixty-seven were male (65.6%) and 35 were female (34.4%).

CCT measured with OB, TOPO, UP and NCP were 534.7 μm (438-629), 544.8 μm (444-634), 553.1 μm (449-674) and 562.9 μm (464-665) in 102 eyes, respectively. The distribution of measurements between the different CCT values measured by the four tonometers are shown in figure 1 by the box-plot diagrams. Repeated measures ANOVA showed that there were statistically significant differences between all pachymeters (p<0.001). The CCT was divided to the three groups according to thickness level by an ultrasound pachymeter including thin (<510 μm), normal (510-580 μm) and thick (580< μm). There were also significant differences between all corneal thickness groups (p<0.001). The thinnest measurements were measured by OB and the thickest measurements measured by NCP in all corneal thickness ranges. Table 1 shows the mean

Table 1. The Mean Values of CCT Obtained By Each Pachymeters In Different CCT Ranges and IOP For Each CCT Ranges

	CCT 449-674 μm	CCT <510 μm (n=18)	CCT, 510-580 μm (n=56)	CCT >580 μm (n=28)
OB	534.7±41.2	473.6±18.6	529.7±18.9	583.1±20.2
TOPO	544.8±41.5	482.1±17.8	540.5±19.5	593.3±18.9
UP	553.1±44.2	487.6±15.4	547.0±20.2	606.3±20.8
NCP	562.9±43.2	499.3±17.9	558.2±21.7	612.3±22.7
IOP	16.2±3.1	14.3±2.3	15.6±2.5	18.5±3.2

All results were given as mean ± standard deviation

CCT: Central Corneal Thickness, OB: Optic Biometry, TOPO: Corneal Topography, UP: Ultrasound Pachymeter, NCP: Non-contact Pachytonometer, IOP: Intraocular Pressure, μm: micrometer

Table 2. Mean Paired Difference (SD) and 95% LoA Values

	Mean paired difference		95% limits of agreement	
	Mean±SE (μm)	p	Lower Limit	Upper Limit
TOPO-UP	-5.44±1.13	<0.001	-27.9	17
UP-NCP	-10.28±1.07	<0.001	-31.6	11
OB-TOPO	-11.11±0.72	<0.001	-25.6	3.3
TOPO-NCP	-15.72±1.08	<0.001	-37.1	5.7
OB-UP	-16.55±0.96	<0.001	-35.6	2.5
OB-NCP	-26.84±0.99	<0.001	-46.6	-7.1

Repeated Measures ANOVA using Bonferroni adjustment for multiple comparisons and Bland-Altman 95% LoA

OB: Optic Biometry, TOPO: Corneal Topography, UP: Ultrasound Pachymeter, NCP: Non-contact Pachytonometer, μm: micrometer

values of the CCT obtained by each instruments for each group.

Respective upper and lower values for 95% LOA between pachymeter pairs were given in Table 2. Based on the results, the mean difference in the CCT was the highest between OB and NCP and lowest between TOPO and UP. The 95% of the LOAs for right eye (ie, the interval within which 95% of differences between measurements by the two methods are expected to lie) are shown on Bland–Altman plots in figure 2. All measurements was only in the confidence interval for OB-UP pachymeters.

The Pearson correlation coefficients were given in Table 3. There were strong correlations between all pachymeters. The correlation between all measurement methods was over 0.950 both eyes.

Table 4 shows the Spearman correlation coefficients between different CCT ranges in different pachymetry methods. When the CCT was divided into the three groups according to the corneal thickness ranges, the correlation was higher than 0.7 in all groups (r=0.72-0.91 for <510 μm, r=0.85-0.95 for 510-580 μm, r=0.82-0.93 for >580 μm). While the correlation was highest between OB and TOPO in thin CCT (r=0.938), it was highest between OB-TOPO (r=0.918) and OB-UP (r=0.908) in thick CCT. Correlation of OB with other devices (OB-UP, OB-TOPO, OB-NCP) was found better than the correlations of other devices (TOPO-NCP, TOPO-UP, UP-NCP) with each other in normal corneal thickness range.

A significant positive correlation was observed between the IOP values and the CCT obtained by all pachymeters with a trend toward increasing the IOP with increasing corneal thickness (Table 5). Figure 3 shows the linear regression graphic between the CCT and IOP obtained by non-contact pachytonometer. The correlation between IOP and CCT was similar by all pachymeters in both eyes.

Discussion

This study analyzed the comparison, correlation and agreement between three non-contact pachymeters and ultrasound pachymeters for the CCT measurements in normal eyes and found

Table 3. Pearson Correlation Analysis Between The Measurements Obtained By Each Pair Of Measurement Methods

	r	p
OB-TOPO	0.984	<0.001
OB-UP	0.976	<0.001
OB-NCP	0.973	<0.001
UP-NCP	0.969	<0.001
TOPO-NCP	0.967	<0.001
TOPO-UP	0.965	<0.001

Pearson Correlation Analysis With Two Way Mixed Model For Absolute Agreement

Table 4. Spearman Correlation Analysis For Pachymeter Methods Between Different CCT (µm) Ranges According To UP Measurements (<510, 510-580, >580)

	<510 µm (n=18)	510-580 µm (n=56)	>580 µm (n=28)
TOPO-NCP	0.829	0.880	0.871
OB-NCP	0.797	0.890	0.867
UP-NCP	0.783	0.911	0.875
OB-TOPO	0.905	0.938	0.918
TOPO-UP	0.780	0.888	0.847
OB-UP	0.783	0.934	0.908

CCT: Central Corneal Thickness, OB: Optic Biometry, TOPO: Corneal Topography, UP: Ultrasound Pachymeter, NCP: Non-contact Pachytonometer, IOP: Intraocular Pressure, µm: micrometer

Table 5. Pearson correlation coefficient Between the IOP Values and CCT Obtained By Different Pachymeters

			NCP	OB	UP	TOPO
IOP	Right (n=102)	r	0.491	0.515	0.519	0.528
		p	<0.001	<0.001	<0.001	<0.001

r= Pearson Correlation

relatively poor numerical agreement despite strong correlations between methods. The correlation between the pachymeters were high in normal corneal thickness, whereas it was slightly lower in the thick and thin cornea.

The Characteristics of Conventional Ultrasonic Measurement Method: Currently, there are several methods to calculate the CCT, although the conventional method is the UP. Corneal thickness measurements can be performed using ultrasonic-based or optic-based techniques. Generally, the optic-based techniques are used in non-contact devices. Previous studies have reported significant differences between measurements of the CCT on the same subjects using different measurement techniques (4-6).

In the current study, mean CCT value with the UP was 18.4 µm higher than the OB, 8.3 µm higher than the TOPO, 9.8 µm lower than the NCP. The CCT obtained by NCP was the highest as compared with UP, OB and TOPO. Many studies reported that UP overestimates the CCT measurements when compared to the noncontact methods (7-10). As such these higher results taken with the UP could also be caused because of the instillation of topical anesthesia that produces epithelial edema during measurements of the CCT. Nam et al reported that the corneal thickness after the anesthesia drops slightly increased (10). The reason for this discrepancy is unclear. According to the previous studies (10-13), the possible answer for the difference in the CCT measurements involve the effect of corneal indentation, decentration of the probe to the cornea, displacement of the precorneal tear film, a possible effect of the topical anesthesia, the variable posterior reflection point and ultrasound speed between the descemet membrane and anterior chamber. The cornea was flattened and compressed by the contact ultrasound probe. In addition, the probe displaces the tear film. The posterior reflection zone may be located possibly

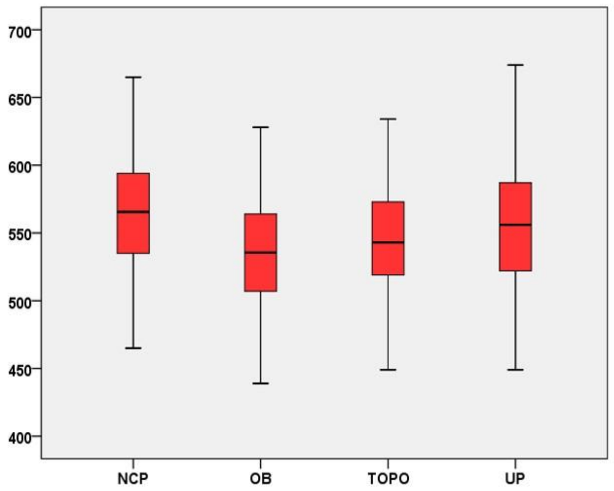

Fig. 1. CCT Values Measured By The Four Tonomete Rs By The Box-Plot Diagrams

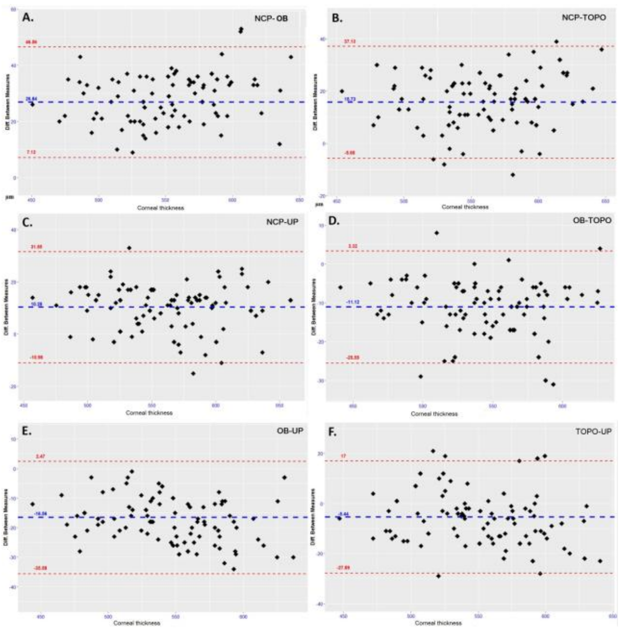

Fig. 2. The 95% of the LOAs for right eye on Bland–Altman plots

between the Descemet membrane and the anterior chamber. Therefore, the accurate location of the anterior and posterior reflection zone is not known in contact measurements (14-15). In contrast, the non-contact devices based on the scheimpflug system detected the CCT when a 475-nm monochromatic blue light beam is reflected from the corneal surfaces with different refractive indices. The distance between the anterior and posterior surfaces was calculated by the devices. Actually, this is not a surprising result because of the differences in the CCT measurement between the non-contact devices and contacts the UP result from different operating principles. Most of the previous studies reported thinner CCT measurement obtained with the Scheimpflug-

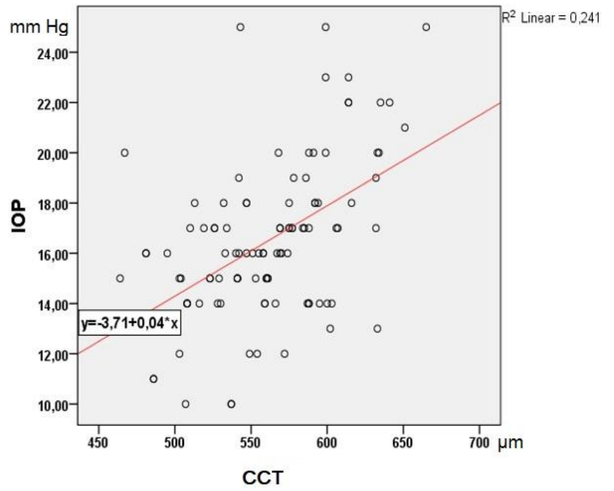

Fig. 3. The Linear Regression Graphic Between The CCT and IOP Obtained By Non-Contact Pachytonometer

based systems compared with the UP measurements (11-14). The difference has been on average measured to be 10 µm thinner than those obtained with the UP similar to our study (11-14). The difference between the TOPO and UP 8.39±0,77 µm (p<0.001).

CCT obtained from the NCP were higher than the UP in our findings. The corneal thickness compared with other pachymeters with a mean difference of 9,82 µm with UP, 18.15 µm with the TOPO, 28.20 µm with the OB (p<0.001). According to our findings, the NCP provides significantly higher CCT measurements (p<0.001) to those offered by commonly used pachymeters, although correlations are fine as in the previous study (15-17). The essential advantage of the tonopachymeters compared with other noncontact tonometers is that it provides CCT corrected IOP measurements.

The Correlation Between Pachymeters In All Corneal Thickness Range: When analyzing the correlation and agreement compared with the UP and other non-contact devices, we found that the all non-contact pachymeters showed the strong correlation with the UP (r=0.965-0.976, p<0.01, Table 3). In addition, there was strong correlation between other non-contact tonometers (r=0.967-0.984, p<0.01, Table 3). These correlations has been shown in many previous studies (4-5,7). Regarding the comparison between the CCT measurements using the OB, TOPO, UP and NCP, we showed that the OB and TOPO were the most correlated by a narrow margin in our study (r=0.984).

The Correlation Between Pachymeters In Different Thickness Range: CCT were divided into 3 groups as thin (<510µm), medium (510-580 µm) and thick (> 580 µm), and correlation analysis was performed using the Spearman correlation test (Table 4). When the correlation between pachymeters is analyzed, it is highest in the group with medium corneal thickness (r=0.88-0.93). The correlation is higher in the group with thick corneal thickness (>580µm), than the group with thin corneal thickness (<510µm) by the Spearman correlation method (r=0.84-0.91, r=0.78-0.90, respectively). The highest correlation was between OB-TOPO at different CCT ranges. OB-UP correlation was very close to OB-TOPO in normal and thick corneal thickness, but it is lower in thin corneal thickness. The correlation of OB-TOPO is upper than 0.9 in all corneal thickness ranges. In all three corneal thickness ranges, only OB-TOPO has a correlation greater than 0.9.

Relationship Between Corneal Thickness and Intraocular Pressure: In our study, we also analyzed the possible impact of the CCT by 4 different pachymeters on the IOP measurements obtained by the NCP in healthy adults. The data revealed the IOP measurements obtained by the NCP were conditioned by the CCT. The amount of variation in the NCP determined the IOP due to the CCT was similar between all pachymeters (Table 5).

In conclusion, despite relatively poor numerical agreement between pachymeters was found in this study, correlation values indicated significant association between all pachymeters. The correlations between the pachymeters were high in normal corneal thickness, whereas it was slightly lower in the thick and thin cornea. According to the correlation analysis, the two most compatible tonometers were determined as OB-TOPO. The correlation of OB-UP was close to OB-TOPO except in eyes with thin corneal thickness. All measurements were only in the confidence interval for OB-UP pachymeters on Bland–Altman plots. A significant positive correlation was observed between IOP and CCT in all pachymeters.

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