



Central Corneal Thickness Measurements with Different Imaging Devices: Ultrasound Pachymetry, Noncontact Specular Microscopy, and Tono-Pachymetry

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Abstract

Objectives: Investigation of the compatibility between central corneal thickness (CCT) measurements in healthy eyes by comparing standard ultrasound pachymetry (USP) with noncontact tono-pachymetry (NCT) and specular microscopy (SM) devices was aimed.

Methods: Forty-five eyes of 45 healthy volunteers aged between 18 and 60 years were included in this study. CCT of all cases was evaluated with USP, NCT, and SM devices. The same examiner performed all examinations. Bland–Altman plots and intraclass correlation coefficients were used to evaluate the agreement between instruments.

Results: The mean age of the patients was 31 ± 10.2 years. Fifteen (33.3%) cases were male and 30 (66.7%) were female. The mean CCT measured using NCT ($559.3 \pm 39 \mu\text{m}$) was significantly higher than those measured using SM ($534.8 \pm 41 \mu\text{m}$) and USP ($542.6 \pm 43 \mu\text{m}$, $p < 0.001$). Bland–Altman analysis showed that the difference between the first, second, and third measurements was evenly dispersed around the mean, with no clear trend toward over- or underestimation by either NCT, USP, or SM. The 95% limits of agreements were 0.30 – $48.72 \mu\text{m}$ for NCT, -12.63 – $46.04 \mu\text{m}$ for the USP, and -24.41 – $8.80 \mu\text{m}$ for the SM. Correlation analysis between the three devices showed a very strong positive correlation ($p < 0.001$).

Conclusion: Significant differences were observed between CCT measurements in healthy individuals used in ophthalmology practice and performed with different devices. This situation should draw attention to the fact that in diseases such as glaucoma and endothelial insufficiency, corneal thickness monitoring should be done with the same device and the devices should not be used interchangeably.

Keywords: Central corneal thickness, ultrasound pachymetry, noncontact tono-pachymetry, specular microscopy

Introduction

Central corneal thickness (CCT) is an important and sensitive indicator of corneal health (1). It is necessary to monitor corneal diseases such as glaucoma, keratoconus, corneal ectasia, Fuchs endothelial dystrophy, and corneal edema, and to evaluate the corneal barrier and endothelial pump func-

tion in various surgical situations (2). It is also an important parameter in patient selection for refractive surgery to prevent postoperative corneal ectasia (3).

Various methods are available to measure CCT including ultrasound, specular microscopy (SM), tono-pachymetry, optical coherence tomography, interferometry, confocal microscopy, and corneal topography (4, 5). Ultrasound

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pachymetry (USP) is the gold standard and determines CCT by measuring the time it takes for the ultrasound wave to return from the corneal endothelium (6). It has very high repeatability and has several advantages such as speed of use and portability (7). Due to the contact nature of the USP, the possibility of epithelial defect, and the possibility of incorrect measurement due to the user, noncontact methods have been preferred more recently.

Noncontact tonopachymetry (NCT) is a technique that combines the functions of tonometer and optical pachymeter. The pachymetry function measures CCT at the apex of the cornea by determining the distance between optical reflections from the anterior and posterior surfaces of the cornea (8).

The noncontact specular microscope (SM) is used to examine endothelial cell density and heterogeneity, especially before cataract and corneal transplant surgery. It measures CCT according to the principle of reflection of light from the anterior and posterior surfaces of the cornea, similar to the NCT device (9).

There are many studies in the literature that compare CCT values measured using different devices but with conflicting results. Although USP was compared with SM or NCT with conflicting results in previous studies, the three devices have not been compared together in terms of measuring the CCT within the same study.

This study aimed to compare the standard USP, NCT, and SM devices for CCT measurements in healthy eyes and to determine the compatibility between them.

Methods

The prospective comparative study was performed according to the revised version of the Declaration of Helsinki from 2013 and was authorized by the Ethics Committee of the Basaksehir Cam and Sakura City Hospital. Written informed consent was obtained from patients after receiving detailed information regarding the nature and purpose of this study.

Forty-five volunteers (15 males and 30 females) were randomly selected from the patients who visited the outpatient ophthalmology clinic. Measurements were taken from right eyes. All subjects after CCT measurement were subjected to routine evaluation of visual acuity, refractive error, slit lamp examination, and indirect ophthalmoscopy.

Primary exclusion criteria for the study participants were patients with a history of previous ocular surgery, anterior segment abnormalities other than cataract, spherical equivalent of more than ± 2 D, and who were unable to cooperate in the examination.

One examiner (A.C.) performed the CCT measurements to minimize technical errors when performing USP. Three consecutive measurements were recorded: NCT

(Canon Full Auto Tonometer TX-20P, Canon INC., Kanagawa, Japan), standard USP (SP-100 Tomey, Tomey Corporation, Nagoya, Japan), and SM (EM-4000, Tomey Corporation, Nagoya, Japan) devices.

The first measurement was made using a noncontact tonopachymeter. The NCT measures intraocular pressure using the air-puff and pachymeter using the specular microscope method. Volunteers were asked to place their heads on the headrest and focus on the fixation target. The transmitted light from a slit in the cornea is reflected by the front and back surfaces of the cornea. It measures the CCT by determining the distance between reflections.

After completing the noncontact examination, USP was executed. First, an anesthetic drop (0.5% topical proparacaine hydrochloride) was instilled on the cornea. After 10 min, the participants were asked to look straight ahead to the fixation target. The ultrasound probe was tried to be contacted as close to the corneal center and perpendicularly as possible. Then, the measurements were repeated eight times for the right eye and they were averaged. After each procedure, the ultrasound probe was sterilized with disinfectant.

Statistical Analysis

The distribution of the samples was analyzed with the Kolmogorov–Smirnov test. For the comparison of the means of the three dependent groups, an analysis of variance test was used followed by a Bonferroni correction for the between-group analysis. The compatibility of the devices was evaluated with the Bland–Altman plot analysis and intraclass correlation coefficient. The correlation was analyzed using Pearson's correlation test. The results were presented as mean \pm standard deviation and 95% was used as the confidence interval. *p*-values below 0.05 were accepted as statistically significant.

The sample size analysis was performed using G*Power (version 3.1). Results from a recent study were used for the sample size calculation (10). The mean CCT data from three different devices were 546.9, 525.3, and 548.1 μm , and the standard deviation was 31 μm . The sample size analysis showed that 42 eyes were sufficient for 99% power for the study. Forty-five eyes were included in the study.

Results

A total of 45 eyes in 45 healthy subjects (only right eyes) were studied. The mean age of the patients was 31 ± 10.2 years. Fifteen (33.3%) of the cases were male and 30 (66.7%) were female.

The between-group comparison of the mean CCT data from three different devices is shown in Table I and their box plot graphs are shown in Figure I. The mean CCT of

NCT ($559.3 \pm 39 \mu\text{m}$) was significantly higher than that of SM ($534.8 \pm 41 \mu\text{m}$) and that of USP ($542.6 \pm 43 \mu\text{m}$, $p < 0.001$).

Bland–Altman analysis showed that the difference between the first, second, and third measurements was evenly dispersed around the mean, with no clear trend toward over- or underestimation by either NCT, USP, or SM (Table I and Fig. 2). The 95% limits of agreement were 0.30 – $48.72 \mu\text{m}$ for NCT, -12.63 – $46.04 \mu\text{m}$ for the USP, and -24.41 – $8.80 \mu\text{m}$ for the SM (Table I).

Correlation analysis between the three devices showed a very strong positive correlation ($p < 0.001$). Intraclass correlation coefficients are shown in Table I.

Discussion

Reliable and validated measurement of CCT is an important parameter in the planning of keratorefractive surgery, diagnosis, and follow-up of diseases such as endothelial failure, and glaucoma. There are many studies in the literature that compare CCT values measured using different devices but with conflicting results. In this study, noncontact methods (NCT and SM) and USP devices were compared.

Measurement of CCT with USP is considered the gold standard. In previous studies, USP and devices that can measure CCT using different methods were compared and different results were obtained. While some studies showed

that CCT is measured thicker by USP than by other devices (11–14), it has also been shown in other studies that CCT is measured thinner by USP (15, 16). Even in a study comparing two different USP devices, the agreement between two different pachymeters was found as poor despite a statistically significant strong correlation (17). This may be related to the operator-dependent nature of the device.

In a study on 216 healthy eyes, measurements of CCT taken with USP and SM were found to be compatible, and USP measured the central cornea $22.8 \mu\text{m}$ thicker than that measured by SM (10). Bovellet et al. compared the SM and USP measurements and found the USP measurement to be $32 \mu\text{m}$ higher on average (18). Similarly, Uçakhan et al. showed that CCT measured with USP was $20 \mu\text{m}$ higher on average than that measured using SM (14). Contrary to the other studies, Ohn et al. showed that CCT measured by USP and SM were compatible and SM measured CCT $15 \mu\text{m}$ thicker than that measured by USP ($p < 0.001$) (16). Similarly, Scotto et al found that the CCT measurement with SM was $10 \mu\text{m}$ thicker than that with USP on average (19). Furthermore, Erdur et al. showed no difference between the mean CCT measured with USP and SM (20). Overall, studies comparing SM and USP found that USP generally measures CCT thicker. Consistent with this, in our study, CCT with USP was measured $8 \mu\text{m}$ thicker than that measured using SM.

Table I. Comparison of the three different devices for the central corneal thickness measurement

Devices compared	Mean difference \pm SD (μm)	95% LoA (μm)	p^a	ICC	Pearson correlation	
					r	p
NCT-SM	24.51 ± 12.40	0.30 – 48.72	< 0.001	0.953	0.954	< 0.001
NCT-USP	16.71 ± 14.97	-12.63 – 46.04	< 0.001	0.934	0.937	< 0.001
SM-USP	-7.80 ± 8.47	-24.41 – 8.80	< 0.001	0.980	0.980	< 0.001

^aRepeated measures analysis of variance (ANOVA) with Bonferroni correction; NCT: Non-contact tonometry; SM: Specular microscopy; USP: Ultrasound pachymetry; SD: Standard deviation; ICC: Intraclass correlation coefficient; LoA: Limits of agreement.

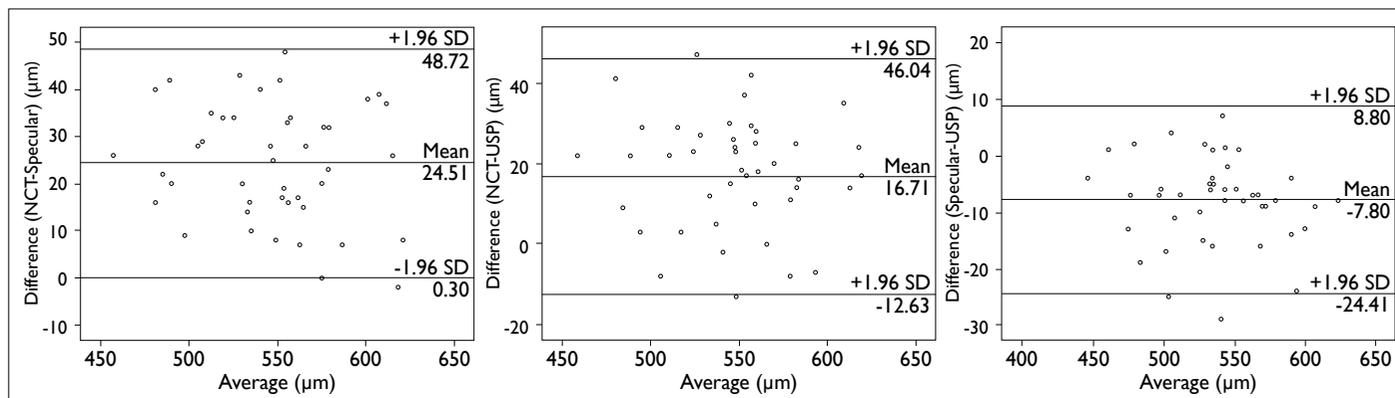


Figure I. Bland–Altman plot analysis of the central corneal thickness measurements between three different devices.

NCT: Noncontact tonometry; SM: Specular microscopy; USP: Ultrasound pachymetry.

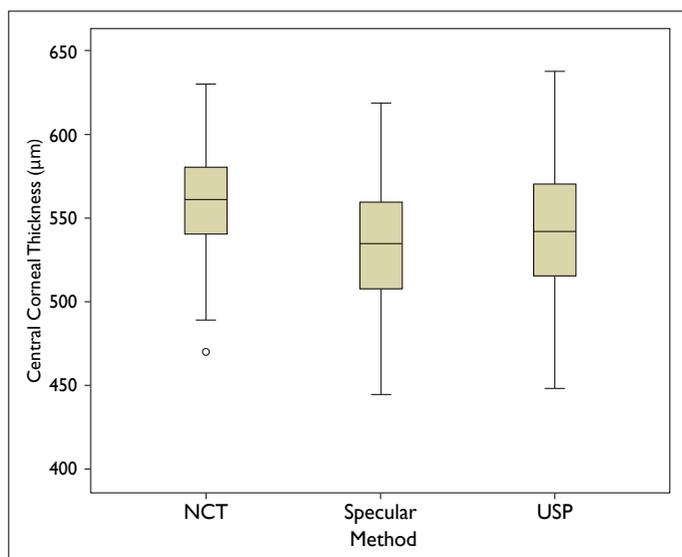


Figure 2. Comparison of three different devices for the measurement of central corneal thickness.

NCT: Noncontact tonometry; SM: Specular microscopy; USP: Ultrasound pachymetry; SD: Standard deviation.

The reason for this difference has not been clearly explained.

There is no study comparing the SM, USP, and NCT at the same time. Despite compatible measurements with NCT, USP, and SM found in our study similar to most studies in the literature, NCT ($559.3 \pm 39 \mu\text{m}$) measured CCT thicker than that measured by USP ($542.6 \pm 43 \mu\text{m}$) ($p < 0.001$) and USP measured CCT thicker than that measured by SM ($534.8 \pm 41 \mu\text{m}$) ($p < 0.001$). Although patients should be followed with the same devices, these differences should be taken into account when patients have to be followed with different devices. However, further studies are needed to better understand their measurement behavior in disease states such as corneal edema.

In the study by González-Pérez et al., CCT was found $33 \mu\text{m}$ thicker on average with USP than with NCT (4). Similarly, Lomoriello et al. found the mean CCT $13 \mu\text{m}$ thicker with USP compared to NCT (21). Garcia-Resua et al. also found that the mean CCT was $20 \mu\text{m}$ lower compared to USP when using the same NCT system (22). Sagdik et al. showed that CCT measurement was $28 \mu\text{m}$ thicker on average with USP than with NCT (23). In our study, contrary to the previous studies, CCT measured with NCT was found to be $17 \mu\text{m}$ thicker on average than that measured with USP ($p < 0.001$).

As both NCT and SM are the most commonly performed techniques to measure CCT, their measurement compatibility should be examined to improve our knowledge of their measurement results. Therefore, our study was designed to contribute to the literature in terms of the comparison of these two devices. In our study, NCT and SM methods were

also compared, and CCT measured with NCT was found to be $24 \mu\text{m}$ thicker on average than that measured with SM ($p < 0.001$). NCT and SM take measurements with the same method. However, no study was found comparing the two. In both of these methods, the slit light, which is reflected on the cornea at a certain angle, is reflected from the anterior and posterior surface of the cornea and is calculated trigonometrically. Despite high compatibility, NCT found CCT thicker than that found by SM in our study. This may be because both devices detect the anterior and posterior surfaces of the cornea from different levels.

The varying results with USP in different studies may be related to obtaining operator-dependent results with the device. In our study, we took care not to put pressure on the cornea, to keep the probe upright, to take the measurement from the center of the cornea, and to measure the CCT by a single operator. In this way, we think that we achieved high compatibility. The reason for the differences in the studies may be the differences in the pressure applied onto the cornea and probe centralization differences between the operators. Compliance of the patients who were measured may also affect the results. This situation can be clarified by studies evaluating the compatibility within and between operators.

The limitations of our study include the absence of other systems to measure CCT such as Scheimpflug-based and anterior segment optical coherence tomography for comparing with the devices included in the study. The second limitation is the single-center design of the study.

In conclusion, this study showed that despite compatibility between USP, SM, and NCT for the measurement of CCT, NCT measured thicker CCT than that measured by USP, and USP measured thicker CCT than that measured by SM in healthy individuals. This situation draws attention to the fact that in diseases such as glaucoma and endothelial insufficiency, corneal thickness monitoring should be performed with the same device and the devices should not be used interchangeably.

Disclosures

Ethics Committee Approval: Ethics Committee of the Basaksehir Cam and Sakura City Hospital, KAEK/2021.06.132.

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Conflict of Interest: None declared.

Authorship Contributions: Involved in design and conduct of the study (AC, YY); preparation and review of the study (AC, IO, BM, YY); data collection (AC, IO); and statistical analysis (AC, BM).

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