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Comparison of corneal thickness measurements using ultrasound pachymetry, noncontact tonopachy, Pentacam HR, and Fourier-domain OCT

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Abstract
We retrospectively compared the central corneal thickness (CCT) obtained by ultrasound pachymetry (USP; SP-3000, Tomey Corp., Nagoya, Japan), non-contact tonopachy (TP) (NT-530P, Nidek Co., Ltd., Gamagori, Japan), Pentacam HR (OCULUS Inc., Wetzlar, Germany), and RTVue optical coherence tomography (OCT) (Optovue Inc., Fremont, CA, USA) in 78 eyes of 78 healthy subjects with myopia. Agreement between the measurement methods was evaluated using 95% confidence intervals for the limits of agreement (LoA). The mean CCT values were 546.9 ± 34.7, 548.1 ± 33.5, 559.2 ± 34.0, and 547.2 ± 34.8 μm for USP, non-contact TP, Pentacam, and RTVue, respectively. The thickest and the thinnest mean CCT values corresponded to those obtained by Pentacam HR and USP, respectively. Plots of the differences against the means showed the best agreement between USP and RTVue (LoA, 10.14–10.70 μm), while the largest discrepancy was observed between RTVue and Pentacam systems (LoA, −25.47–1.44 μm). Our data showed that CCT measurements using these 4 instruments were well correlated. However, the results from Pentacam differed significantly from those of the other instruments.

Abbreviations: CCT = central corneal thickness, LoA = limits of agreement, OCT = optical coherence tomography, TP = tonopachy, USP = ultrasound pachymetry.

Keywords: corneal pachymetry, optical coherence tomography, Pentacam, tonopachy, ultrasound pachymetry

1. Introduction

Central corneal thickness (CCT) measurement is an integral component of ophthalmic examination. In glaucoma, a thin CCT is a significant risk factor for intraocular pressure (IOP) underestimation.[1,2] Accurate measurement of CCT is required when evaluating candidates for refractive surgery. Low residual stromal bed thickness is a risk factor for development of keratectasia after surgery.[3] Corneal thinning is known to be associated with keratoconus progression.[4] Additionally, CCT reflects the progression of Fuchs endothelial corneal dystrophy.[5] For patients with corneal problems, CCT measurements allow determination of disease status.

Several instruments are available for the measurement of CCT, each of which is based on specific principles. Contact ultrasound pachymetry (USP) is the most commonly accepted method.[6,7] In USP, a probe in contact with the anterior surface of the cornea detects the interface where the speed of sound changes. While USP is considered the gold standard in pachymetry, its measurement can be influenced by several factors. The probe should be placed perpendicular to the center of the cornea. To avoid possible corneal indentation, the operator must be trained properly and the patient must cooperate well during the examination. Moreover, this method carries additional risks such as corneal infection and erosion.[8]

Other instruments used for pachymetry are mostly automated and do not involve direct contact with the cornea. The Pentacam system (OCULUS Inc., Wetzlar, Germany) uses a rotating Scheimpflug camera to acquire cross-sectional images of the cornea. From these images, which contain up to 25,000 data points, Pentacam can calculate CCT, corneal curvature, anterior chamber angle, and anterior chamber depth.[9] RTVue (Optovue Inc., Fremont, CA, USA) is a high-speed, high-resolution optical coherence tomography (OCT) system. With the corneal anterior module option, RTVue examines the cornea and anterior segment. Non-contact tonopachy (TP) (NT-530P, Nidek, Japan) is a combination unit equipped with a non-contact tonometer and a pachymeter. The NT-530P system measures CCT with

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Scheimpflug camera and displays the compensated IOP, which is calculated from the measured CCT. The reliability of non-contact tonopachymeters has not been widely tested. Additionally, pachymetry evaluation is essential to confirm CCT-corrected IOP.

The purpose of this study was to compare CCT measurements obtained with USP, noncontact TP, the Pentacam system, and RTVue OCT in healthy subjects with myopia.

2. Materials and methods

2.1. Subjects

This retrospective case series study assessed 78 eyes of 78 patients who underwent preoperative examination for refractive surgery at B and Viit Eye Center between January 2017 and August 2017. To avoid inter-eye correlation, only right eye from each patient was included. This study was approved by the Institutional Review Board of Daejeon St. Mary's Hospital (DC20RISI0031) and conducted in accordance with the tenets of the Declaration of Helsinki. Patients with any of the following were excluded: history of previous ocular surgery, corneal disease, soft contact lens wear within one-week, dry eye, or ocular or systemic medication use that would likely affect corneal thickness. Four instruments were used for the measurement of corneal thickness: an NT-530P (Nidek Co., Ltd., Gamagori, Japan) for non-contact TP, an RTVue OCT (Optovue, Inc., Fremont, CA, USA) for spectral domain OCT, a Pentacam Scheimpflug imaging system (Pentacam, Oculus, Wetzlar, Germany), and an SP-3000 (Tomey Corp., Nagoya, Japan) for USP. Three non-contact measurements were followed by the application of a topical anesthetic to obtain USP data. Two examiners performed the measurements, and the mean value was used for further analysis.

2.2. CCT measurements with non-contact tonopachy

Non-contact TP measures corneal thickness using Scheimpflug imaging and calculates the compensated IOP based on the measured thickness.[10] Measurements were obtained automatically after approximately focusing the mires on the screen. CCT values were recorded for each of the 3 IOP measurements. Mean CCT values were used for the analysis.

2.3. CCT measurements with a rotating Scheimpflug camera

Pentacam HR was used to acquire Scheimpflug data.[11,12] An image was built from 50 slit-beam images using a single rotating Scheimpflug camera. CCT was recorded from the corneal thickness at the pachy apex (0, 0) displayed by Pentacam software.

2.4. CCT measurements with RTVue OCT

RTVue has a depth resolution of 5 μm in tissue for a light source working at 830 nm.[13] A corneal anterior module was added to image the anterior segment and to obtain the corneal thickness. The scans were centered on the coaxially fixating corneal light reflex observed by the central bright reflection on the OCT scan. A pachymetry map was created automatically with 3 zones: central (0–2 mm), pericentral (2–5 mm), and transitional (5–6 mm). The corneal thickness value in the central 2-mm zone was used for the analysis.

2.5. CCT measurements with ultrasound pachymetry

After applying 1 drop of 0.5% proparacaine hydrochloride, patients were asked to look at a distant, fixed point in sitting position. The USP probe was placed perpendicular to the central surface of the cornea. Three consecutive measurements were acquired, and the mean value was used for the analysis.

2.6. Statistics

All data were analyzed using SPSS for Windows software (version 19.0; Microsoft Corp., Redmond, WA, USA). Normal distributions were confirmed using the Kolmogorov-Smirnov test. CCT was compared using one-way repeated measures analysis of variance (ANOVA). Paired comparisons were further evaluated using Bonferroni adjustment. Bland–Altman plots were used to evaluate the agreement between test instruments. The limits of agreement (LOA) were calculated as the mean difference between 2 measurements ± 1.96 times the standard deviation of the difference. The R-values between the instruments were obtained using Pearson's correlation. The percentage of corneas measured within a 5-μm difference was calculated between different measurements.

3. Results

This study included 78 eyes from 78 refractive surgery candidates. Table 1 shows demographic data of the patients including their sex, mean age, median age, and spherical equivalent refraction. Table 2 displays the mean CCT with standard deviations and the CCT range of each instrument. The Pentacam and USP systems provided the thickest and the thinnest CCT values, respectively. The differences in CCT values obtained from USP compared to TP, Pentacam, and RTVue systems were 1.22 ± 5.47, 12.29 ± 5.87, and 0.28 ± 5.32 μm, respectively. Table 3 shows the mean bias, bias range, LOA, width of limits, significance level for Bonferroni analysis, R-value, and percentage of corneas measured within a 5-μm difference.

All instruments showed a high correlation between measurements ($R = 0.980$–0.988). However, Bonferroni analysis showed that Pentacam CCT measurements differed significantly from those of other 3 instruments, whose values showed little or no

Table 1
Demographic data.

Characteristics	Value
Candidates/eyes	78/78
Sex	42% male, 58% female
Mean age, yr	25.5 ± 6.6
Median age, yr	23 (18 to 55)
Spherical equivalent refraction, Diopters	−4.44 ± 2.08 (−11.625 to −0.75)

Table 2
Mean results of ultrasound pachymetry, tonopachy, Pentacam, and RTVue.

Device	CCT values (Mean ± SD) (μm)	Minimum (μm)	Maximum (μm)
USP	546.9 ± 34.7	469	605
TP	548.1 ± 33.5	470	607
Pentacam	559.2 ± 34.0	481	624
RTVue	547.2 ± 34.8	473	608

CCT = central corneal thickness, SD = standard deviation, TP = tonopachy, USP = ultrasound pachymetry.

Table 3

Differences between ultrasound pachymetry, noncontact tonopachy, Pentacam, and RTVue.

Parameter	TP-USP	Pen-USP	RTVue-USP	Pen-TP	RTVue-TP	RTVue-Pen
Mean bias in CCT (μm)	1.22	12.29	0.28	11.08	−0.94	−12.01
SD (μm)	5.47	5.87	5.32	6.54	5.78	6.87
Maximum (μm)	15	30	18	28	14	7
Minimum (μm)	−12	−2	−9	−7	−14	−26
95% CI for the mean (μm)	−0.02 to 2.45	10.97 to 13.62	−0.92 to 1.48	9.60 to 12.55	−2.24 to 0.37	−13.56 to -10.47
LOA (μm)	−9.50 to 11.93	0.78 to 23.81	−10.14 to 10.70	−1.75 to 23.90	−12.27 to 10.39	−25.47 to 1.44
Width of limits (μm)	21.43	23.03	20.84	25.65	22.66	26.91
95% CI for the LOA	−11.61 to 14.04	−1.49 to 26.07	−12.19 to 12.75	−4.28 to 26.43	−14.5 to 12.63	−28.12 to 4.09
P (one-way ANOVA, Bonferroni)	0.316	<0.01	1.000	<0.01	0.941	<0.01
R-value	0.988	0.986	0.988	0.981	0.986	0.980
Within 5-μm difference (%)	73.1	10.3	71.8	19.2	69.2	17.9

ANOVA = analysis of variance, CCT = central corneal thickness, CI = confidence interval, LOA = limits of agreement, Pen = Pentacam, SD = standard deviation, TP = tonopachy, USP = ultrasound pachymetry.

difference (Table 3). The mean difference in CCT was largest between Pentacam and RTVue measurements. The percentage of corneas measured within a 5-μm difference was greatest, 73.1%, between USP and TP measurements. The smallest percentage was 10.3% between Pentacam and USP measurements.

The Bland–Altman plots in Figure 1 provide a graphical representation of the mean difference and LOA. The solid line represents the mean value, and the dotted lines show the agreement limits, with the smallest limit of agreement between RTVue and USP results.

4. Discussion

Our study investigated the agreement in CCT measurements using USP, non-contact TP, Pentacam, and RTVue OCT systems. The results revealed well-correlated CCT values. However, the measurements obtained by Pentacam differed significantly from those by other 3 instruments, while non-contact TP measurements were comparable to USP measurements.

In our study, USP, RTVue, TP, and Pentacam showed average CCT values in descending order. The difference between measurements was smallest by 0.28 μm in RTVue and USP. The differences were also small between RTVue and TP values and between TP and USP values. A comparison between TP and USP measurements showed that values from 73.1% of the eyes were within 5 μm. However, Pentacam measurements differed significantly from those of other 3 instruments. The largest gap of 12.29 μm was observed between Pentacam and USP readings; values from only 10.3% of eyes were within 5 μm. However, the variability in agreement was within the LOA. The limits were narrowest between RTVue and USP values (20.84 μm) and widest between RTVue and Pentacam values (26.91 μm).

Non-contact CCT measurement has recently gained much attention as it offers several advantages over contact methods. For example, contact with the corneal surface causes patient's discomfort, which can interfere with accurate measurements. Instilling an anesthetic eye drop can be bothersome in some patients. Additionally, probe contact can lead to corneal erosion and infection.

Among non-contact measurement methods, TP measures the corneal thickness and provides corrected IOP as opposed to other conventional tonometers. Accurate measurement of corneal thickness is a prerequisite for providing a precisely corrected IOP. Therefore, it would be important to investigate the reliability of CCT measurements in the TP.

Our results showed that TP measurements did not differ significantly from USP measurements: the average difference was 1.22 μm. Our results contradict those of earlier studies. Gonzalez-Perez et al compared non-contact TP with standard USP and found that TP underestimated CCT by 33.1 ± 33.3 μm.[14] However, their TP approach adopted a specular microscope method for pachymetric analysis.

In a separate study, Bao et al compared CCT obtained by 3 non-contact specular microscopes with that obtained by USP in 70 healthy subjects.[15] The mean CCTs measured by 3 non-contact microscopes were 513.66 ± 33.14, 529.12 ± 33.22, and 549.06 ± 40.27 μm, and the mean CCT obtained by USP was 539.01 ± 35.73 μm. Although non-contact specular microscopes and USP showed high intra-operator repeatability, the inter-device agreement was poor. Other studies have also found that non-contact specular microscopes underestimated CCT compared to USP.[16,17] Taken together, these outcomes imply the importance of scrutinizing corneal thickness measurements using non-contact pachymetric machines. In this study, TP used the Scheimpflug imaging principle to measure corneal thickness.

The accuracy of Pentacam CCT measurements, compared to USP has been challenged. While in some studies Pentacam system underestimated CCT,[18,19] in other studies Pentacam measurements were comparable to[20,21] or overestimated[22–24] CCT compared to USP. In our study, Pentacam yielded overestimation of CCT. Al-Ageel et al considered the effect of ultrasound probe displacing 7 to 40-μm-thick tear film, resulting in thinner measurements.[25] They also suggested that differences in corneal hydration after local corneal anesthesia could affect differences in measurement.[25] Also, USP probe may indent the corneal epithelium.[26]

Non-contact TP using the Scheimpflug principle provided results that were similar to those obtained with USP method. However, Pentacam, which uses a rotating Scheimpflug camera, overestimated CCT. It is unclear why the measurements differed between the 2 instruments that use the same principle. One possibility could be the incorporation of a correction factor by the manufacturer; Orbscan manufacturers recommend incorporating an acoustic factor to compensate for overestimation.[27] Another explanation is that the same principle does not necessarily produce the same results. For example, a study comparing CCT measurements obtained with GALILEI, a dual Scheimpflug system, and Pentacam indicated a difference of 18.26 μm, with a thicker measurement obtained using the GALILEI system.[18]

Several studies comparing corneal thickness readings between Pentacam and RTVue systems found Pentacam measurements to be thicker than RTVue measurements by 5.16 ± 19.09, 10.52 ± 5.28, 10.9 ± 5.93, and 21.9 ± 10.6 μm.[24,28–30] In our study,
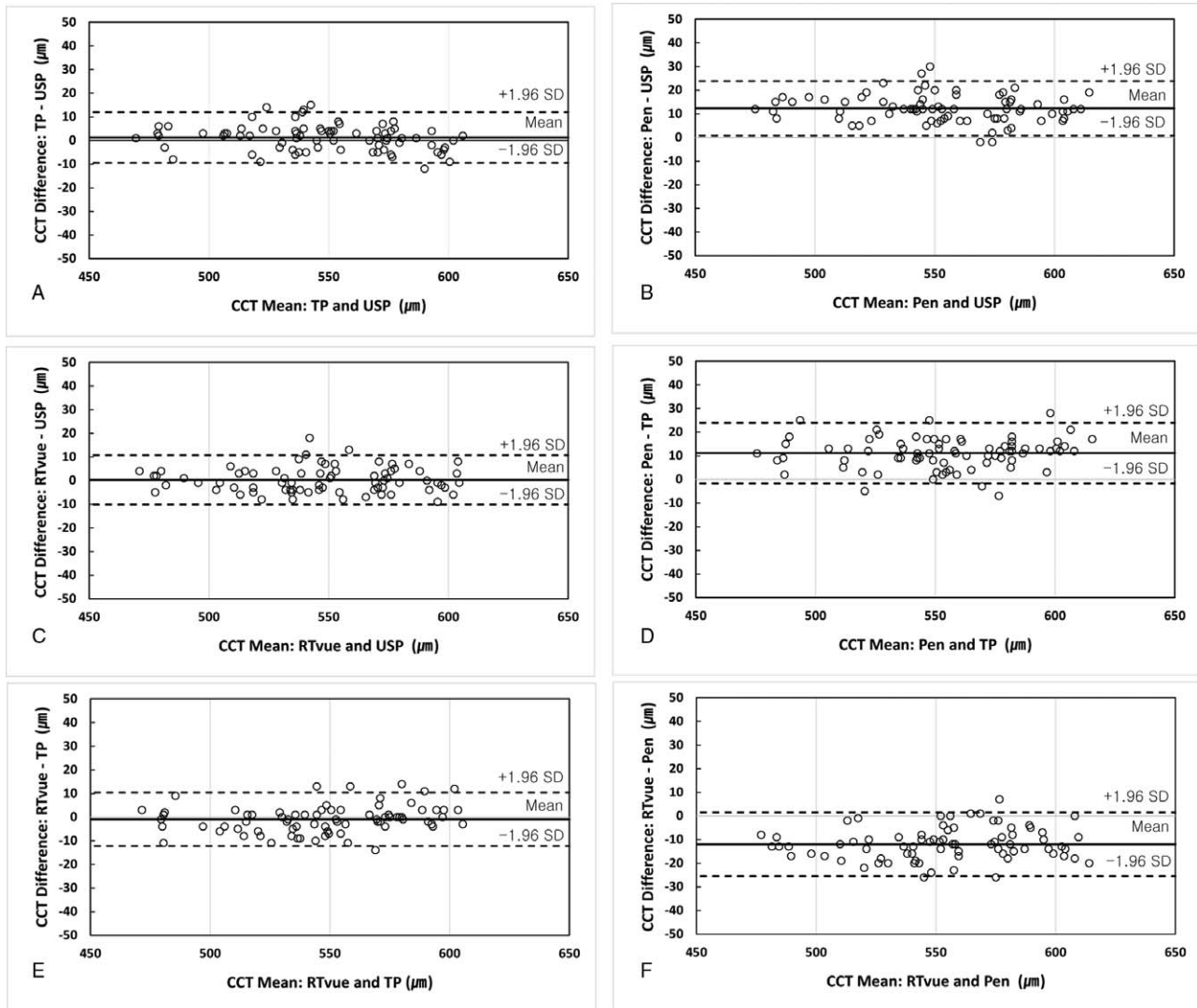
Figure 1. Bland–Altman plots comparing the central corneal thicknesses measured by (A) tonopachy (TP) and ultrasound pachymetry (USP), (B) Pentacam and USP, (C) RTVue and USP, (D) Pentacam and TP, (E) RTVue and TP, and (F) RTVue and Pentacam. The solid line represents the mean difference, and the dashed lines show the 95% confidence intervals for the limits of agreement.

Pentacam reading was thicker than that of RTVue system by $12.01 \pm 6.87 \mu m$, which was approximately at middle range of previous reports.

Two recent reports compared corneal thicknesses obtained with swept-source optical coherence tomography (CASIA SS-1000; Tomey, Nagoya, Japan or CASIA2; Tomey, Nagoya, Japan) and Pentacam.[31,32] Both reports found that Pentacam CCT measurements were thicker than SS-OCT (swept-source optical coherence tomography), by 4.91 and 9.64 μm, respectively. Zhao et al insisted that SS-OCT outperformed the Scheimpflug-based corneal topographic map in measuring corneal thickness. The coefficients of variation for corneal thickness measurements were smaller with CASIA SS-1000 than with Pentacam HR.[31] Li et al emphasized that SS-OCT has the advantage of shorter scanning time and utilizing an infrared light source to minimize the effects of instrument light on pupil movement.[32]

Our study had certain limitations. First, all subjects included in this study were myopic patients who underwent examinations for refractive surgery. Patients with emmetropia or hyperopia were not included in this study. Second, we did not explore instrumental correction factors. Third, the data collection may have been flawed. Armstrong suggested that if both eyes are to be included in an evaluation, the inter-eye correlation should be assessed using the intraclass correlation coefficient.[33] Also, the author viewed that eye should be randomly selected if only one of 2 eligible eyes should be included.[33] Unfortunately, we evaluated a non-random data set, uniformly including only right eye of each patient. Murdoch et al suggested that in a condition where either eye can be equally affected, analyses made on only right, or on only left, or on a randomly selected eye are statistically equivalent.[34] Our participants were normal in terms of eye structure except for myopia, and we deemed that laterality would not influence corneal thickness in otherwise normal subjects. However, 2 concerns persist. First, only half of the available data were included in the analysis. Second, selection bias may have been in play considering that only right eye, instead of randomly selected eye, was included in this study. However, it should be mentioned that all subjects

were candidates for refractive surgery with normal best-corrected visual acuity in both of their eyes, providing a rationale for our selection of right eyes.

In this study, we measured and compared CCT with 4 different instruments, and found that their readings were closely correlated in general. However, CCT measurements made using Pentacam system were significantly thicker than those using other 3 systems. The difference in average thickness between-RTVue-and-USP was minimal.

Author contributions

Conceptualization: Jung Sub Kim.
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Formal analysis: Jung Sub Kim.
Investigation: Jung Sub Kim, Chang Rae Rho.
Methodology: Chang Rae Rho, Yeon Woo Cho.
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Supervision: Jeongah Shin.
Validation: Chang Rae Rho, Yeon Woo Cho.
Visualization: Yeon Woo Cho.
Writing – original draft: Jung Sub Kim, Chang Rae Rho.
Writing – review & editing: Jeongah Shin.

Correction

The asterisk indicating corresponding author was incorrectly placed on Dr. Jung Sub Kim in the byline. It has been corrected to Dr. Jeongah Shin.

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