Reliability and agreement of measuring central cornea thickness on RTVue Fourier-domain optical coherence tomography, Pentacam, and ultrasonic pachymeter

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Directed by Professor Kyoung Yul Seo

The Master's Thesis
submitted to the Department of Medicine,
the Graduate School of Yonsei University
in partial fulfillment of the requirements for the degree
of Master of Medical Science

Sang Min Nam

June 2009

This certifies that the Master's Thesis of Sang Min Nam is approved.

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June 2009

ACKNOWLEDGEMENTS

I thank Chan Young Im, MD, for his thoughtful supports on deciding study topics, supplying instruments, collecting data, and lively discussions. I am also grateful for all staffs at Ian Eye Center. This study would have not been accomplished without their heartful contributions. KORYO EyeTech gave me technological advices about RTVue. Professor Kyoung Yul Seo not only supervised my thesis, but also inspired me to go through research.

Finally, I dedicate this thesis to my beloved wife, daughter and parents. They are love of my life and help me keep my passion as an eye doctor.

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<ABSTRACT>

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Objective: To compare reliability and verify agreement in measuring central corneal thickness (CCT) using the following technologies: the newly developed RTVue Fourier-domain optical coherence tomography (OCT), the Pentacam, and the ultrasonic pachymeter (USP).

Design: Evaluation of diagnostic test.

Participants: 104 eyes from 52 healthy subjects (mean age, 28.6 ± 4.8 (SD) years).

Methods: In order to test for reliability, one eye of each subject was randomly assigned to repeatability test, in which three successive measurements were performed by a single operator. The other eye underwent an interoperator reproducibility test performed by three operators. Two centering methods of RTVue and three types of corneal thickness measurements on Pentacam were used. For USP, one drop of topical anesthetic was administered, and 90 seconds later, measurement was initiated. Concordance among these different methods was evaluated with limits of agreement (LoA), which were calculated from the average of the three measurements in repeatability test.

Main Outcome Measures: Measurements of central zone average and minimum thickness with RTVue centering on the vertex or the pupil, thickness at pupil center, apex, thinnest location measured by Pentacam, and mean CCT of five repeated measurements by USP were compared. The reliability of these measurements was assessed with the repeatability or reproducibility coefficient (Rco), the coefficient of variation (CV), and the intraclass correlation coefficient (ICC). Bland-Altman plots were used to analyze concordance.

Results: Rco of CCT by RTVue was around 4 to 5 µm, which was comparable with USP and lower than the Rco of Pentacam (10-11 µm). Rco did not depend on the centering methods of RTVue or the types of CCT on Pentacam. The location of minimum thickness measured by RTVue was less reliable than that of Pentacam. The three instruments were in good agreement with each other, within about 20-µm LoAs. The central zone average calculated by RTVue was larger than the thickness measured at the pupil center or apex with Pentacam. The measured CCT of USP was the thinnest among the technologies.

Conclusions: RTVue was a fast and accurate non-contact means of measuring CCT, but seems to require an automatic centering system to improve its reliability in measuring minimum thickness.

Key words : RTVue Fourier-domain optical coherence tomography, Pentacam, Ultrasonic pachymeter, Central corneal thickness, Reliability, Repeatability, Reproducibility, Agreement

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I. INTRODUCTION

Precisely measuring central corneal thickness (CCT) is a critical step in preoperative and postoperative evaluation for refractive surgery and an essential test for diagnosis and management of patients with glaucoma.[1] With the accurate CCT, we can have one of valuable indices to avoid devastating iatrogenic keratectasia from refractive surgery and we can monitor the exact intraocular pressure of glaucoma patients for the proper anti-glaucoma medication.

Ultrasonic pachymeter (USP) is the most common method used to measure CCT. However, USP is a method that requires contact with the cornea and its reliability is affected by variable factors such as the administration of topical anesthesia and operator skill. In fact, USP is a very delicate procedure, because the USP probe needs to be manually placed at the center of the cornea at as perpendicular of an angle as possible.

In contrast, Pentacam is a non-contact and more convenient method than USP, but Pentacam's reliability is reported to be comparable to[2] or lower than that of USP[3, 4], except for one study on interobserver reproducibility[3]. Therefore, Pentacam seems to be less reliable in CCT measurement than USP. Additionally, reports comparing Pentacam and USP report controversial results. Some articles report that the measured CCT of Pentacam is 6.1 to 9.8 μm thinner than that of USP.[2-5] Others state that the measured CCT of Pentacam is 6.5 to 8.2 μm thicker than that of USP.[6, 7]

RTVue is also a non-contact method and does not require any topical anesthesia. An operator aligns the CCD camera to the cornea using the joystick, and then clicks the button in the joystick to capture the image. Therefore, RTVue does not make any artifical changes to the cornea with drugs or mechanical instrumentation. Moreover, RTVue has a rapid imaging speed that overcomes eye movement velocity and ensures high resolution image while prioritizing patient comfort.

RTVue is the first Fourier-domain optical coherent tomography (OCT) system approved by the Food and Drug Administration. In 2007, a cornea adaptor module (CAM) was also approved and made 5-μm resolution and high magnification imaging of the cornea possible in 0.04 seconds. To date, RTVue is a means to measure CCT in a convenient, comfortable, and accurate way.

The high measurement velocity of RTVue is achieved with a stationary reference mirror. In older time-domain OCT systems, the scan speed is limited due to the back-and-forth mechanical movement of a reference mirror over a range of several millimeters.[8] RTVue eliminates this mechanical restraint on speed, simultaneously collects signals from the entire range of interest, and analyzes data using the spectral interferogram and a fast Fourier transformation.[9]

In spite of those promising technological advances of RTVue, there are limited data comparing RTVue to pre-existing technologies. For comparison of the reliability or validity of RTVue, we selected USP and Pentacam. USP is regarded as a gold standard of CCT measurement, and Pentacam is an another non-contact method that uses a rotating Scheimpflug camera that provides a three-dimensional scan of the anterior portion of the eye. To avoid possible effect of topical anesthetics on the cornea, we cautiously designed the way of topical anesthesia in USP measuring. All three kinds of CCT from Pentacam, such as CCTs at the corneal apex, the pupil center, and the thinnest corneal location, were included for comprehensive study.

II. MATERIALS AND METHODS

1. Subjects

We examined 104 eyes of 52 healthy volunteers. Our exclusion criteria included pregnancy, contact lens history within three days, corrected vision less than 20/20, intraocular pressure over 21 mmHg as measured by non-contact tonometry, pathologic changes of the lid, conjunctiva, or cornea on slit lamp examination, endothelial cell counts below 2000 cells/mm^2, and any history of ophthalmic surgery which could affect ocular surface. One eye of each volunteer was randomly selected for repeatability testing and the other eye was assigned for interoperator reproducibility testing. This study was approved by the Institutional Review Board with informed consent and adhered to the tenets of the Declaration of Helsinki.

2. Repeatability and Interoperator Reproducibility of Corneal Thickness Measurements

All measurements were performed from 9:30 AM to 5:30 PM after volunteers had been awake for at least one hour, in order to minimize diurnal change and any ophthalmologic effects from sleep and eye closure. Room temperature was around 23°C, and relative humidity was about 35%. The Pentacam (software version 1.16, Oculus Inc., Germany), RTVue (software version 3.5, Optovue Inc, Fremont, Calif, USA), and USP (Pocket-II, software version 1.02, Quantel Medical Inc., Bozeman, MT, USA; ultrasound velocity, 1620 m/s) were placed in the same dim-lit room.

The right eye of each volunteer was measured first, followed by the left eye. There were two types of RTVue measurements, according to landmarks such as the vertex and the pupil for centering the corneal map. Two types of RTVue measurements and Pentacam measurement were assigned to each eye, and the order of measurements was randomly arranged for each volunteer. In all volunteers, USP was performed last, because it required topical anesthesia and contact of the ultrasound probe, which may have skewed RTVue or Pentacam measurements. For repeatability testing, a single operator measured three successive times with each instrument. For interoperator reproducibility, three operators consecutively and randomly obtained a single measurement of the selected eye with each instrument. Each operator was blinded to the results of the other operators. All sequential measurements were taken with a 15-second interval between each during which the volunteer was encouraged to blink normally.

A CAM-L lens adapter with low magnification was attached to the RTVue. The volunteer was positioned on a headrest and asked to look at a blue, round target at the center of the camera. One of two centering methods was performed. The vertex-centered scan was made by adjusting the position of the OCT system until a bright, vertical flare line was seen on the real-time OCT image and was placed at the center of the image. Alternatively, the pupil-centered scan was obtained by aligning the aiming circle to the center of the pupil on the real-time OCT image. The adjusted scan was captured, reviewed, and calculated.

For Pentacam measurements, the volunteer was seated with a headrest and asked to focus on the target at the center of the camera. The operator moved the Pentacam joystick until arrows on the display were aligned with the horizontal, vertical, and anteroposterior axes in focus. As soon as the image was perfectly aligned, the volunteer was asked to keep his or her eye open, after which the scanning process started. Automatic release was used to reduce variables. The 25-images mode was chosen, so that the rotating camera acquired 25 scans within one second.

After RTVue and Pentacam, the cornea was anesthetized with one drop of 0.5% proparacaine (Alcaine, Alcon Puerto Rico Inc, Fort Worth, TX, USA) followed by 10-second eye closure. To avoid a possible increase of corneal thickness secondary to topical anesthesia, the measurement began after 90 seconds of normal blinking.[10] Then, repeatability and interoperator reproducibility testing were performed as previously described. The calibration was verified with a built-in, plastic test-block (880 ± 10 μm). The ultrasound probe was manually placed at as perpendicular of an angle as possible to the center of the cornea while the volunteer was instructed to gaze at a distant target. The measurement would only be taken if the probe was within ten degrees of the perpendicular. Given the instrument's default settings, five consecutive measurements were automatically averaged to obtain a single value for CCT.

3. Statistical Analysis of Repeatability and Reproducibility

Statistical analyses were performed using SPSS (version 15.0, SPSS Inc., Chicago, IL, USA) and SigmaStat (version 3.11, Systat Software Inc., San Jose, CA, USA). Using the three measurements of each eye from repeatability or reproducibility testing, we calculated the within-subject standard deviation (Sw), repeatability or reproducibility coefficient (Rco), coefficient of variation × 100 (CV), and intraclass correlation coefficient (ICC).

Sw assumes that the subject standard deviation should be independent of the subject mean. This assumption was checked by plotting the individual subject's standard deviations against their means and analyzing with Kendell's tau correlation. In addition, extreme outliers with standard deviations that were more than three times the box width in a boxplot were excluded. A one-way analysis of variance (ANOVA) was used to calculate Sw.[11] The standard error of Sw was estimated by the equation, $Sw/[2n(m - 1)]^{1/2}$, in which “n” represented the number of subjects and “m” represented the number of observations per subject.[12] Rco, defined as $1.96 \times 2^{1/2} \times Sw$, signifies the difference between two repeated measurements for the same subject and the disparity is expected to be less than Rco for 95% of the pairs of observations.[11] CV was calculated with a logarithmic method.[13] CV can be referred to even when the assumption of Sw is not satisfied. Smaller CVs are regarded as representative of better repeatability or reproducibility. ICC and its 95% confidence interval (CI) were computed with SPSS using a two-way mixed model and absolute agreement. ICC approaches 1.000 as repeatability or reproducibility improves.

4. Agreement of Corneal Thickness Measurements and Statistical Interpretation

Agreement of CCT measurements among RTVue, Pentacam, and USP was investigated with a Bland-Altman plot.[14] Three successive measurements from repeatability testing were averaged for each eye, except for USP measurements in which the first single CCT was chosen. The mean difference of the averaged corneal thickness between two methods was calculated. Because some of the repeated measurement errors had been removed by averaging values, the standard deviation of the difference was corrected. The corrected standard deviation was used to estimate the 95% CI of mean differences and limits of the agreement (LoAs).[15] Then, 95% of mean differences would be expected to lie between the upper and lower LoAs. When LoAs were small enough to be allowed clinically, two instruments were deemed to be in good agreement. Additionally, the standard error of upper and lower LoAs is equal to $(3s^2/n)^{1/2}$, where “s” is the corrected standard deviation of the difference between two methods and “n” is the sample size.[14] The smallest LoAs, that is, the most optimistic estimations, were picked up from 95% CIs of upper and lower LoAs.

III. RESULTS

The mean age of the 52 volunteers was 28.6 ± 4.8 (SD) years. Our study included 12 men and 40 women. One volunteer worn soft contact lens four days ago. Mean spherical errors of 52 eyes with repeatability testing and interoperator reproducibility testing were −5.35 ± 3.26 (SD) and −5.44 ± 3.28 (SD) diopters, respectively.

1. Reliability of Central and Minimum Corneal Thickness Measurements by RTVue

The reliability of corneal thickness measurements was evaluated with repeatability and interoperator reproducibility testing (Table 1, Table 2, and Table 3). The reliability of RTVue was superior to Pentacam and equivalent to USP. The reliability of RTVue did not depend on which centering method was used. There was no difference in reliability among three types of CCT from Pentacam. The interoperator reproducibility of USP was not worse than the repeatability of USP (Table 1 and Table 2).

Although the minimum thickness measured on RTVue was a single-point value, the reliability was comparable with its measured central zone average (Table 1, Table 2, and Table 3). However, coordinates of the minimum thickness measured with RTVue were more variable than the thinnest location measured with Pentacam. Repeatability coefficients of the x-coordinate of RTVue and Pentacam were 0.930 mm (95% CI, 0.801-1.059 mm) and 0.40 mm (95% CI, 0.34-0.45 mm), respectively. Repeatability coefficients of the y-coordinate of RTVue and Pentacam were 1.018 mm (95% CI, 0.877-1.159 mm) and 0.27 mm (95% CI, 0.23-0.31 mm), respectively. Hence, the minimum thickness measured with RTVue was located more dispersively than the thinnest thickness measured with Pentacam (Figure 1). But, the location measured with RTVue was strongly correlated with that of Pentacam (Pearson correlation; x-coordinate of the right eye, $P = 0.007$; y-coordinate of the right eye, $P < 0.001$; x-coordinate of the left eye, $P < 0.001$; y-coordinate of the left eye, $P < 0.001$).

Table 1. Comparison of Repeatability with Three Successive Measurements of Central Corneal Thickness Using RTVue Fourier-Domain OCT, Pentacam, and Ultrasonic Pachymeter[a]

	Mean (SD), µm	**Rco (95% CI), µm[b]**	**CV (95% CI), %**	**ICC (95% CI)**
pRTV	548.0 (27.0)	4.7 (4.0 – 5.3)	0.31 (0.27 – 0.35)	0.996 (0.994 – 0.998)
vRTV	548.9 (26.9)	3.9 (3.4 – 4.4)	0.26 (0.22 – 0.29)	0.997 (0.996 – 0.998)
P_{PC}	541.3 (26.2)	10.0 (8.6 – 11.4)	0.67 (0.58 – 0.77)	0.981 (0.970 – 0.989)
P_{CA}	540.6 (26.2)	10.0 (8.7 – 11.4)	0.68 (0.58 – 0.77)	0.981 (0.970 – 0.989)
US[c]	534.7 (26.8)	4.9 (4.2 – 5.6)	0.34 (0.29 – 0.38)	0.996 (0.993 – 0.997)

[a]The total eye number was 50. Two extreme outliers (one for RTVue and the other for Pentacam) were excluded. Rco represents the repeatability coefficient; CV, coefficient of variation; ICC, intraclass correlation coefficient; CI, confidence interval; pRTV, 2-mm central zone average of corneal thickness by RTVue centered on the pupil; vRTV, 2-mm central zone average of corneal thickness by RTVue centered on the vertex; P_{PC}, corneal thickness at the pupil center on Pentacam; P_{CA}, corneal thickness at the apex on Pentacam; and US, central corneal thickness of ultrasonic pachymeter.

[b]One-way analysis of variance was used to compute Rco. Each eye's standard deviation was not correlated with each eye's mean.

[c]Each single corneal thickness value was calculated from the average of five successive measurements.

Table 2. Comparison of Interoperator Reproducibility of Central Corneal Thickness by Three Operators Using RTVue Fourier-Domain OCT, Pentacam, and Ultrasonic Pachymeter[a]

	Mean (SD), μm	**Rco (95% CI), μm[b]**	**CV (95% CI), %**	**ICC (95% CI)**
pRTV	548.3 (27.4)	4.0 (3.5 – 4.6)	0.27 (0.23 – 0.30)	0.997 (0.996 – 0.998)
vRTV	549.6 (26.8)	4.9 (4.2 – 5.5)	0.32 (0.28 – 0.36)	0.996 (0.993 – 0.997)
P_{PC}	540.7 (27.2)	11.4 (9.8 – 12.9)	0.77 (0.66 – 0.87)	0.977 (0.965 – 0.986)
P_{CA}	540.0 (27.0)	11.7 (10.1 – 13.3)	0.79 (0.68 – 0.90)	0.976 (0.962 – 0.985)
US[c]	535.2 (26.7)	5.2 (4.5 – 5.9)	0.35 (0.30 – 0.40)	0.995 (0.992 – 0.997)

[a]The total eye number was 52. There were no extreme outliers. Rco represents the reproducibility coefficient; CV, coefficient of variation; ICC, intraclass correlation coefficient; CI, confidence interval; pRTV, 2-mm central zone average of corneal thickness by RTVue centered on the pupil; vRTV, 2-mm central zone average of corneal thickness by RTVue centered on the vertex; P_{PC}, corneal thickness at the pupil center on Pentacam; P_{CA}, corneal thickness at the apex on Pentacam; and US, central corneal thickness of ultrasonic pachymeter.

[b]One-way analysis of variance was used to compute Rco. Each eye's standard deviation was not correlated with each eye's mean.

[c]Each single corneal thickness value was calculated from the average of five successive measurements.

Table 3. Repeatability and Reproducibility of Minimum Corneal Thickness Measurements with RTVue Fourier-Domain OCT and Pentacam[a]

	Repeatability[b] (n = 52)		**Reproducibility[c] (n = 52)**	
	Rco (95% CI), μm	**CV (95% CI), %**	**Rco (95% CI), μm**	**CV (95% CI), %**
pRTVm	5.0 (4.3 – 5.7)	0.33 (0.29 – 0.38)	4.3 (3.7 – 4.9)	0.29 (0.25 – 0.33)
vRTVm	5.1 (4.4 – 5.8)	0.34 (0.29 – 0.38)	4.3 (3.8 – 4.9)	0.29 (0.25 – 0.33)
P_{TL}	10.9 (9.4 – 12.4)	0.73 (0.63 – 0.83)	11.3 (9.7 – 12.8)	0.77 (0.66 – 0.87)

[a]Rco represents the repeatability or reproducibility coefficient; CV, coefficient of variation; CI, confidence interval; pRTVm, minimum corneal thickness of RTVue centered on the pupil; vRTVm, minimum corneal thickness of RTVue centered on the vertex; and P_{TL}, corneal thickness at the thinnest location on Pentacam.

[b]Three successive measurements were made for each eye.

[c]Each of three operators measured a single corneal thickness value in random order for each eye.

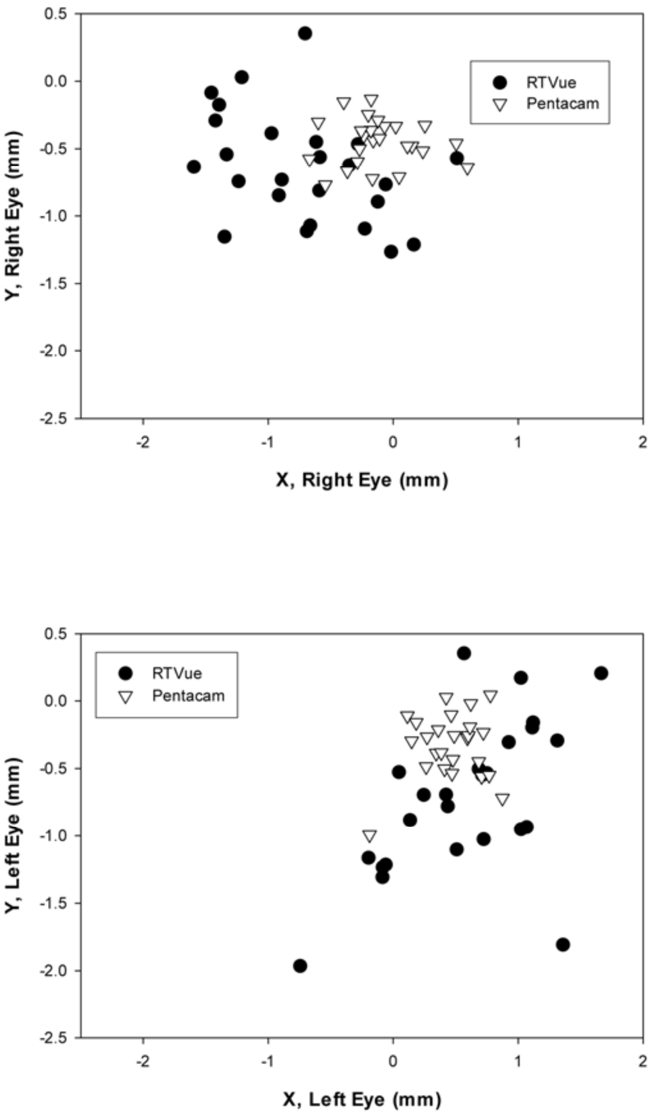


Figure 1. Distribution of the minimum thickness of the cornea as measured on RTVue Fourier-domain OCT and the thinnest location as measured on Pentacam of the right eye (top) and the left eye (bottom). RTVue was centered on the vertex for comparison with the coordinates from Pentacam, which are automatically centered on the apex. Three repeated coordinates were averaged for each subject. The total subject number was 25 for each eye. Two extreme outliers, one for RTVue in a right eye and the other for Pentacam in a left eye, were removed.

2. Agreement of Measurements Between RTVue or Penatacam and Ultrasonic Pachymeter

To evaluate agreement of measurements between two methods, a Bland-Altman plot was used (Figure 2). At least 95% of the data were randomly distributed between upper and lower LoAs (other plots were not shown except Figure 2).

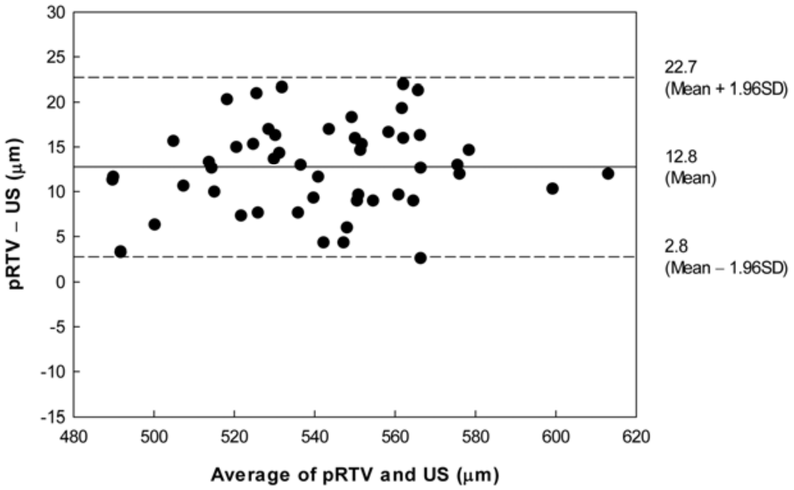
The CCT measured with RTVue or Pentacam was thicker than that of USP (Table 4). Mean differences between RTVue and USP were larger than those between Pentacam and USP. The mean difference was not affected by the various centering methods of RTVue or types of corneal thickness measurement of Pentacam. The most optimistic estimates of LoA were about 20 μm between RTVue and USP and 15 μm between Pentacam and USP, which could be regarded as good agreement in general practice.

3. Agreement of Measurements Between RTVue and Pentacam

The central zone average calculated by RTVue was thicker than the relevant CCT measured with Pentacam (Figure 2 and Table 4). However, the minimum thickness measured with RTVue was very close to the thinnest thickness measured with Pentacam. Specifically, the most optimistic estimates of LoA were about 17 μm between the central zone average measured with RTVue and CCT measured with Pentacam and 11-13 μm between the minimum thickness measured with RTVue and the thinnest thickness measured with Pentacam, which all were clinically acceptable.

4. Agreement of Measurements between RTVue Centering Methods

The central zone average measurements of RTVue did not significantly vary according to centering method (Table 4). However, the minimum thickness measured with RTVue was slightly smaller when centered at the pupil compared to when centered at the vertex.



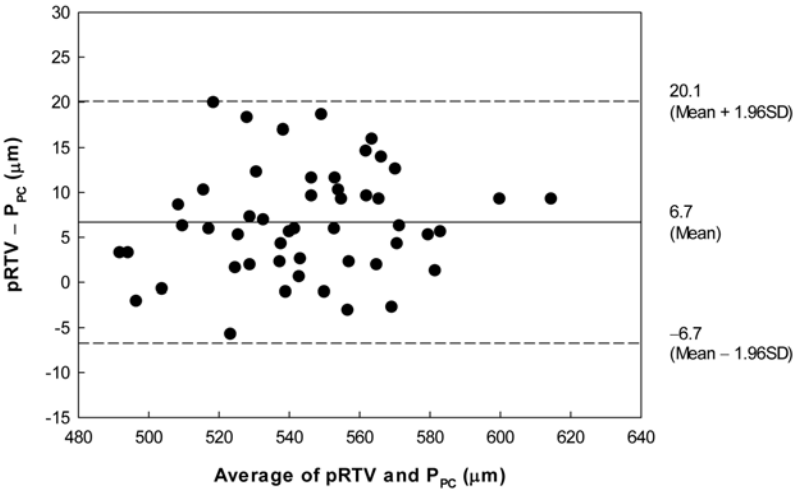


Figure 2. Bland-Altman plots of the difference between RTVue Fourier-domain OCT and ultrasonic pachymeter (top) and between RTVue Fourier-domain optical coherence tomography and Pentacam (bottom). pRTV indicates the mean of 3 repeated central zone averages of RTVue that was centered on the pupil. US indicates the first single central corneal thickness measured with ultrasonic pachymeter. P_{PC} indicates the mean of 3 repeated corneal thickness measurements at the pupil center with Pentacam. SD was corrected because the SDs of pRTV and P_{PC} had decreased by removal of their measurement errors when

they were averaged. Two extreme outliers (one for RTVue and the other for Pentacam) were excluded and the total subject number was 50. 95% of the subject data would be expected to be within the upper and lower LoA in both plots.

Table 4. Agreement of Central and Minimum Corneal Thickness Measurements with RTVue Fourier-Domain OCT, Pentacam, and Ultrasonic Pachymeter[a]

	Mean Difference (95% CI), μm	**Upper LoA (95% CI), μm**	**Lower LoA (95% CI), μm**
Between RTVue and USP[b]			
pRTV - US	12.8 (11.3 to 14.2)	2.8 (0.3 to 5.3)	22.7 (20.2 to 25.2)
vRTV - US	13.7 (12.3 to 15.0)	4.4 (2.1 to 6.7)	22.9 (20.6 to 25.3)
Between Pentacam and USP[b]			
P_{PC} - US	6.1 (4.3 to 7.9)	−6.3 (−9.4 to −3.2)	18.4 (15.3 to 21.5)
P_{CA} - US	5.4 (3.6 to 7.2)	−7.1 (−10.2 to −3.9)	17.8 (14.7 to 20.9)
Between RTVue and Pentacam			
pRTV – P_{PC}[b]	6.7 (4.7 to 8.6)	−6.7 (−10.1 to −3.4)	20.1 (16.7 to 23.5)
vRTV – P_{CA}[b]	8.3 (6.5 to 10.1)	−4.2 (−7.4 to −1.1)	20.9 (17.7 to 24.0)
pRTVm – P_{TL}[c]	0.2 (−1.8 to 2.1)	−13.8 (−17.2 to −10.4)	14.1 (10.7 to 17.6)
vRTVm – P_{TL}[c]	2.2 (0.1 to 4.2)	−12.2 (−15.7 to −8.7)	16.5 (13.0 to 20.0)
Within RTVue			
pRTV − vRTV[b]	−0.9 (−1.8 to 0.0)	−6.9 (−8.4 to −5.4)	5.1 (3.6 to 6.6)
pRTVm - vRTVm[c]	−2.0 (−2.8 to −1.2)	−7.8 (−9.2 to −6.4)	3.8 (2.4 to 5.2)
Within Pentacam[b]			
P_{PC} − P_{CA}	0.7 (−0.6 to 2.0)	−8.1 (−10.3 to −5.9)	9.5 (7.3 to 11.7)

[a]See the “Materials and Methods” section for a description of how the values in this table were calculated. CI represents the confidence interval; LoA, limits of the agreement; USP, ultrasonic pachymeter; pRTV, 2-mm central zone average of corneal thickness by RTVue centered on

the pupil; US, central corneal thickness of ultrasonic pachymeter; vRTV, 2-mm central zone average of corneal thickness by RTVue centered on the vertex; P_{PC}, corneal thickness at the pupil center on Pentacam; P_{CA}, corneal thickness at the apex on Pentacam; pRTVm, minimum corneal thickness of RTVue centered on the pupil; P_{TL}, corneal thickness at the thinnest location on Pentacam; and vRTVm, minimum corneal thickness of RTVue centered on the vertex.

[b]The total eye number was 50. Two extreme outliers (one for RTVue and the other for Pentacam) were excluded.

[c]The total eye number was 52. There were no extreme outliers.

V. DISCUSSION

In this study, RTVue was a reliable and accurate method for measuring CCT. The measurement error between two successive measurements was estimated to be only about 5 μm, and 95% of the measurements were expected to be within about 20 μm from USP measurement. RTVue measured this precise corneal thickness in 0.31 seconds with high-quality tomography of the cornea. Furthermore, RTVue can be applicable to various ophthalmic fields such as the anterior chamber, glaucoma, and the retina.

There are two reasons for the high reliability of corneal thickness measurements by RTVue. First, RTVue gives the central zone average of the corneal thickness in contrast to a single-point thickness on Pentacam. The central zone average is more reliable than an individual value. This reasoning also explains the high reliability of CCT measurements by USP, in which 5-repeated measurements are averaged to output a single value. Moreover, each CCT measurement of USP was a small-zone value given the 1.2-mm diameter of the probe tip. Second, RTVue has a high enough resolution through fast scanning to overcome motion artifact. This makes even a single-point value, for example, the minimum thickness, more reliable than the thinnest thickness measured with Pentacam (Table 3). In addition, the measured minimum thickness was as reliable as the calculated central zone average.

In contrast, coordinates of the minimum thickness measured with RTVue were less reliable than the thinnest locations measured with Pentacam. Because the minimum thickness measurement itself was very reliable, RTVue’s lower reliability of the measured coordinates may not result from measurement error, but from the instability of the reference point, which is determined by manual centering. Pentacam, on the other hand, automatically finds the location of the apex as a reference point after scanning (Figure 1).

Another caution for RTVue and Pentacam was an extreme outlier. While the percentage of outliers was less than 2% for each method, we recommend obtaining at least two measurements to avoid an unexpected value.

Measurements made by RTVue were in good agreement with the USP and Pentacam. However, an acceptable value for LoA is determined with a clinical decision, not with statistics. Therefore, our results should be applied depending on the clinical purpose. In general, a LoA less than 20 μm is acceptable. For example, Goldmann applanation tonometric intraocular pressure (IOPG) is correlated with CCT by 0.02 to 0.07 mmHg/CCT(μm).[1] Therefore, a 20-μm measurement error results in a 1 mmHg IOPG error.

In LASIK, a 20-μm LoA will not affect estimation of residual stromal thickness. Errors of residual stromal thickness estimation mainly originate from imprecision of microkeratome cuts and laser ablation depth. The mean difference between the actual and predicted flap thickness is −55 ± 24.3 (SD) μm,[16] −35.2 ± 18.5 μm,[17] −24 ± 29 μm,[18] or 20 ± 26 μm[18] depending on the type of head. Even by femtosecond laser, the mean flap thickness is 114 ± 14 μm with an intended thickness of 130 μm.[18] Additionally, actual ablation depth is more than predicted ablation depth by an average of 14.6 ± 16.7 μm[17] or 38 μm (SD was not given)[16]. Therefore, 20 μm is not significant compared with the mean size of total error and its standard deviation.

Although agreement was clinically good between RTVue and USP, the central zone average calculated by RTVue was statistically larger than the CCT measured with USP (Table 4). Two reasons for this finding are hypothesized and also explain why the CCT measured with Pentacam was larger than that of USP. First, applanation force by the ultrasonic probe may push away the tear film when the probe touches the surface with thinning the epithelium of the cornea or not. Because the thickness of the tear film is reported to be up to about 40 μm,[19] partial removal of the tear volume by the probe can make a change of tens of micrometers in thickness. The thinning effect of USP was also evident in our data. The second measured thickness of USP from repeatability testing was on average, 0.8 μm thinner than the first measured thickness (paired *t*-test, $P = 0.03$). Again, the third measurement was 1.0 μm thinner than the second measurement (paired *t*-test, $P = 0.003$). Second, a temporal thickening effect secondary to topical anesthetics was minimized in our study. Although some study argues against a temporal increase in corneal thickness following topical anesthesia,[20] a topical eye drop can augment the tear film with its water content or swell the epithelium secondary to chemicals.[10, 21] In our study, only one drop was instilled, followed by 90 seconds of normal blinking prior to measurement. These procedures lessened the possible increase of corneal thickness, which probably resulted in lower than usual thickness measurements.

In addition, the central zone average calculated by RTVue was thicker than its corresponding thickness measurement with Pentacam (Table 4). This result was predictable because corneal thickness increases as one proceeds closer to the periphery of the normal cornea. Therefore, central and thicker pericentral areas were included into the central 2-mm zone average calculated by RTVue. In contrast, the CCT measured with Pentacam is a single-point value near the center. Therefore, the single-point value measured with RTVue, the minimum thickness, was similar to the corresponding thinnest thickness measured with Pentacam (Table 4).

V. CONCLUSION

In conclusion, RTVue was a fast and accurate method used to measure CCT. RTVue could discriminate a 5-μm change in CCT with one shot and without disturbing the surface of the cornea. Because of RTVue's averaging calculation and non-contact set-up, the central zone average calculated by RTVue was slightly larger than the CCT measured with Pentacam or USP. An automatic centering system seems to be necessary to improve reliability, especially with regard to the coordinates of the minimum thickness.

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< ABSTRACT(IN KOREAN)>

RTVue 푸리에 도메인 광학집속단층촬영, Pentacam, 초음파 측정법 등을 이용한 중심각막두께의 신뢰도 및 합치도

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연구목적: 새로 개발된 RTVue 푸리에 도메인 광학집속단층촬영 기구로 중심각막두께를 측정하였을 때 신뢰도 및 타당도를 Pentacam 및 초음파 측정법 결과와 비교하여 알아본다.

연구대상: 평균 나이 28.6 ± 4.8 (SD) 세의 젊고 건강한 성인 남녀 52명을 대상으로 총 104개 안구에 대해 검사하였다.

연구방법: 신뢰도 평가를 위해서 각 연구 대상자의 한쪽 안구를 무작위로 선택하여 한 검사자가 연속 3회 측정함으로써 반복성을 알아보았다. 이때 다른 쪽 안구는 검사자 세 명이 1회씩 연속으로 3회 측정하여 검사자 간 재현성을 알아보았다. RTVue에서 이용되는 두 가지 중심 맞추기 방법과 Pentacam에서 제공하는 세 가지 각막 두께에 대해 평가하였다. 초음파 측정법 때는 점안 마취제를 단 한 방울 투약하고 90초 후에 측정하였다. 서로 다른 측정 방법 간 합치도를 분석하기 위해 초음파 측정법을 제외한 다른 검사에서는 반복성 검사 때 얻은 세 번 측정값을 평균을 내었다. 합치도는 합치도 한계 (limit of the agreement)를 계산하여 알아보았다.

분석방법: RTVue에서는 두 가지 중심맞추기 방법에 대해 중심영역평균과 최소두께를 얻었다. Pentacam에서는 홍체중심두께, 각막꼭지점두께, 최소두께를 얻었다. 초음파 측정법에서는 다섯 번 연속 측정값을 평균하여 일 회 측정값을 얻었다. 신뢰도 평가를 위해 반복성 또는 재현성 계수 (Rco), 변동계수, 급내상관계수 등을 구하였다. Bland-Altman 그림으로 합치도를 보았다.

결과: RTVue의 중심영역평균 두께에 대한 Rco는 4-5 μm로 초음파 검사법과 비슷했고 10-11 μm인 Pentacam보다 우수하였다. Rco는 RTVue의 중심맞추기방법 또는 Pentacam상 서로 다른 중심각막두께에 따라 달라지지 않았다. RTVue의 최소두께 위치는 Pentacam에 비해 신뢰도가 낮았다. 세 가지 기구 간에 합치도 한계는 약 20μm로 양호한 합치도를 보였다. RTVue의 중심영역평균값은 상응하는 Pentacam상 각막두께보다 두꺼웠다. 초음파 측정에 의한 중심각막두께 이 중 제일 얇았다.

결론: RTVue는 중심각막두께를 빠르고 정확하게 알 수 있는 비접촉성 측정 도구였으나 최소두께에 대한 신뢰도를 향상 시키려면 자동 중심맞추기 기능이 필요해 보인다.

핵심되는 말 : RTVue 푸리에 도메인 광합집속단층촬영, Pentacam, 초음파 측정법, 중심각막두께, 신뢰도, 반복성, 재현성, 합치도