

# To compare central corneal thickness measurements obtained by Pentacam with those obtained by IOLMaster 700, Cirrus anterior segment optical coherence tomography and Tomey specular microscopy in normal healthy eyes

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**Purpose:** To compare central corneal thickness measurements obtained by Pentacam with those obtained by IOL Master 700, Cirrus Anterior segment optical coherence tomography and Tomey Specular microscopy in normal healthy eyes. **Methods:** Two hundred and six eyes of healthy subjects were included in the study. Each subject was assessed by four different methods of measuring central corneal thickness using Pentacam, IOL Master 700, Cirrus AS-OCT and Tomey Specular microscopy by a single examiner. **Results:** The mean CCT [ $\pm$  standard deviation (SD)] for Pentacam, IOL Master 700, Cirrus AS-OCT and Tomey Specular microscopy were Pentacam (Oculus), AS-OCT (Cirrus), IOL Master 700 and Specular microscopy (Tomey) were 523.75 ( $\pm$ 27.75), 525.29 ( $\pm$ 28.81), 517.13 ( $\pm$ 28.43) and 512.82 ( $\pm$ 27.60)  $\mu$ m, respectively. All the means were significantly different from one another ( $P < 0.000$ ). The differences between pairs of mean central corneal thickness (CCT) for Pentacam and IOL Master, Pentacam and anterior segment- optical coherence tomography (AS-OCT), and Pentacam and Specular microscopy are statistically significant. Bland-Altman plots showed that pentacam and IOL Master 700 have the closest agreement, followed by AS-OCT. Specular microscopy was found to have the poorest agreement with Pentacam. **Conclusion:** We found that CCT measurements of Pentacam did not correlate with measurements of IOL Master, or AS-OCT or Specular microscopy. In clinical practice, the devices analyzed should not be used interchangeably due to low agreement regarding CCT values.

**Key words:** Agreement, AS-OCT, central corneal thickness, IOL master, pentacam, specular microscopy

Central corneal thickness (CCT) measurements are clinically important in the diagnosis and monitoring of corneal diseases such as pseudophakic or aphakic bullous keratopathy, Fuchs' endothelial dystrophy, endotheliitis, keratoconus, pellucid marginal degeneration, preoperative evaluation in refractive surgery and interpretation of intraocular pressure (IOP) measured by applanation tonometry. Central corneal thickness varies widely in normal subjects. The mean CCT is 511.4  $\pm$  33.5 microns.<sup>[1]</sup>

Therefore, the measurement of CCT is important in many clinical applications such as glaucoma management, diagnosis of corneal ectatic conditions, corneal physiology, and contact lens research.

There are several systemic, ocular and technical factors affecting central corneal thickness measurements which include diabetes, corneal irregularities, corneal scarring, band shaped keratopathy, corneal edema, measurement done over a soft contact lens and technical errors in measuring CCT. The outcome and success rate of refractive surgical procedure rely on accuracy of pachymetry measurements.<sup>[2]</sup>

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Until recently, ultrasound pachymetry was the most commonly used clinical method to measure central corneal thickness and is considered as the gold standard method.<sup>[3]</sup> However, patients' discomfort, the risk of epithelial lesion (abrasion), risk of transmission of infections due to the probe in contact with the cornea and interobserver variability lead to alternatives of noncontact methods that provide rapid, reliable, and objective measurements of the central corneal thickness such as rotating scheinpluf imaging, optical coherence tomography, scanning slit pachymetry, specular microscopy, and corneal confocal microscopy. These devices use different measurement technologies and may give different results. In this present study we have compared central corneal thickness measurements done by Pentacam with that of IOL Master, AS-OCT and Specular microscopy.

## Methods

A prospective study was conducted in a tertiary eye care center in south India from October 2019 to January 2020. Two hundred

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and six eyes from one hundred and three health professionals were enrolled into the study, in which we included subjects with no ocular pathology and willingness to provide informed written consent. Health professionals with previous ocular surgery, corneal ectasias, glaucoma, on topical medication for any ocular condition, prior history of contact lens wear and those who did not give consent were excluded from the study.

Each subject was assessed by four different methods of measurements using a dual Scheimpflug imaging device (Oculus Pentacam Rotating Scheimpflug Camera; Oculus, Wetzlar, Germany), optical biometer (Zeiss; IOL Master 700), optical coherence tomography (Stratus OCT, version 4.0.7; Carl Zeiss Meditec, Inc, Dublin, CA) and the specular microscope (Tomey, Nagoya, Japan) by a single examiner. The order of optical devices was random as they are non-contact devices. Measurements were performed at least 3hrs after waking up to avoid the effects of diurnal variation on corneal thickness.

The pentacam (Oculus Pentacam Rotating Scheimpflug Camera; Oculus, Wetzlar, Germany) is a newer imaging system that uses a single Scheimpflug camera to measure the corneal thickness, keratometry, anterior and posterior elevations, anterior segment OCT and grading of cataractous lens.<sup>[4]</sup> The light source is a blue light-emitting diode (LED) with a wavelength of 475 nm. Subjects were examined under dim lighting conditions in sitting position with their chin on chin rest and forehead touching the forehead bar looking at the fixation target. Images were automatically captured by the machine after focusing the image (defining the pupil edge and the central and corneal apex) by monitoring the ocular images. The device can capture a 25-slit image of the anterior chamber and prepare the corneal pachymeter map in less than 2 seconds. Pachymetry values are automatically calculated by the device for the centre of the cornea.

In contrast, the Zeiss Cirrus 5000 HD-OCT (Carl Zeiss Meditec, Dublin, CA, USA) is based on Spectral Domain (SD) OCT principle which uses Coherence interferometry thus measuring the delay of back-reflected light. 27,000 A-scans per second are captured by this device with axial resolution of  $5\mu$ .<sup>[5]</sup> It can evaluate both anterior and posterior segment structures. There are two external Anterior Segment (AS) lenses (cornea and anterior chamber) available to view cornea and anterior chamber in detail. The cornea-lens captures anterior segment images by producing telecentric scans. The "Pachymetry" scan pattern settings in the OCT were used and the cornea was mapped with the help of high magnification (short) lens. The distance between anterior and posterior boundaries of the cornea was measured. Irido-corneal angles, angle-to-angle distances, anterior chamber dimensions, and crystalline lens are other parameters that can be measured with the use of anterior chamber lens. With the patient in sitting position the head was stabilized with a chin and forehead rest and gaze was fixed with an internal fixation target. The OCT image was displayed as a real-time video to help in alignment.

The IOL Master 700 (Carl Zeiss Meditec AG, Jena, Germany) is an optical biometry device based on the principle of Mach-Zehnder partial coherence interferometry (PCI).<sup>[6]</sup> The device measures six variables, including the axial length (AL), keratometry (K) readings, CCT, anterior chamber depth (ACD), white-to-white (WTW) distance, and pupil size by using

infrared laser diode (SS-OCT) whose wavelength varies from 1035 nm to 1095 nm. The measurement of CCT occurs at the corneal vertex.

In performing non-contact specular microscopy with the Tomey EM-3000 (Tomey, Nagoya, Japan), the subject was positioned on the chin rest and forehead rest and asked to fixate on the red target.<sup>[7]</sup> On proper alignment on the center of the cornea, a bright central specular image of the central corneal endothelial cells was obtained. If the endothelial image displayed on the monitor was not in focus, the process was repeated. The device is equipped with an autofocus, digital image-capturing system, and automated image analysis software for ECD and CCT assessment. The optical magnification of the device is 3190 and the display resolution is 1.14 mm. Up to 300 cells per image are counted in a fixed area of  $0.135\text{ mm}^2$  ( $0.25 \times 0.54\text{ mm}$ ). CCT measurements from well-focused images obtained using NCSM were considered acceptable and used in this study.

### Statistical methods

The summary statistics was done by using mean, SD, and correlation coefficient. The inferential statistics was done by using repeated measure ANOVA with Bonferroni post hoc test, correlation test. Bland Altman plot was also done. All the measurements were done using SPSS 23.0. A value of  $P < 0.05$  was considered as statistically significant.

### Results

All subjects taken were included in the study as they met the necessary criteria. Subjects were divided into three groups consisting of age less than 20 years, 21 to 25 years and more than 25 years. Maximum subjects belonged to the age group less than 20 years (44.7%), followed by more than 25 years (29.1%) followed by 21 to 24 years (26.2%). The mean age of the subjects was 24.03 years (range: 17–34 years) out of which 80.58% of subjects were women.

The mean CCT ( $\pm$ SD) for the Pentacam (Oculus), AS-OCT (Cirrus), IOL Master 700 and Specular microscopy (Tomey) were 523.75 ( $\pm$ 27.75), 517.13 ( $\pm$ 28.43), 525.29 ( $\pm$ 28.81), and 512.82 ( $\pm$ 27.60)  $\mu\text{m}$ , respectively. The maximum and minimum values of CCT from each machine obtained are also shown in Table 1.

Difference of mean CCT of Pentacam and mean CCT of IOL Master, AS-OCT and specular microscopy is as shown in Table 2. Upper bound and lower bound values are also mentioned. Pearson's correlation is also applied to each of the difference in mean CCT of Pentacam with that of other three instruments as shown in Table 3. Analysis showed that the F-ratio value is 131.69. The  $P$  value is  $<0.00001$ . All the means were significantly different from one another ( $P < 0.05$ ) as shown in Table 3.

The Bland-Altman plots were also used to examine the agreement between means of Pentacam and IOL Master Values as shown in Fig. 1. The difference of mean CCT values obtained by Pentacam and IOL Master was 1.56  $\mu\text{m}$ . Standard deviation (SD) of difference was 5.47. Differences of means of CCT obtained from Pentacam and IOL Master values that lie within 95 percent confidence interval is 12.28 and -9.16. Values are scattered all over the plot and thus values obtained through these machines cannot be correlated.

**Table 1: Mean CCT & SD of all the instruments**

	Mean CCT	Minimum CCT	Maximum CCT	Standard Deviation
Pentacam	523.75	457.00	596.00	27.75
AS-OCT	517.13	456.00	607.00	28.43
IOL MASTER	525.29	458.00	603.00	28.81
Specular microscopy	512.82	446.00	590.00	27.60

Mean=Minimum and maximum CCT in microns. SD=Standard deviation

**Table 2: Difference of mean CCT Of Pentacam and Others**

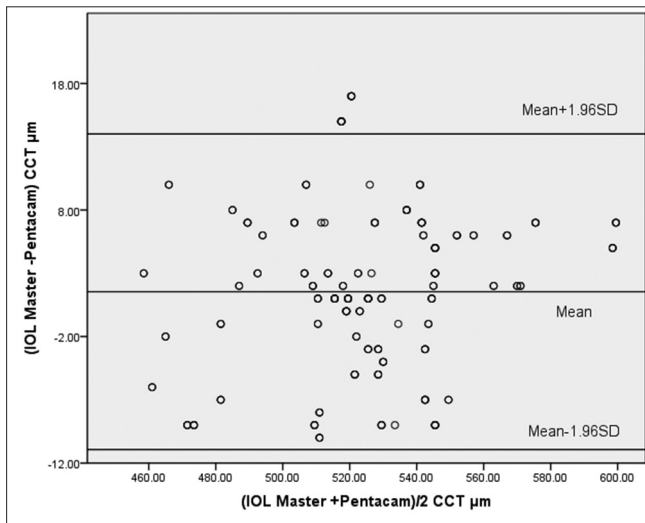
(I) CCT	(J) CCT	Mean Difference (I-J)	SE	P	95% Confidence Interval for Difference	
					Lower Bound	Upper Bound
Pentacam	IOL MASTER	-1.539*	0.444	0.004	-2.721	-0.357
	AS- OCT	6.617*	0.528	0.000	5.209	8.024
	Specular microscopy	10.927*	0.938	0.000	8.430	13.425

SE - Standard error, I - Pentacam mean CCT in microns, J - Mean CCT of IOL Master, AS\_OCT, Specular microscopy in microns, lower bound- difference of mean CCT (I-J) -2 × SE, upper bound=difference of mean CCT (I-J) +2 × SE

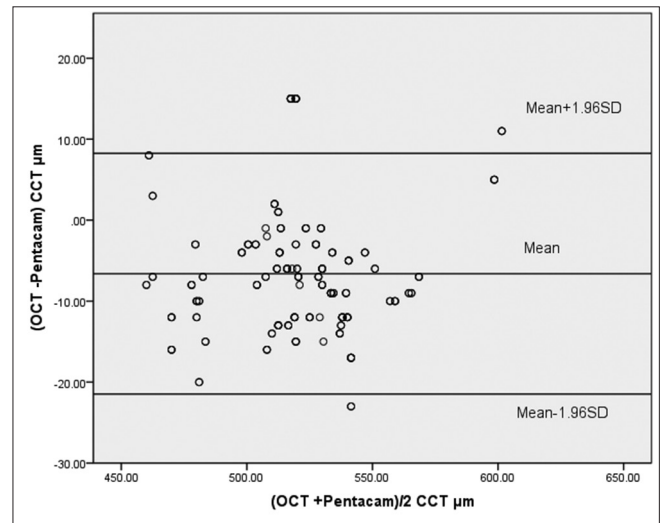
**Table 3: Pearson’s correlation**

	CCT-IOL MASTER	CCT-AS-OCT	CCT-Pentacam	CCT-Specular microscopy
CCT-Pentacam				
Pearson Correlation	0.975**	0.964**	1	0.882**
P	0.000	0.000		0.000
N	206	206	206	206

\*\*Correlation is significant at the 0.01 level (2-tailed). P=Positive correlation, N=Negative correlation



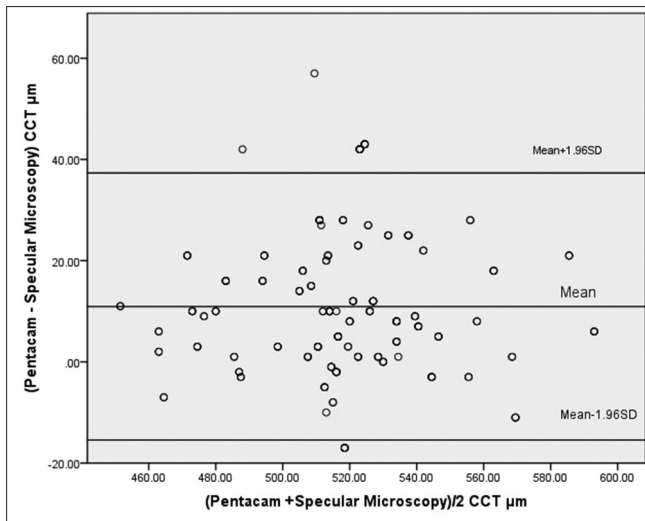
**Figure 1: Bland-Altman plots for IOL Master and Pentacam**



**Figure 2: Bland-Altman plots for OCT and Pentacam**

Similarly, the Bland–Altman plots were also used to examine the agreement between means of Pentacam and AS-OCT Values as shown in Fig. 2. The difference of mean CCT values obtained by Pentacam and AS-OCT was 2.6 μm. Standard deviation (SD) of difference was 5.65. Differences of means of CCT obtained from Pentacam and IOL Master values that lie within 95 percent confidence interval is 14.28 and -9.08. Values are scattered all over the plot and thus values obtained through these machines again cannot be correlated.

The Bland–Altman plots the agreement between means of Pentacam and Specular microscope Values is as shown in Fig.3. The difference of mean CCT values obtained by Pentacam and Specular microscope was 10.92 μm. Standard deviation (SD) of difference was 13.45. Differences of means of CCT obtained from Pentacam and Specular microscopy values that lie within 95 percent confidence interval is 37.45 and -13.08. Values are scattered all over the plot and thus values obtained through these machines cannot be correlated.



**Figure 3:** Bland-Altman plots for Pentacam and Specular microscopy

## Discussion

There are different methods available to measure CCT in normal and diseased eyes. Newer devices have made CCT measurement easy and safe in routine ophthalmic examination. The two most important factors in monitoring an individual patient require high repeatability and reliability of that particular instrument, thus standardizing the instrument. Interchangeability between different available instruments to measure CCT is of utmost importance. Two potential sources of errors in measurement of CCT can be caused by a human factor or by the instrument itself. This is of utmost importance in refractive patients to obtain best refractive outcomes followed by glaucoma patients in whom the calculation of corrected intraocular pressure depends on CCT measurements. Our results are in line with the findings of other studies in measuring CCT. Barkana and coauthors reported an excellent repeatability and reproducibility for the Pentacam Scheimpflug device, hence stating that it gives a reliable estimate of CCT.<sup>[8]</sup> A single reading is sufficient and independent of the operator.

There were many studies done to compare the values of CCT obtained by Pentacam with that of the gold standard Ultrasound pachymetry. Few studies did find comparable results of values of CCT measurements between Pentacam and Ultrasound pachymetry, for example, Nam *et al.* also showed that Pentacam can provide comparable and high repeatability of CCT.<sup>[9]</sup> Hani S *et al.* and coauthors studied that pentacam can be considered as a reliable instrument to measure CCT.<sup>[10]</sup> Whereas there were few studies that did not find a good correlation between the values obtained by these two machines like a study conducted by Módis *et al.*, compared CCT as measured by two independent observers using Pentacam HR and ultrasound pachymetry in 46 healthy subjects.<sup>[11]</sup> The CCT values from the Pentacam examination were significantly higher ( $572 \pm 33$  and  $575 \pm 31$  mm) in both investigators than when measured by Ultrasound pachymetry ( $546 \pm 27$  and  $548 \pm 28$  mm) ( $P < 0.0001$ ). Wu *et al.*, reported higher CCT measurements with the Pentacam compared to ultrasound pachymetry in normal healthy corneas, but the Pentacam tended to underestimate the CCT in keratoconic eyes.<sup>[12]</sup>

In this present study, the differences in pachymetry values from different instruments were statistically significant. Nature of the radiation, wavelength, reflection of radiation emitted, principle involved and the area where measurement is taken are some of the reasons for such differences in measurements of CCT. The devices use different reference points for central measurements (apex or pupil).

Since the IOLMaster is unable to directly measure the corneal thickness, no prior data for comparing CCT were available. A study conducted by Ozyol *et al.* compared CCT measurements with Zeiss IOL Master 700 which showed it had good repeatability with an ICC of 0.965 and coefficient of variation (CoV) of 0.49.<sup>[13]</sup> Excellent repeatability of CCT values was also reported by Kiraly *et al.* with a high intraobserver ICC of 0.999 [95% confidence interval 0.998–0.999] for Zeiss IOL Master 700.<sup>[14]</sup> Laszlo Kiraly *et al.* conducted a study to estimate repeatability and comparability of CCT with IOLMaster 700, Pentacam HR, and Cirrus HD-OCT. The comparison of CCT measurements revealed statistically significant differences between Pentacam HR versus IOLMaster 700 ( $P < 0.0001$ ). The Pentacam HR exhibited higher CCT values than the IOL Master 700 (on average  $10.99 \mu\text{m}$ ). PelinÖzyola *et al.* conducted a study in which they compared CCT and anterior segment parameters with Pentacam and IOL Master and the results showed that both these instruments generated the mean difference for CCT of  $5.05 \mu\text{m}$  for normal eyes.<sup>[15]</sup> The Pentacam exhibited significantly lower CCT measurements ( $P < 0.001$ ). In this study, mean CCT by Pentacam was lower than the mean CCT values by IOL Master by a mean difference of  $1.56 \mu\text{m}$  ( $P < 0.000$ ) which was statistically different and hence the CCT values of both these machines cannot be used interchangeably.

When we compared Pentacam with AS-OCT, we found that the value of CCT measured by pentacam was higher than that measured by AS-OCT with a mean difference of  $6.61 \pm 1.05 \mu\text{m}$  with a  $P$  value of 0.000. There are several studies which agree with our results. One such study conducted by Kanellopoulos *et al.* showed that there was a significant difference of  $12.2 \pm 10.01 \mu\text{m}$  ( $P = 0.0002$ ) in value of CCT as measured by a Scheimpflug imaging system to that of a spectral domain OCT.<sup>[16]</sup> Another study conducted by Chen *et al.* found a significant difference of  $10.9 \pm 5.93 \mu\text{m}$  (95% LoA,  $-0.7$  to  $22.5 \mu\text{m}$ ) when they compared the Pentacam HR with a Fourier-domain OCT.<sup>[17]</sup> Study by Yap *et al.* were also consistent with our results showing that highest CCTs were obtained using the Pentacam compared with OCT in normal eyes.<sup>[18]</sup>

Saleh Al-Ageel *et al.* conducted a study to compare central corneal thickness (CCT) measurements taken with Pentacam, NCSM, and ultrasound pachymetry in normal and post-laser *in situ* keratomileusis (LASIK) eyes, found out that the average values of CCT taken were significantly different for Pentacam vs. NCSM ( $P = 0.046$ ).<sup>[19]</sup> Ucakhan *et al.* found that NCSM CCT measurement to be thinner than Pentacam by  $21.9 \mu\text{m}$  and this agrees with this study.<sup>[20]</sup>

Another study conducted by Fujioka *et al.* also found that NCSM CCT measurement to be thinner than Pentacam (by  $7.45 \mu\text{m}$ ).<sup>[21]</sup> In this present study when we compared Pentacam mean CCT value with mean CCT of NCSM, it was evident that Pentacam gave higher values with a difference in

mean CCT of  $10.92 \pm 1.83 \mu\text{m}$  ( $P < 0.000$ ) which was statistically significant and hence cannot be used interchangeably.

A study conducted by Reem Hassan Ibrahim Azzam *et al.* to measure central corneal thickness by different techniques showed that the mean CCT measurements by pentacam ( $532.88 \pm 34.15 \mu\text{m}$ ) were thicker than those measured by specular microscopy ( $531.92 \pm 33.64 \mu\text{m}$ ) by  $0.96 \mu\text{m}$ , with  $P$  value of 0.824 (nonsignificant) thus stating that any of these devices can be easily substituted by the other for the measurement of CCT.<sup>[22]</sup>

In our study CCT measurements by Oculus Pentacam were statistically higher than that of Cirrus AS-OCT and Tomey EM-3000 and statistically lower than that of IOL Master 700 and the interchangeability of CCT values between these methods is not possible because of bias and wide variation which can be largely attributed to distinct methodologies of measurement techniques.

There are several limitations in our study including its modest sample size. A potential limitation of our study is that the population consisted of only young, healthy participants with normal corneas. The results may differ in eyes that have experienced refractive surgery or in keratoconus patients. Further investigations are needed to assess these instruments in diseased patients, in operated eyes, in elderly patients, in eyes with irregular corneas, including those with keratoconus; and in eyes that have undergone corneal surgery. It is also advisable to have further studies with larger population to find correlation between the instruments.

## Conclusion

From our study we would like to conclude that the three devices cannot be used interchangeably since there was statistically significant variation between values obtained by each method. Pentacam's CCT measurements tend to be thinner than IOL Master whereas AS-OCT and noncontact specular microscopy yielded thicker values than Pentacam. Further studies with greater sample size are needed to compare the corneal thickness using Pentacam, IOL Master, AS-OCT and Specular microscopy before we can use these instruments interchangeably.

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## Conflicts of interest

There are no conflicts of interest.

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