

# Variability of Central Corneal Thickness Measurements—Comparing Zeiss IOL Master and Tomey Corneal Specular Microscope

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**Purpose:** The aim of this study was to compare the intraobserver repeatability and agreement of central corneal thickness (CCT) measurements by 2 commonly available instruments, Zeiss IOL Master 700 (SS-OCT-based optical biometry device) and Tomey corneal specular microscope EM-3000 (Noncontact specular microscopy).

**Design:** Retrospective study.

**Methods:** This is a retrospective analysis of data from routine clinical practice in which preoperative CCT measurements of 105 patients scheduled for cataract surgery were analyzed. Two consecutive CCT measurements were measured using Zeiss IOL Master 700 and Tomey corneal specular microscope EM-3000 by the same examiner. The repeatability of CCT measurements was analyzed by mean intraobserver difference, coefficient of repeatability (CR), and intraclass correlation. The agreement between the 2 methods was analyzed by mean difference and limits of agreement (LoA) using the Bland-Altman method.

**Results:** The mean absolute intraobserver difference between the 2 measurements by Zeiss and Tomey were  $3.41 \pm 3.98 \mu\text{m}$  and  $8.62 \pm 9.52 \mu\text{m}$  ( $P < 0.0001$ ), respectively. For Zeiss, the CR was  $10.3 \mu\text{m}$  with 95% LoA of  $-10.5$  to  $10.1 \mu\text{m}$ . For Tomey, the CR was  $25.2 \mu\text{m}$  with 95% LoA of  $-25.2$  to  $25.2 \mu\text{m}$ . The mean CCT measurements  $\pm$  standard deviation by Zeiss and Tomey were  $544.0 \pm 38.1 \mu\text{m}$  and  $532.6 \pm 40.0 \mu\text{m}$ , respectively ( $P = 0.003$ ). The 95% LoA in CCT between the 2 methods was  $-15.8$  to  $38.7 \mu\text{m}$ .

**Conclusions:** Zeiss IOL Master 700 has superior intraobserver repeatability and consistency than Tomey EM-3000. Zeiss produced higher CCT measurements than Tomey; hence, in clinical practice, interchangeability between these 2 methods is limited.

**Key Words:** agreement, central corneal thickness, optical coherence tomography, repeatability, specular microscopy

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Central corneal thickness (CCT) measurements are clinically important in ophthalmology, particularly in the diagnosis and monitoring of corneal diseases, interpretation of intraocular pressure (IOP) measured by applanation tonometry, detection of glaucoma, and for preoperative evaluation in refractive surgery.<sup>1</sup> Ultrasound pachymetry is the most commonly used method and

criterion standard for the measurement of CCT.<sup>2</sup> However, as ultrasound pachymetry is a contact method requiring topical anesthesia, it poses limitations such as variability of measurements due to probe placement and pressure application and risks of epithelial abrasions and infection.<sup>3</sup>

Due to these limitations, noncontact optical methods such as optical biometry and specular microscopy, are alternatives that provide rapid, reliable, and objective measurements of the CCT.<sup>4</sup> Noncontact specular microscope (NCSM) is commonly used in clinical practice to evaluate corneal endothelial cell density and morphology and has also been shown to provide reliable measurements of CCT.<sup>5,6</sup> Swept-source optical coherence tomography (SS-OCT) such as Zeiss IOL Master 700 (Carl Zeiss Meditec AG, Jena, Germany) is commonly used for the calculation of intraocular lens (IOL) power and desired postoperative refraction. It can obtain multiple measurements of various biometric eye data such as CCT, anterior chamber depth, anterior aqueous depth, lens thickness, and axial length in a single capturing process.<sup>4</sup>

CCT is becoming more routine in clinical examination and it is useful to understand the agreement and repeatability of CCT measurements between different instruments. Although numerous studies have been performed to compare different CCT measurement methods, to our knowledge, no study has directly compared Zeiss IOL Master 700 and Tomey EM-3000. The aim of this study is to evaluate and compare the intraobserver repeatability and quantify the agreement of CCT measurements by 2 commonly available instruments, Zeiss IOL Master 700 and Tomey corneal specular microscope EM-3000.

## METHODS

### Subjects

The study population was composed of 105 cataract subjects between December 2017 and June 2018. All measurements were taken 1 to 2 weeks before cataract surgery. Two measurements were taken from each instrument for validation and accuracy assurance, which is routine protocol at this medical practice. All measurements were taken as part of routine ophthalmological examination performed by the same senior ophthalmologist (K.O.). Routine examination included but not limited to imaging of the corneal endothelium with Tomey EM-3000 and measurement of IOL power with Zeiss IOL Master 700. Patients with pathological corneal features and previous corneal refractive surgery were excluded from the study.

### Equipment

Tomey EM-3000 NCSM (Tomey, Nagoya, Japan) was used as previously described.<sup>5–7</sup> CCT measurements from

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well-focused images obtained using NCSM were considered acceptable and used in this study. Readings obtained from poor-quality images were not recorded by the instrument. The measurement process was repeated until 2 acceptable measurements were obtained. Zeiss IOL Master 700 (Carl Zeiss Meditec AG, Jena, Germany) utilizes SS-OCT technology that uses a laser with variable wavelength to generate optical B-scans or optical cross-sections to determine biometric eye data including keratometry, CCT, anterior chamber depth, anterior aqueous depth, lens thickness, horizontal white-to-white corneal diameter, pupil size, and axial length.<sup>4,8</sup> Only 2 measurements were performed using Zeiss IOL master 700 as correct fixation and alignment was checked before scan. The order of CCT measurements was consistent and performed in the order Zeiss IOL Master 700 then Tomey EM-3000 NCSM. The interval between measurements with the 2 devices was within 5 minutes. The subjects were asked to perform several blinks just before each measurement was taken.

**Statistical Analysis**

All data were analyzed using the Statistical Package for Social Sciences for Windows version 23.0 SPSS (Windows version 23.0; IBM Corp, Armonk [NY], US). The normality of all data distributions was confirmed by the Kolmogorov-Smirnov test ( $P > 0.05$ ).

CCT measurements are presented as means  $\pm$  SD. Mean difference  $\pm$  SD between the paired measurements was calculated. The coefficient of repeatability and 95% limits of agreement (LoA) as recommended by Bland and Altman method were used to assess repeatability between the paired measurements.<sup>9</sup> Bland-Altman plots were used to assess the differences between first and second measurements as a function of their average. 95% LoAs were defined as the mean difference  $\pm$  1.96 SD of the differences. Repeatability was also assessed using intraclass correlation coefficients (ICCs) determined based on analysis of variance for 2-way mixed-effects model. In general, an ICC of  $>0.9$  is considered excellent repeatability of measurements.

Comparison of the mean CCT values for the 2 devices was conducted by Student *t* test. The linear correlation between measurements (Pearson coefficient of correlation) with values of  $>0.7$  was considered indicative of good correlation between the 2 methods. Bland-Altman plots including 95% LoA were also used to assess the agreement of CCT measurements between the 2 methods.

**RESULTS**

The mean age  $\pm$  SD of subjects was  $68.0 \pm 8.3$  years with 52% ( $n = 55$ ) being female.

**Repeatability of CCT Measurements of Zeiss IOL Master 700 and Tomey EM-3000**

Measurements of CCT were highly repeatable with both Zeiss IOL Master 700 and Tomey EM-3000 (Table 1). For Zeiss IOL Master 700 and Tomey EM-3000, the mean absolute intra-observer differences between the 2 measurements were  $3.41 \pm 3.98 \mu\text{m}$  and  $8.62 \pm 9.52 \mu\text{m}$  ( $P < 0.0001$ ). The ICC for Zeiss IOL Master700 was 0.995 and for Tomey EM-3000 was 0.974. Bland-Altman analysis showed that the difference between the first and second measurements was evenly spread around the mean difference independent of CCT values, with no demonstration of over or underestimation by either instrument (Fig. 1). Tomey EM-3000 demonstrated greater variability between first and second CCT measurements than Zeiss IOL Master 700 with 95% LoA between  $-10.49 \mu\text{m}$  and  $+10.06 \mu\text{m}$  compared to  $-25.23 \mu\text{m}$  and  $+25.19 \mu\text{m}$ .

**Agreement of CCT Measurements Between Zeiss IOL Master 700 and Tomey EM-3000**

Mean CCT measurements by Zeiss IOL Master 700 and Tomey EM-3000 were  $544.03 \pm 38.04 \mu\text{m}$  and  $532.57 \pm 39.99 \mu\text{m}$ , respectively. CCT measurements by Zeiss were on average  $11.46 \pm 13.90 \mu\text{m}$  greater than those determined by Tomey ( $P = 0.003$ , Table 2). Bland-Altman analysis demonstrated that Zeiss IOL Master 700 exhibited higher CCT values compared to Tomey EM-3000, with 95% of the differences between  $-15.78$  and  $38.70 \mu\text{m}$  (Fig. 2). The maximum difference between the 2 methods was  $52 \mu\text{m}$ . There was high linear correlation in scatter plot ( $r = 0.954$ ,  $P < 0.001$ ).

**DISCUSSION**

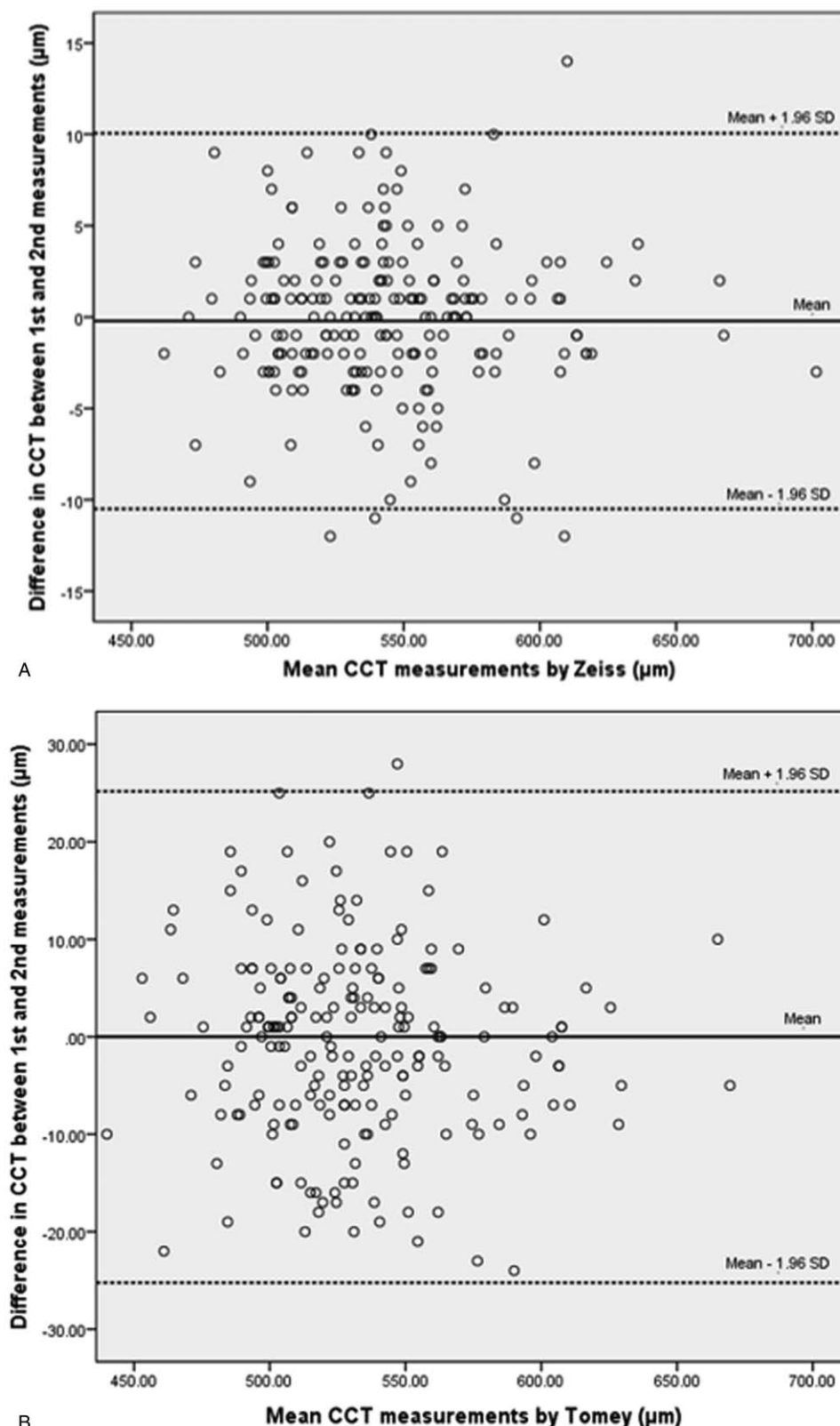
Measuring CCT has been made easier to incorporate in routine ophthalmic examinations with the emergence of new devices and technology. Longitudinal assessments in monitoring patients require techniques with high repeatability and low variability. It is important to standardize the interchangeability between different available methods to allow clinicians to detect real changes in patient’s status and make informed diagnostic and therapeutic decisions.

In the present study, we showed that intraobserver repeatability of CCT measurements was high with both Zeiss IOL Master 700 and Tomey EM-3000 as both methods demonstrated ICC  $>0.9$ . Our results agree with previously reported results for SS-OCT and NCSM systems. Comparison of CCT measurements with 4 non-contact devices by Ozyol and Ozyol<sup>4</sup> revealed SS-OCT optical biometer such as Zeiss IOL Master 700 had good repeatability with

**TABLE 1.** Intraobserver Repeatability of Zeiss IOL Master 700 and Tomey EM-3000 in Measuring CCT ( $n = 210$ )

	Zeiss	Tomey
Mean of first measurement $\pm$ SD, $\mu\text{m}$	543.92 $\pm$ 38.00	532.56 $\pm$ 40.45
Mean of second measurement $\pm$ SD, $\mu\text{m}$	544.13 $\pm$ 38.27	532.58 $\pm$ 40.55
Mean difference $\pm$ SD, $\mu\text{m}$	3.41 $\pm$ 3.98	8.62 $\pm$ 9.52
CR	10.27	25.21
CoV	0.44	1.15
95% LoA, $\mu\text{m}$	-10.49 to 10.06	-25.23 to 25.19
ICC (95% CI)	0.995 (0.994–0.996)	0.974 (0.966–0.980)
Pearson correlation		
<i>R</i>	0.991	0.950
<i>P</i> value	<0.001	<0.001

CCT indicates central corneal thickness; CI, confidence interval; CR, coefficient of repeatability; ICC, intraclass correlation coefficient; LoA, limits of agreement.



**FIGURE 1.** Bland-Altman plots of the mean differences between the first and second measurements against the mean CCT values by Zeiss IOL Master 700 (A) and Tomey EM-3000 (B). The mean difference between the 2 measurements is represented by the solid line and the 95% confidence limits are represented by the dotted lines.

an ICC of 0.965 and coefficient of variation (CoV) of 0.49. Excellent repeatability was reported by Kiraly et al<sup>10</sup> with a high intraobserver ICC of 0.999 [95% confidence interval (CI) 0.998–0.999] for Zeiss IOL Master 700. Similarly, Kunert et al<sup>11</sup> reported high repeatability for SS-OCT with a CoV of 0.411 which is

comparable to our results. With regard to Tomey EM-3000, Bao et al<sup>5</sup> reported CoV and ICC values as 0.65 and 0.989 respectively (95% CI 0.984–0.993) based on analysis of 70 normal eyes. Similarly, Modis et al<sup>6</sup> reported an ICC of 0.94 (95% CI 0.89–0.97) with 95% LoA  $-25.13$  to  $+18.06$   $\mu\text{m}$  using NCSM.

**TABLE 2.** Mean CCT Measurements by Zeiss IOL Master 700 and Tomey EM-3000, Zeiss and Tomey Mean CCT Difference ± SD, Paired *t* Test, LoA, and Pearson Correlation Values

Mean CCT Zeiss, μm	Mean CCT Tomey, μm	Zeiss – Tomey Mean Difference ± SD, μm	<i>P</i> Value	95% LoA, μm	Pearson Correlation	
					<i>r</i>	<i>P</i> Value
544.03 ± 38.04	532.57 ± 39.99	11.46 ± 13.90	0.003	–15.78 to 38.70	0.954	<0.001

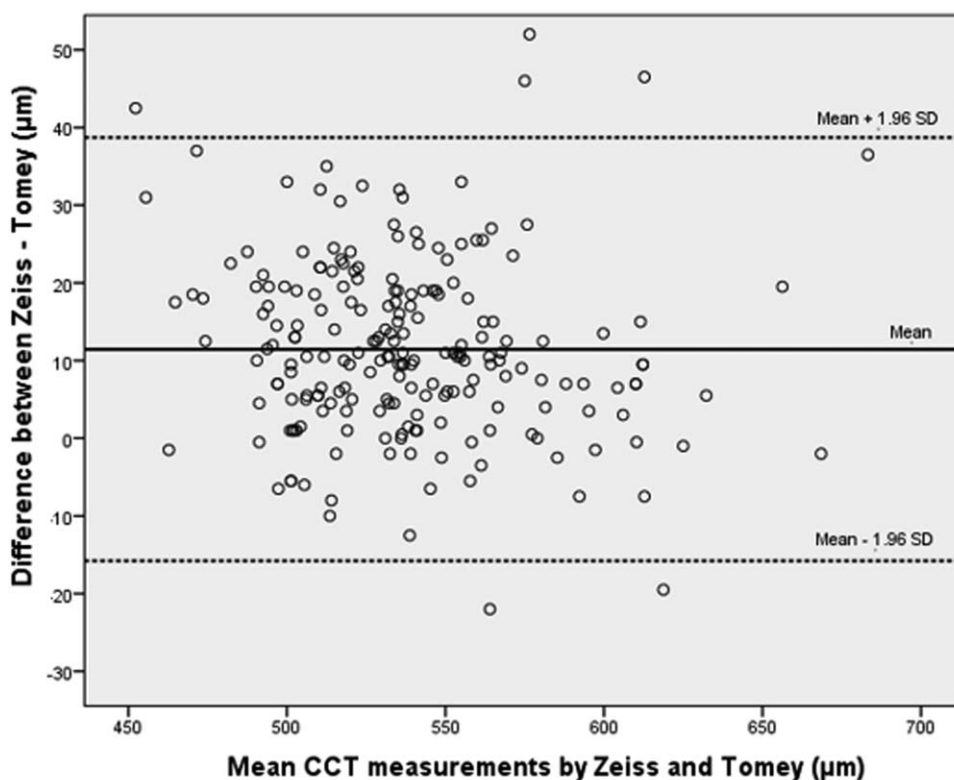
CCT indicates central corneal thickness; LoA, limits of agreement.

Although both methods demonstrated high ICC values, that is >0.95, it is evident that Zeiss IOL Master 700 demonstrated better intraobserver repeatability than Tomey EM-3000. Bland-Altman graphs depict both systematic bias and random error as shown by the width of 95% LoA. Bland-Altman graphs demonstrated small mean intraobserver difference between CCT measurements for both Zeiss IOL Master 700 and Tomey EM-3000. However, the 95% LoA for Tomey EM-3000 was significantly wider than that of Zeiss IOL Master 700; –25.23 to 25.19 μm compared to –10.49 to 10.06 μm. No clear trend regarding over- or underestimation depending on CCT values was identified by either method. The superior repeatability of Zeiss IOL Master 700 can be attributed to the fact that SS-OCT technology is able to present the mean CCT value from 6 measurements from a single scan, which reduces random error and variability. Kunert et al<sup>11</sup> previously showed that swept-source biometry exhibited high repeatability performance for all biometric parameters including axial length, anterior chamber depth, lens thickness, and CCT. Additionally, CCT measurements made by Tomey EM-3000 can be reliant on the degree of focus of the endothelial images. If the endothelial image displayed on the Tomey EM-3000 monitor is not properly focused, the generated CCT value will not be

accurate which represents a potential source of error for clinicians. Hence, clinicians should check the focus of the images and only include CCT values obtained from a well-focused endothelial image with bright corneal reflections.

CCT measurements are particularly important for the correct measurement of IOP. Kohlhaas et al<sup>12</sup> reported that the measured and real IOP was significantly dependent on CCT (*P* < 0.001). Thin corneas may lead to an underestimation and thick corneas may lead to an overestimation of applanation IOP measurements. The authors reported an association between IOP and CCT of approximately 1-mm Hg correction for every 25-μm deviation from a CCT of 550 μm. A meta-analysis by Doughty and Zaman<sup>1</sup> showed that a 10% difference in CCT may result in an approximately 3.4 ± 0.9 mm Hg change in IOP. These results highlight the need for consideration of both CCT and IOP in the diagnosis and understanding of various types of glaucoma.<sup>13</sup> Although the influence of CCT on the accuracy of IOP measurements has been recognized, there is no existing reliable formula to “correct” the measured IOP.

CCT measurements by Zeiss IOL 700 were statistically higher than that of Tomey EM-3000 and the interchangeability of CCT values between the 2 methods is limited because of bias



**FIGURE 2.** Bland-Altman plots comparing CCT measurements made by Zeiss IOL Master 700 and Tomey EM-3000. The mean difference between the 2 methods is represented by the solid line and the 95% confidence limits are represented by the dotted lines.

and wide variation which can be largely attributed to distinct methodologies of measurement techniques. Although clinicians should not use CCT measurements obtained from different devices interchangeably, the differences in CCT measurements may not be clinically significant for the management of glaucoma.

### CONCLUSION

In conclusion, Zeiss IOL Master 700 demonstrated superior repeatability compared with Tomey EM-3000. Zeiss IOL Master 700 also produced statistically significantly higher CCT measurements than Tomey EM-3000.

Noncontact methods can provide accurate and repeatable measurements of ocular biometry. However, biometric measurements taken by different devices should not be considered equivalent and clinicians should be aware of the potential systematic bias when using these different devices.

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