

Multimodal Imaging Device Comparison for Central Corneal Thickness Assessment in Primary Open-Angle Glaucoma and Non-Glaucomatous Eyes

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ABSTRACT

Purpose: To compare central corneal thickness (CCT) in eyes with primary open-angle glaucoma (POAG) and non-glaucomatous eyes using four different devices, and to evaluate the agreement and comparability of these devices in both groups.

Study Design: Cross sectional study.

Place and Duration of Study: Tertiary hospital in Semarang City from May 2025 to February 2026.

Methods: CCT in right eye was measured using standard ultrasonic pachymetry (USP), optical coherence tomography (OCT), non-contact tono-pachymetry (NCT), and specular microscopy (SM). Differences, correlation levels, and agreement between the measurement results were assessed.

Result: A total of 69 participants participated in this study (33 patients with glaucoma and 36 without glaucoma). The mean CCT measured using NCT (580.50 ± 27 mm), USP (578.50 ± 26 mm), SM (569.50 ± 28 mm), and OCT (564.50 ± 27 mm) did not differ statistically in the non-glaucoma group. Similar results were seen in glaucoma group with NCT (528 ± 22 mm), USP (527 ± 22 mm), SM (518 ± 25 mm), and OCT (518 ± 27 mm) ($p > 0.05$). The difference between the two groups was statistically significant ($p < 0.001$). A strong positive correlation was observed among the four devices within each group ($p < 0.001$). Bland-Altman analysis comparing each device to the USP gold standard showed bias values of 2.6 (NCT), -12.03 (SM), and -6.03 (OCT) in the glaucoma group, and 9.8 (NCT), -9.1 (SM), and -14.6 (OCT) in the non-glaucoma group.

Conclusion: The CCT measurements using NCT, SM, and OCT were aligned with the USP measurements in both groups. This finding highlights that CCT monitoring may be interchangeable between devices.

Keywords: Central Corneal Thickness, Non-Contact Tono-Pachymetry, Optical Coherence Tomography Specular Microscopy, Ultrasound Pachymetry.

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INTRODUCTION

Central corneal thickness (CCT) contributes to the accuracy of intraocular pressure (IOP) measurements

which are essential for glaucoma diagnosis and management.^{1,2} Open angle glaucoma is the most common type of glaucoma occurring in the United States, affecting over 2.7 million persons.^{3,4} IOP measurements may be overestimated or underestimated because of variations in CCT, which may result in incorrect diagnosis or inappropriate treatment decisions.^{5,6} Thinner CCT is linked to more severe optic nerve damage.⁷ Nevertheless, research also indicates that although CCT is correlated with the degree of optic nerve damage upon diagnosis, it might not have a major impact on how glaucomatous damage

develops over time.^{8,9}

The gold standard for IOP measurement is the Goldmann Applanation Tonometer (GAT), which is affected by the CCT. IOP measurements from thinner corneas may be underestimated, whereas those from thicker corneas may be overestimated. Because of this potential discrepancy, measuring CCT is important to ensure a more accurate assessment of IOP.¹⁰⁻¹² Mendelian randomization analysis indicates that a higher risk of POAG may be linked to a higher CCT. These findings suggest that the association between CCT and glaucoma is more complex than previously thought, and further investigation is therefore needed to completely comprehend these systems.¹³

Ultrasound, confocal microscopy, corneal topography, interferometry, tonopachymetry, optical coherence tomography (OCT), and specular microscopy (SM) are some of the methods that may be used to quantify CCT. Ultrasonic pachymetry (USP) is regarded as the gold standard for measuring CCT among these methods, as it determines corneal thickness by calculating the time required for an ultrasound wave to travel to the corneal endothelium and return.¹⁴⁻¹⁶ USP offers higher accuracy but it also needs corneal contact, which may introduce observer variability and infection risks. Although it is more expensive, OCT offers non-contact, high resolution measurements with good consistency. On the other hand, SM evaluates both CCT and endothelial health. Tono-pachymetry trades precision in favor of convenience by combining IOP and CCT measurements. These differences significantly impact glaucoma management. The objectives of this research are to compare the CCT measurement among non-glaucoma patients and POAG patients using 4 different methods: USP, NCT, SM, and OCT.

METHODS

This cross-sectional study was conducted at a tertiary care hospital in Semarang City after receiving ethical approval from the university ethics committee (**No. 16347/EC/KEPK-RSDK/2025**). Written informed consent was obtained from all participants before enrollment. The study included adults aged ≥ 18 years who were diagnosed with primary open-angle glaucoma (POAG) based on standard clinical criteria, including optic disc evaluation, visual field assessment, and intraocular pressure (IOP) measurement. Participants with a history of ocular

trauma or surgery, coexisting ocular or systemic conditions known to influence CCT, such as keratoconus or diabetes mellitus, refractive error exceeding ± 2.00 diopters spherical equivalent, unreliable visual field test results, or inability to cooperate during ophthalmic examination were excluded.

The study population was divided into two groups: (1) a non-glaucoma group, comprising individuals without clinical evidence or a history of glaucoma, and (2) a glaucoma group, consisting of patients with POAG diagnosed according to optic nerve head assessment and visual field defects based on the Hodapp–Parrish–Anderson classification. Demographic and clinical data, including age, sex, intraocular pressure, and refractive error, were recorded for all participants.

Participants were recruited consecutively from the outpatient ophthalmology clinic. Only the right eye of each participant was included in the analysis to eliminate inter-eye correlation. Following CCT assessment, all participants underwent a comprehensive ophthalmic examination, including measurement of best-corrected visual acuity, refraction, slit-lamp biomicroscopy, and dilated fundus examination by indirect ophthalmoscopy.

To minimize measurement variability, all CCT assessments were performed by a single experienced examiner. Measurements were obtained consecutively using four different instruments: ultrasound pachymetry (USP) (US-4000 Echoscanner, NIDEK Co., Japan), non-contact tonometer/pachymeter (NCT; NT-530P Non-Contact Tono/Pachymeter, NIDEK Co., Japan), anterior segment optical coherence tomography (AS-OCT; Cirrus HD-OCT 5000, Carl Zeiss Meditec, Germany), and a specular microscope (CEM-530 Specular Microscope, NIDEK Co., Japan). For each device, three consecutive measurements were obtained, and the mean value was used for analysis unless otherwise specified. Measurements were performed in the following sequence: NCT, AS-OCT, and USP.

The initial CCT measurement was obtained using the NCT. Participants were instructed to rest their chin and forehead on the support and fixate on the internal target throughout the examination. The pachymetry function of the NCT determines corneal thickness by analyzing reflections from the anterior and posterior corneal surfaces, while the integrated air-puff

tonometer simultaneously measures intraocular pressure. The distance between the reflected light signals from the two corneal surfaces is automatically calculated to determine the central corneal thickness.

Subsequently, anterior segment OCT imaging was performed. This non-contact imaging modality generates high-resolution cross-sectional images of the anterior segment using low-coherence interferometry. Light reflected from the ocular tissues is captured and processed to reconstruct cross-sectional images of the cornea. Central corneal thickness is calculated as the perpendicular distance between the anterior epithelial surface and the posterior endothelial surface of the cornea.

Ultrasound pachymetry was performed after completion of the non-contact examinations to avoid potential epithelial disruption affecting optical measurements. Before measurement, one drop of 0.5% proparacaine hydrochloride was instilled for topical anesthesia. After approximately 10 minutes, participants were instructed to fixate on a distant target while the ultrasound probe was positioned perpendicular to the central cornea with minimal pressure. Eight consecutive measurements were obtained from the right eye, and their average was recorded as the final CCT value. The ultrasound probe was disinfected after each examination according to the manufacturer's recommendations.

Statistical analysis was done using IBM SPSS Statistics. A paired-sample one-way analysis of variance was used to assess differences in CCT measurements. When significant differences were identified, multiple comparisons between groups were conducted using the Bonferroni post hoc correction. The intraclass correlation coefficient (ICC) was used to evaluate the measurements' repeatability. ICC coefficients indicate the degree of similarity among measurements within the same group. Bland-Altman

plots were used to assess agreement between measurement techniques and calculate the 95% limits of agreement (LoA). These plots show the mean of the two procedures on the x-axis and the difference between the two measurement approaches on the y-axis. The 95% LoA was defined as the interval within ± 1.96 SD of the mean difference.

RESULTS

The study included 36 eyes in the non-glaucoma group and 33 eyes in the glaucoma group. There was no significant difference ($p > 0.05$) between mean CCT values using one-way ANOVA analysis (Table 1).

An independent-samples *t*-test was used to compare central corneal thickness (CCT) measurements between the glaucoma and non-glaucoma groups. A statistically significant difference in mean CCT was observed between the two groups across all four measurement devices ($p < 0.05$), indicating that CCT differed significantly between glaucomatous and non-glaucomatous eyes.

The agreement between the four CCT measurement devices was assessed using correlation analysis. All pairwise comparisons demonstrated a **very strong positive correlation** (Pearson's $r > 0.80$), with all correlations reaching statistical significance ($p < 0.001$), indicating excellent consistency among the instruments.

Bland-Altman plots were created for each procedure in comparison to the gold standard measurement, the USP device (Figure 1). The bias values determined were 9.8, -9.1, -14.6 in non-glaucoma group and 2.6, -12.03, -6.03 in glaucoma group for NCT, SM and OCT respectively (Table 3).

Table 1: Four distinct approaches were used to calculate the mean central corneal thickness value.

Group	Ultrasound pachymetry(μm)	Non-contact pachymetry(μm)	Specular Microscopy(μm)	Optical coherence tomography(μm)	<i>p</i> -value
Non-Glaucoma	578.50 $\pm$ 27	580.50 $\pm$ 27	569.50 $\pm$ 28	564.50 $\pm$ 27	0.68
Glaucoma	527 $\pm$ 22	528 $\pm$ 22	518 $\pm$ 25	518 $\pm$ 27	0.81

Notes: Data was presented mean $\pm$ SD. $P < 0.05$ was considered statistically significant

Table2: Correlation analysis between various methodologies' CCT results.

Pearson Correlation	OCT	USP	Tono-pachy	SM
<i>Non-glaucoma</i>				
OCT	-	0.910*	0.895*	0.850*
USP	0.910*	-	0.959*	0.962*
Tonopachy	0.895*	0.959*	-	0.932*
SM	0.850*	0.962*	0.932*	-
<i>Glaucoma</i>				
OCT	-	0.953*	0.944*	0.931*
USP	0.953*	-	0.988*	0.957*
Tono-pachy	0.944*	0.988*	-	0.956*
SM	0.931*	0.957*	0.956*	-

Notes: Pearson correlation coefficients were used for all analyses;
 *Correlation is significant at $p < 0.001$ (2-tailed). CCT: Central corneal thickness, OCT: Optical coherence tomography, SM: Specular microscope, USP: Ultrasonic pachymetry.

DISCUSSION

The present study compared CCT measurements in participants with POAG and non-glaucomatous controls using four different instruments: USP, the reference standard; NCT; SM; and AS-OCT. Within each study group, the mean CCT values obtained with the four devices did not differ significantly ($p > 0.05$), suggesting good consistency among the instruments for CCT measurement.

These findings are consistent with recent studies demonstrating that although different pachymetry devices may yield small variations in CCT measurements, such differences are generally not clinically meaningful in routine practice.^{17,18} Similarly, Ucak et al, compared six CCT measurement modalities, including USP, OCT, and specular

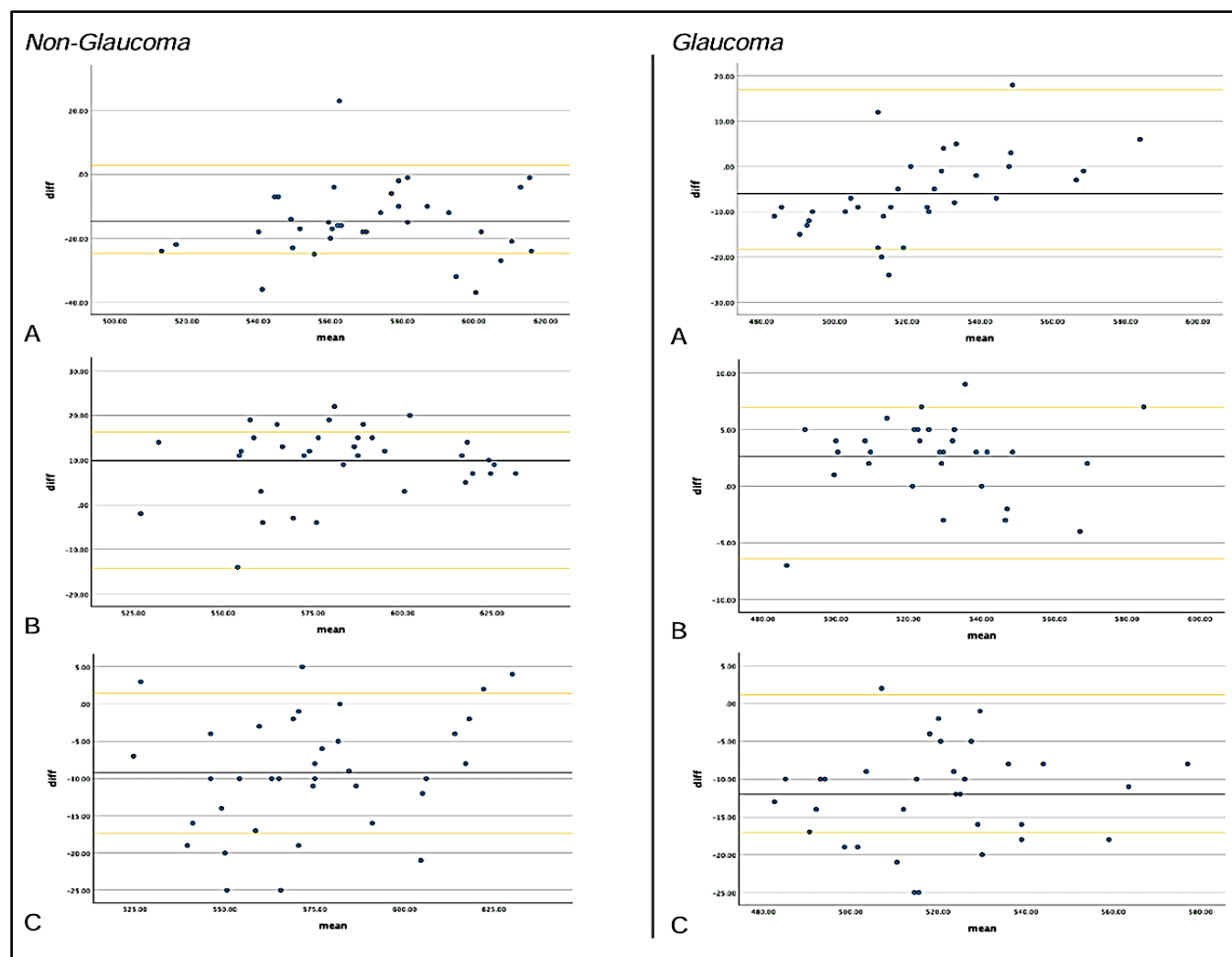


Figure 1: Bland-Altman plots comparing the CCT results between devices in non-glaucoma and glaucoma groups. (A) Optical coherence tomography and USP, (B) Non-contact pachymeter and USP, (C) Specular Microscopy and USP.

Table3: Bland-Altman limits of agreement and ICC for CCT measurements from devices compared with ultrasound pachymetry, stratified by glaucoma status.

Groups	Mean	LoA	Parameter	ICC
Non-glaucoma				
OCT	-14.6	2.76and-24.76	One measurement	0.910
			Average measurement	0.953
Tono-pachy	9.8	16.32and-14.32	One measurement	0.958
			Average measurement	0.978
SM	-9.1	1.45and-17.38	One measurement	0.958
			Average measurement	0.978
Glaucoma				
OCT	-6.03	17.04and-18.3	One measurement	0.934
			Average measurement	0.966
Tono-pachy	2.6	6.94and-6.40	One measurement	0.988
			Average measurement	0.994
SM	-12.03	1.16and-17.09	One measurement	0.957
			Average measurement	0.978

Notes: ICC: Interclass correlation coefficient; LoA: Limits of agreement

microscopy, in healthy eyes and found no statistically significant differences among the devices ($p = 0.18$), despite minor absolute variations in measured values.¹⁴ Their study reported excellent inter-device agreement, with intraclass correlation coefficients (ICC) exceeding 0.90, while Bland–Altman analysis demonstrated only minimal systematic bias (e.g., OCT bias of $-0.53 \mu\text{m}$ relative to USP). These findings support the conclusion that differences among commonly used pachymetry devices rarely exceed clinically relevant limits in healthy individuals. Nevertheless, the authors cautioned that device-dependent discrepancies may become more pronounced in eyes with corneal pathology, such as corneal edema, ectatic disorders, or following corneal surgery, where differences in measurement principles and image acquisition may influence CCT estimation. Therefore, caution should be exercised when interpreting measurements from different devices in these clinical settings.

In the present study, patients with POAG exhibited significantly thinner CCT than non-glaucomatous controls across all four measurement devices ($p < 0.001$), reinforcing the well-established association between reduced CCT and glaucoma.⁵ The consistency of this finding across USP, NCT, SM and AS-OCT further support the reliability of these instruments in detecting clinically relevant differences in CCT.

Our findings agree with the landmark Ocular Hypertension Treatment Study (OHTS) and the European Glaucoma Prevention Study (EGPS), both of which established thinner CCT as an independent risk factor for the development and progression of

POAG.^{5,19} Two principal mechanisms have been proposed to explain this association. First, from a tonometric perspective, thinner corneas (typically $<520 \mu\text{m}$) may lead to underestimation of intraocular pressure by approximately 2–3 mmHg when measured using Goldmann applanation tonometry, potentially delaying the diagnosis and treatment of glaucoma.^{20,21} Second, from a biomechanical perspective, a thin cornea may reflect generalized structural weakness of the ocular connective tissues, including the lamina cribrosa and optic nerve head, thereby increasing susceptibility to glaucomatous optic nerve damage at a given level of intraocular pressure.²²

The consistent observation of reduced CCT in glaucomatous eyes across all four measurement modalities highlights the clinical importance of incorporating pachymetry into routine glaucoma evaluation. Furthermore, a recent meta-analysis reported that the risk of glaucoma increases by approximately 10% for every 10- μm reduction in CCT.¹⁴ Collectively, these findings emphasize that, irrespective of the measurement technique employed, CCT remains an essential parameter for glaucoma risk stratification, accurate interpretation of intraocular pressure measurements, and comprehensive clinical assessment of patients with or at risk of glaucoma.

Here is a refined, journal-ready version of your discussion and limitations section with improved scientific language, logical flow, and reduced redundancy.

Bland–Altman analysis demonstrated consistent, device-specific measurement biases relative to USP. In

the non-glaucoma group, the NCT overestimated CCT by a mean of 9.8 μm , whereas AS-OCT and SM underestimated CCT by 14.6 μm and 9.1 μm , respectively. A similar pattern of systematic bias was observed in the glaucoma group, although the magnitude of the differences was slightly smaller. These findings indicate that, despite good overall agreement, each instrument exhibits characteristic measurement bias relative to USP. Consequently, clinicians should be aware of these device-specific differences when interpreting CCT measurements, particularly when comparing values obtained from different instruments or when switching devices during longitudinal patient follow-up.^{23,24}

Despite these systematic differences in absolute CCT values, all four instruments demonstrated excellent reliability and strong inter-device agreement. ICCs ranged from 0.910 to 0.988, with all comparisons reaching statistical significance ($p < 0.001$). These findings indicate that each device provides highly reproducible CCT measurements and can be considered reliable for routine clinical use. However, because systematic measurement biases exist between devices, serial CCT assessments should ideally be performed using the same instrument to ensure consistency and accurate longitudinal comparisons. Our findings are consistent with previous studies reporting excellent repeatability and reproducibility of contemporary pachymetry devices, supporting their utility for long-term monitoring when the same measurement platform is used consistently.⁹⁻¹¹

This study has several limitations. First, the relatively modest sample size may limit the generalizability of the findings. Second, Scheimpflug-based imaging systems, which are widely used for corneal assessment, were not included in the comparison. Future studies should incorporate a larger and more diverse study population, including additional pachymetry technologies such as Scheimpflug imaging, and evaluate device performance in eyes with corneal pathologies or altered corneal biomechanics, including keratoconus, corneal edema, and post-refractive surgery eyes. Furthermore, the development and validation of device-specific correction algorithms for intraocular pressure measurement, particularly in eyes with abnormal corneal biomechanics, may improve the accuracy of glaucoma diagnosis and management.

CONCLUSION

In conclusion, this study demonstrates that optical coherence tomography, specular microscopy, and non-contact tonometry provide CCT readings that are therapeutically similar to ultrasound pachymetry. Clinicians should ensure that the devices used for long-term monitoring are consistent and watch out for measurement biases specific to a given device. As technology advances, ongoing analysis and platform standardization will be necessary to optimize glaucoma therapy and risk assessment.

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Patient's Consent: Researchers followed the guidelines set forth in the Declaration of Helsinki.

Conflict of Interest: Authors declared no conflict of interest.

Ethical Approval: The study was approved by the Institutional review board/Ethical review board (16437/EC/KEPK-RSDK/2025)

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Authors Designation and Contribution

Teuku Muhammad Agra Setianto; Resident: Concepts, Design, Literature search, Data acquisition, Data analysis, Statistical analysis, Manuscript preparation, Manuscript editing, Manuscript review

Maharani; Consultant Ophthalmologist: *Concepts, Design, Literature search, Data acquisition, Data analysis, Statistical analysis, Manuscript preparation, Manuscript editing, Manuscript review.*

