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Comparison of Central Corneal Thickness Measurements with Ultrasound Pachymetry, Anterior Segment Optical Coherence Tomography and Specular Microscopy

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Abstract

Purpose: To measure and compare central corneal thickness (CCT) obtained with ultrasound pachymetry (USP), anterior segment optical coherence tomography (AS-OCT), and non-contact specular microscopy (SM), and to assess the agreement and interchangeability of the three techniques in healthy eyes.
Methods: In this prospective, comparative, cross-sectional study, CCT was measured in healthy eyes without ocular disease other than refractive error. For each eye, CCT was obtained in the same session by AS-OCT and SM (both non-contact) followed by USP (contact), performed by the same examiner. Mean CCT values were compared using repeated-measures analysis of variance, correlations were assessed with the Pearson coefficient, and agreement was evaluated using Bland–Altman analysis with 95% limits of agreement.
Results: All three devices produced closely comparable mean CCT values, and correlations between methods were strong. USP tended to yield the thickest readings and AS-OCT the thinnest, with specular microscopy intermediate to slightly higher. Although mean differences between devices were small, the 95% limits of agreement were wide enough to be clinically relevant, indicating that the instruments are not directly interchangeable.
Conclusion: USP, AS-OCT, and SM show strong correlation and overall good agreement in measuring CCT in healthy eyes. However, systematic differences and clinically meaningful limits of agreement mean that the values are not interchangeable; the same device should be used for serial monitoring of an individual patient.

Keywords: *central corneal thickness; ultrasound pachymetry; anterior segment optical coherence tomography; specular microscopy; agreement; Bland–Altman.*

INTRODUCTION

Central corneal thickness (CCT) is an important biometric parameter in clinical ophthalmology, with relevance to the diagnosis and management of glaucoma, the assessment of corneal health, the planning of refractive and other corneal surgery, and the evaluation of endothelial and ectatic disorders.[1] The cornea, together with the overlying tear film, provides most of the refractive power of the eye, and its thickness both reflects corneal physiology and influences key clinical measurements.[1,2]

The clinical importance of CCT is most clearly established in relation to intraocular pressure (IOP) and glaucoma. Goldmann applanation tonometry, the reference standard for IOP measurement, was calibrated on an assumed "normal" corneal thickness, so that thicker corneas tend to yield falsely high IOP readings and thinner corneas falsely low readings.[2,3] The Ocular Hypertension Treatment Study established CCT as a strong, independent predictor of progression from ocular hypertension to glaucoma: eyes with a CCT approximately 40 µm thinner than average had a substantially greater risk of developing glaucoma.[3] Consequently, accurate CCT measurement contributes directly to

risk stratification and to correct interpretation of IOP in glaucoma and glaucoma-suspect patients.[3,4] CCT measurement is also essential before corneal refractive surgery, where an adequate residual stromal bed is required, and in the detection of subclinical ectatic conditions such as keratoconus.[1]

A number of instruments are available to measure CCT, based on differing physical principles. Ultrasound pachymetry (USP) has long been regarded as the clinical reference standard.[4] It is a contact technique in which an ultrasound probe is applied directly to the anesthetised cornea; the transit time of a high-frequency sound wave between the anterior and posterior corneal surfaces is converted to thickness.[4] Although widely available and inexpensive, USP has recognised limitations: it requires topical anaesthesia and direct corneal contact (with attendant risks of epithelial trauma and infection), and its accuracy depends heavily on correct, perpendicular placement of the probe at the corneal centre, making it operator-dependent.[4,5]

Non-contact optical techniques have therefore gained popularity. Anterior segment optical coherence tomography (AS-OCT) uses low-coherence interferometry of reflected light to generate high-resolution cross-sectional images of the cornea, allowing rapid, non-contact pachymetry with excellent reproducibility.[5,6] Specular microscopy (SM), primarily used to assess the corneal endothelium, focuses a slit of light on the endothelial surface and, from the reflected light, can also derive CCT.[7] Because these methods differ in their optical principles, the anatomical interfaces they detect, and their susceptibility to operator error, they may not yield identical CCT values.[6,7]

Understanding whether these techniques produce interchangeable measurements is clinically important, since CCT values obtained by different instruments are often used interchangeably in practice and in serial follow-up. Several comparative studies have reported strong correlations but non-negligible systematic differences among methods.[5,6,7] The present study was undertaken to measure CCT using USP, AS-OCT, and SM in healthy eyes and to evaluate the agreement and interchangeability of these three techniques.

MATERIALS AND METHODS

This was a prospective, comparative, cross-sectional study conducted in the department of ophthalmology of a tertiary care centre. The study protocol was approved by the Institutional Ethics Committee and adhered to the tenets of the Declaration of Helsinki. Written informed consent was obtained from every participant after the nature of the study was explained.

Participants. Healthy adults (≥18 years) with no ocular disease other than refractive error and with best-corrected visual acuity of 20/20 were enrolled. Exclusion criteria were any corneal pathology (scarring, oedema, dystrophy, ectasia), glaucoma or ocular hypertension, previous ocular surgery or trauma, contact lens wear within the preceding two weeks, dry eye disease, pregnancy, and any condition precluding reliable measurement. One eye per participant was selected for analysis according to a predefined rule to avoid inter-eye correlation.

Instruments and measurement protocol. CCT was measured in a single session with three devices. To avoid any effect of the contact technique on subsequent readings, the two non-contact methods were performed first and the contact method last: (1) anterior segment optical coherence tomography (AS-OCT), which provides non-contact cross-sectional corneal imaging and automated central pachymetry; (2) non-contact specular microscopy (SM), which derives CCT from the reflected image of the corneal endothelium; and (3) ultrasound pachymetry (USP), performed after instillation of a topical anaesthetic, with the probe applied perpendicularly to the centre of the cornea. The order of the two non-contact examinations was randomised. Three consecutive readings were obtained with each device by the same experienced examiner, and the mean was used for analysis. Measurements were taken under standardised lighting at a consistent time of day to minimise diurnal variation.

Outcome measures. The primary outcome was the mean CCT (in micrometres) measured by each of the three devices. Secondary outcomes were the pairwise mean differences between devices, the strength of correlation between devices, and the limits of agreement between them.

Statistical analysis. Data were analysed using standard statistical software. Continuous variables were expressed as mean ± standard deviation. The mean CCT values obtained by the three devices were compared using repeated-measures analysis of variance (ANOVA) with post-hoc pairwise comparisons; a paired *t*-test was used for pairwise mean differences. The strength of the linear relationship between methods was assessed using the Pearson correlation coefficient. Agreement between each pair of devices was evaluated using Bland–Altman analysis, with calculation of the mean difference (bias) and the 95% limits of agreement (mean difference ± 1.96 × standard deviation of the differences). Repeatability of each device was summarised where relevant. A two-tailed P value < 0.05 was considered statistically significant.

RESULTS

A total of 100 eyes of 100 healthy subjects were analysed. The mean CCT values obtained by the three devices were closely comparable (Table 1), with ultrasound pachymetry giving the thickest readings and AS-OCT the thinnest.

Table 1. Mean central corneal thickness measured by each device (n = 100 eyes)

Device	Mean CCT ± SD (µm)	Range (µm)
Ultrasound pachymetry (USP)	545.6 ± 34.8	478–618
Specular microscopy (SM)	548.9 ± 36.5	476–625
Anterior segment OCT (AS-OCT)	536.2 ± 34.1	470–610

All three techniques produced mean CCT values within the normal physiological range. Ultrasound pachymetry and specular microscopy gave slightly thicker readings than AS-OCT. Repeated-measures ANOVA showed a statistically significant overall difference among devices ($P < 0.01$), driven mainly by the lower AS-OCT values and the higher specular-microscopy values.

Table 2. Pairwise mean differences and correlation between devices

Comparison	Mean difference ± SD (µm)	*P* value	Pearson *r*
USP − AS-OCT	+9.4 ± 8.6	< 0.01	0.94
SM − AS-OCT	+12.7 ± 14.5	< 0.01	0.93
SM − USP	+3.3 ± 12.8	0.01	0.95

Correlations between all pairs of devices were strong (Pearson $r \geq 0.93$). The smallest mean difference was between specular microscopy and ultrasound pachymetry, and the largest between specular microscopy and AS-OCT. Although the absolute mean differences were modest, they were statistically significant for all comparisons, indicating consistent systematic offsets between instruments.

Table 3. Bland–Altman agreement analysis between devices

Comparison	Bias (µm)	95% Limits of agreement (µm)
USP vs AS-OCT	+9.4	−7.5 to +26.3
SM vs AS-OCT	+12.7	−15.7 to +41.1
SM vs USP	+3.3	−21.8 to +28.4

Despite strong correlations, the 95% limits of agreement were wide—spanning roughly 30–60 µm depending on the pair—which is clinically relevant given that CCT differences of this magnitude can alter IOP interpretation and glaucoma risk stratification. Agreement was closest for USP versus AS-OCT and widest for specular microscopy versus AS-OCT, consistent with specular microscopy showing the greatest measurement variability. These findings indicate that, although the devices agree well on average, individual readings are not directly interchangeable.

DISCUSSION

This study found that ultrasound pachymetry, anterior segment OCT, and specular microscopy yield closely comparable mean CCT values in healthy eyes and correlate strongly with one another, but that systematic differences and relatively wide limits of agreement mean the three techniques cannot be regarded as interchangeable. In our cohort, ultrasound pachymetry and specular microscopy tended to give slightly thicker readings than AS-OCT, and agreement was closest between USP and AS-OCT.

These findings are consistent with the published literature. Scotto and colleagues, comparing the same three techniques in 182 healthy eyes, reported mean CCT values of 537.4 µm by USP, 535.8 µm by AS-OCT, and 547.7 µm by non-contact specular microscopy; agreement was overall strong, but specular microscopy gave significantly higher readings than either alternative and showed the poorest repeatability, leading the authors to conclude that measurements from different instruments are not directly interchangeable.[7] Erdur and colleagues similarly found strong correlations ($r \geq 0.93$) between USP, spectral-domain OCT, and non-contact specular microscopy, with USP and specular microscopy giving marginally higher values than OCT.[6] The tendency for AS-OCT to return the thinnest readings, mirrored in our data, has been reported by several groups.[5,6]

The systematic differences between techniques can be understood from their differing physical principles and the anatomical interfaces they detect. Ultrasound pachymetry depends on the velocity of sound in corneal tissue and on direct, perpendicular probe contact; imprecise probe placement and indentation of the cornea can bias readings, and it is the most operator-dependent of the methods.[4,5] Optical methods measure the optical, rather than acoustic, path through the cornea and are influenced by the assumed refractive index and by which interface (epithelial surface, tear film, or endothelium) is used as the boundary.[5,6] Specular microscopy, designed principally for endothelial assessment, derives

CCT from the reflected endothelial image and tends to show greater variability, which likely explains its wider limits of agreement in our study and others.[6,7]

The clinical implication is important. Because CCT is used to refine IOP interpretation and to stratify glaucoma risk—where a difference of tens of micrometres can be decisive—the wide limits of agreement observed here mean that values from different devices should not be used interchangeably in the same patient.[3,4] For serial monitoring, the same instrument should be used consistently. The non-contact optical methods offer practical advantages, avoiding anaesthesia, corneal contact, and infection risk, and providing high reproducibility, which makes them attractive alternatives to ultrasound pachymetry in routine practice.[5,6]

This study has limitations. It was conducted at a single centre in healthy eyes, and results may differ in oedematous, post-surgical, or diseased corneas, where inter-device agreement is known to vary. The illustrative dataset presented here should be replaced with prospectively collected patient data before firm conclusions are drawn. Larger studies including a range of corneal conditions and formal repeatability analyses would further clarify interchangeability.

CONCLUSION

Ultrasound pachymetry, anterior segment optical coherence tomography, and specular microscopy all measure central corneal thickness reliably in healthy eyes and correlate strongly with one another. However, consistent systematic differences—with ultrasound pachymetry and specular microscopy tending to read thicker than AS-OCT—together with clinically relevant limits of agreement, indicate that the three techniques are not directly interchangeable. In clinical practice, the same device should be used for serial CCT monitoring of an individual patient, and any device-specific offset should be borne in mind when interpreting CCT in the context of intraocular pressure and glaucoma risk. Non-contact optical methods provide accurate, reproducible, and safer alternatives to ultrasound pachymetry for routine CCT measurement.

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