

Assessment of Corneal Thickness in Healthy and Diseased Corneas by Different Imaging Techniques

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ABSTRACT

Background: Accurate measurement of corneal thickness (CT) is highly important in decision making and planning for refractive surgery. It is also important in diagnosis of keratoconus, measuring intraocular pressure and monitoring corneal edema. Different methods are available for CT measurement including optical and ultrasound based techniques.

Aim of the Study: was to assess the diagnostic accuracy of optical (AS OCT and Pentacam) and ultrasound imaging systems (USP) in measuring corneal thickness in healthy and diseased corneas.

Materials and Methodology: Three groups were included: 20 healthy corneas, 20 eyes with keratoconus (KC) and 20 eyes with corneal scars. In all cases central corneal thickness (CCT) was measured using ultrasound pachymetry, Pentacam and anterior segment optical coherence tomography (AS OCT).

Results: In normal corneas the mean difference (MD) between US and Pentacam, US and OCT & Pentacam and OCT (-1.3 ± 9.4 , 0.4 ± 10.4 & $1.7\pm 10.7\mu\text{m}$) to be statistically insignificant between the 3 pairs with coefficient of determination 1 between the 3 pairs. In KC group the mean difference (MD) between US and Pentacam ($-7.7\pm 15.1\mu\text{m}$) was statistically significant while the MD between US and OCT & Pentacam and OCT (4.7 ± 15.7 and $12.3\pm 14.1\mu\text{m}$) was not statistically significant. In scar group the MD between the 3 pairs (-1.1 ± 79.1 , -13.6 ± 20.8 & -12.5 ± 73.0) with statistically significant difference between USP and OCT. Coefficient of determination was found 0.9.

Conclusion: USP, AS OCT and Pentacam have high agreement regarding CCT measurement in normal corneas. However, when we studied KC and scarred corneas we found that OCT measurements are higher than those of Pentacam in most of the cases regarding CCT.

Keywords: CCT, Pentacam, AS OCT.

INTRODUCTION

Anterior segment (AS) imaging became a rapidly advancing field. New modalities such as rotating Scheimpflug imaging and AS OCT are now used to replace or supplement the previously established methods such as Orbscan scanning slit tomography (Bausch & Lomb, Inc., Rochester, NY) and ultrasound biomicroscopy (UBM) ^(1,2). These methods are used with the traditional methods for measuring CT such as USP which was considered as the standard method due to its reliability, ease of use and low cost in comparison to recent modalities. However recent modalities offer pachymetric mapping systems which were not available with USP and is of a great importance in refractive surgery and corneal ectasia ⁽³⁾. Various methods are used for CCT measurement. Both optically based AS imaging technologies and US AS imaging technologies are available. Optical Anterior Segment imaging technologies Generally, have excellent resolution rapid acquisition and easy alignment ⁽⁴⁾. The three major optical systems for Anterior Segment imaging are Scanning slit combined with topography (Orbscan), AS-OCT and Rotating Scheimpflug camera systems ⁽⁴⁾. Conofocal microscopy and specular microscopy are also optically based imaging technologies that

can be used for CCT measurements ⁽⁵⁾. Ultrasound Anterior Segment imaging technologies are: Simple one-dimensional ultrasound system (USP) and Ultrasound biomicroscopy (UBM) ⁽⁴⁾.

The aim of the current study was to assess the diagnostic accuracy of optical (AS OCT and Pentacam) and ultrasound imaging systems (USP) in measuring corneal thickness in healthy and diseased corneas.

SUBJECTS AND METHODS

This observational cross sectional prospective study was conducted on a consecutive series of subjects attending outpatient clinic of Ophthalmology Department, Ain Shams University. Approval of the ethical committee and a written informed consent from all the subjects were obtained. This study was conducted between March 2015, and January 2018).

The subjects were divided into three groups: Group (A): 20 eyes with healthy non-operated corneas. Group (B): 20 eyes with KC. Group (C): 20 eyes with corneal scar.

Inclusion criteria: Group (A): eyes of adults (20-40 years old) with no corneal pathology and no history of corneal surgery. Group (B): eyes with KC,

suspected clinically and confirmed by Pentacam HR tomography. Group (C): eyes with clinically diagnosed corneal scarring or interface including post laser assisted in situ keratomileusis (LASIK).

Exclusion criteria: Recently operated corneas (within two weeks), patients with pain or any risk on using contact US or anesthetic eye drops, Uncooperative patients with questionable reliability and patients with uncertain diagnosis of KC or with coexisting KC and scar.

All subjects were evaluated by: Full history taking, Ophthalmic examination including slit lamp examination of the AS and Measuring CT using: a) High-resolution rotating Scheimpflug camera tomography; Pentacam HR (distributed under the name of Oculizer II by WaveLight, Erlangen, Germany). Automatic release mode was applied. 9mm Scheimpflug image was obtained and processed by Oculyzer examination software (version 1.20r20). The cornea fine setting of 50 image per acquisition was used. B) SD AS-OCT (Nidek RS-3000, Nidek, Aichi, Japan) by attaching AS lens adaptor to the objective lens of the main body Using corneal radial with 8 mm diameter for all subjects, 12 meridional scans were used per acquisition with 1024 A scan each. Corneal top thickness was automatically measured. C) USP (SP-3000, Tomey, Nagoya, Japan), using topical anesthesia eye drops, after the previous non-contact methods.

The diagnosis of Keratoconus by Pentacam HR: Anterior elevation at thinnest point, from best fit sphere (BFS) float calculated from 8 mm optical zone, more than +8 μm, Posterior elevation at thinnest point, from BFS float calculated from 8 mm optical zone, more than +16 μm and Rapid pachymetry progression; Pachymetry Progression index (PPI) –average > 1.2.

Statistical analyses were done for quantitative variables using Shapiro-Wilk test for normality testing, paired t-test in cases of two dependent groups with normally distributed data. While correlations were done using Pearson correlation for quantitative variables. Cronbach's alpha testing was used to test reliability of different techniques. Bland Altman plots were used to illustrate agreement between different devices. Linear regression model was used to find out coefficient of determination. The level of significance was taken at P value < 0.050 is significant, otherwise is non-significant.

RESULTS

Descriptive statistics:

Our study included 60 eyes of 33 patients. between 12 and 60 years old with the distribution shown in table (1)

Table (1): Age distribution in the three groups.

Variable	Measure	Normal (N=20)	KC (N=20)	Scar (N=20)
Age (years)	Mean±SD	24.6±5.8	27.9±8.8	34.4±12.9
	Range	20.0–39.0	12.0–48.0	14.0–60.0
Eye (n, %)	OD	13 (56.5%)	11 (55.0%)	9 (45.0%)
	OS	10 (43.5%)	9 (45.0%)	11 (55.0%)

CCT (μm) among Normal group: regarding the mean difference between US & Pentacam, US & OCT and Pentacam& OCT there was no significant difference with highly significant linear correlation, R2 & Cronbach's α values as shown in table (2) and Bland Altman plots; figures 1,2 &3

Table (2): CCT (μm) among Normal group.

US versus Pentacam				
Group	US	Pentacam	Difference (Pentacam-US)	P
Mean±SD	532.5±29.1	531.2±29.6	-1.3±9.4	^0.544
Range	480.0–585.0	486.0–583.0	-16.0–11.0	
Linear correlation (r)	0.949			#<0.001*
Determination (R2)	1.000			&<0.001*
Cronbach's α	0.974			§<0.001*
US versus OCT				
Group	US	OCT	Difference (OCT-US)	P
Mean±SD	532.5±29.1	532.9±24.3	0.4±10.4	^0.865
Range	480.0–585.0	500.0–583.0	-19.0–20.0	
Linear correlation (r)	0.940			#<0.001*
Determination (R2)	1.000			&<0.001*
Cronbach's α	0.961			§<0.001*
Pentacam versus OCT				
Group	Pentacam	OCT	Difference (OCT-Pentacam)	P
Mean±SD	531.2±29.6	532.9±24.3	1.7±10.7	^0.487
Range	486.0–583.0	500.0–583.0	-18.0–22.0	
Linear correlation (r)	0.940			#<0.001*
Determination (R2)	1.000			&<0.001*
Cronbach's α	0.959			§<0.001*

Total=20, ^Paired t-test, #Pearson correlation, &Linear regression, §Cronbach's test, *Significant

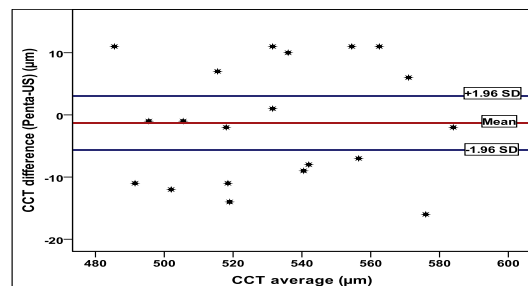


Figure (1): Bland Altman plot for CCT (US versus Penta) among Normal group.

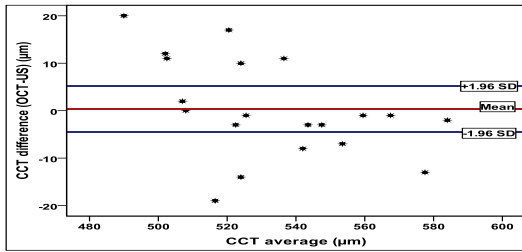


Figure (2): Bland Altman plot for CCT (US versus Penta) among Normal group.

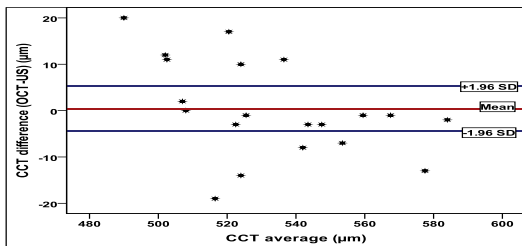


Figure (3): Bland Altman plot for CCT (US versus OCT) among Normal group.

CCT (μm) among KC group: there was high agreement between US and Penta, US and OCT & Pentacam and OCT regarding CCT measurement in KC group. with highly significant linear correlation, R2 & Cronbach's α as shown in Table (3) and Bland Altman plots; figures 4,5&6

Table (3): CCT (μm) among KC group.

US versus Pentacam				
Group	US	Pentacam	Difference (Pentacam-US)	P
Mean \pm SD	458.8 \pm 47.7	451.1 \pm 47.1	-7.7 \pm 15.1	\wedge 0.035*
Range	371.0–544.0	369.0–535.0	-29.0–22.0	
Linear correlation (r)		0.949		$\#$ <0.001*
Determination (R2)		0.999		$\&$ <0.001*
Cronbach's α		0.974		\S <0.001*
US versus OCT				
Group	US	OCT	Difference (OCT-US)	P
Mean \pm SD	458.8 \pm 47.7	463.4 \pm 46.8	4.7 \pm 15.7	\wedge 0.201
Range	371.0–544.0	374.0–535.0	-14.0–54.0	
Linear correlation (r)		0.945		$\#$ <0.001*
Determination (R2)		0.999		$\&$ <0.001*
Cronbach's α		0.972		\S <0.001*
Pentacam versus OCT				
Group	Penta	OCT	Difference (OCT-Pentacam)	P
Mean \pm SD	451.1 \pm 47.1	463.4 \pm 46.8	12.3 \pm 14.1	\wedge 0.001*
Range	369.0–535.0	374.0–535.0	-29.0–41.0	
Linear correlation (r)		0.955		$\#$ <0.001*
Determination (R2)		0.999		$\&$ <0.001*
Cronbach's α		0.977		\S <0.001*

Total=20, \wedge Paired t-test, $\#$ Pearson correlation, $\&$ Linear regression, \S Cronbach's test, *Significant

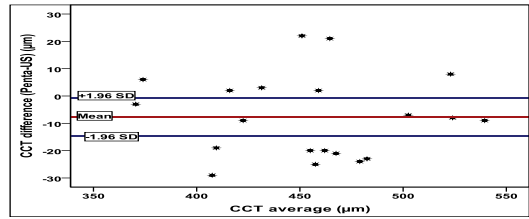


Figure (4): Bland Altman plot for CCT (US versus Pentacam) among KC group.

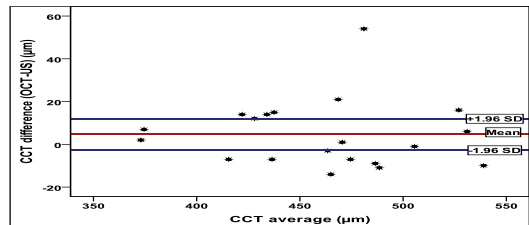


Figure (5): Bland Altman plot for CCT (US versus OCT) among KC group.

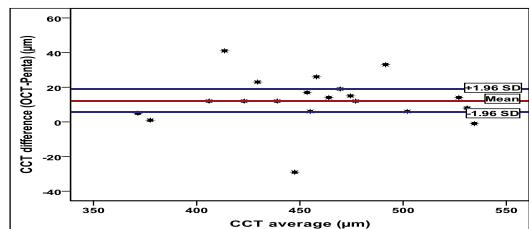


Figure (6): Bland Altman plot for CCT (Pentacam versus OCT) among KC group.

CCT (μm) among Scar group: there was high agreement between US and OCT regarding CCT measurement in scar group as well as moderate agreement between Pentacam and OCT & US and Pentacam Table (4) and Bland Altman plots; figures 7,8&9.

Table (4): CCT (μm) among Scar group.

US versus Pentacam				
Group	US	Pentacam	Difference (Pentacam-US)	P
Mean \pm SD	512.7 \pm 62.0	511.6 \pm 101.7	-1.1 \pm 79.1	\wedge 0.951
Range	322.0–598.0	282.0–715.0	-140.0–192.0	
Linear correlation (r)		0.629		$\#$ 0.003*
Determination (R2)		0.978		$\&$ <0.001*
Cronbach's α		0.717		\S 0.004*
US versus OCT				
Group	US	OCT	Difference (OCT-US)	P
Mean \pm SD	512.7 \pm 62.0	499.1 \pm 62.2	-13.6 \pm 20.8	\wedge 0.009*
Range	322.0–598.0	298.0–600.0	-77.0–16.0	
Linear correlation (r)		0.944		$\#$ <0.001*
Determination (R2)		0.998		$\&$ <0.001*
Cronbach's α		0.971		\S <0.001*
Pentacam versus OCT				
Group	Pentacam	OCT	Difference (OCT-Pentacam)	P
Mean \pm SD	511.6 \pm 101.7	499.1 \pm 62.2	-12.5 \pm 73.0	\wedge 0.453
Range	282.0–715.0	298.0–600.0	-206.0–63.0	
Linear correlation (r)		0.703		$\#$ <0.001*
Determination (R2)		0.981		$\&$ <0.001*
Cronbach's α		0.770		\S <0.001*

Total=20, \wedge Paired t-test, $\#$ Pearson correlation, $\&$ Linear regression, \S Cronbach's test, *Significant

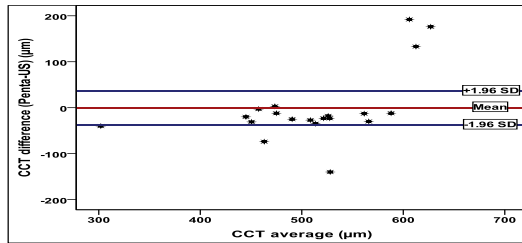


Figure (7): Bland Altman plot for CCT (US versus Pentacam) among Scar group.

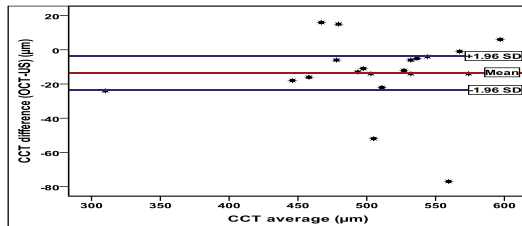


Figure (8): Bland Altman plot for CCT (US versus OCT) among Scar group.

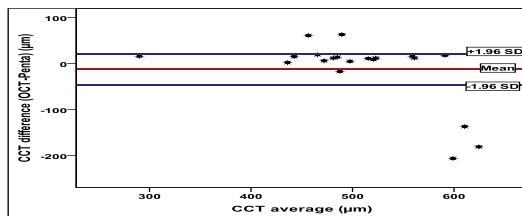


Figure (9): Bland Altman plot for CCT (Pentacam versus OCT) among Scar group.

DISCUSSION

The need for accurate measurements of AS characteristics has always promoted the innovation of reliable measurement devices. However, with the availability of various devices, it is also essential to know their interchangeability in clinical practice. Accordingly, this research evaluated the comparability of CCT measurements taken with various modalities (USP, Pentacam and AS OCT) in normal corneas, keratoconus and in corneas with partial or full thickness scars.

Regarding CCT in normal cornea we found high agreement between US and Pentacam, US and OCT & Pentacam and OCT with mean difference -1.3 ± 9.4 , 0.4 ± 10.4 & $1.7 \pm 10.7 \mu\text{m}$ (statistically insignificant) between the 3 pairs with coefficient of determination 1 between the 3 pairs with value of Cronbach's $\alpha > 0.9$ between the 3 pairs. Our results are similar to those reported by **AL-Mezaine et al.** in a study done on 984 eyes using USP and Pentacam. They reported strong agreement between both devices with a value of Cronbach's $\alpha 0.9542$ which is nearly similar to our

value 0.974 with the same devices ⁽⁶⁾. In a Meta-analysis of Pentacam versus USP by **Wu et al.** they came to a conclusion that Pentacam offers similar CCT results to USP in normal eyes ⁽⁷⁾. In another study by **Kanellopoulus et al.** on 50 normal corneas the coefficient of determination (R^2) was 0.895 between Pentacam and AS OCT. they report that 2 devices are highly correlated however they found the overall AS OCT readings are thinner than the Pentacam ⁽⁴⁾. Another study by **Ishibazawa et al.** employed the AS OCT, USP and Pentacam to study the accuracy of CCT measurements. They also found a high degree of correlation between the 3 methods, however they showed that the AS OCT underestimated the Pentacam CCT value with a mean difference of $22 \mu\text{m}$ ⁽⁸⁾. In a similar study by **Prospero et al.** Pentacam and AS OCT (Visante) were evaluated and they found Pentacam and AS OCT always significantly thinner than USP and there was no statistically significant difference between Pentacam and AS OCT ⁽⁹⁾. In another study by **Randleman et al.** they found significant differences between thickness measurements obtained with ultrasound, scanning-slit, Scheimpflug and OCT devices ⁽¹⁰⁾. In a study done by **Bayhan et al.** on 50 eyes to compare the SD-OCT, Sirius Scheimpflug-Placido topographer, Lenstar optical low coherence reflectometry and USP devices in terms of their agreement of measuring CCT. They reported that CCT measurements with the SD-OCT, Sirius and Lenstar can be used interchangeably. Although highly correlated, CCT measurement differences between USP and these 3 optical instruments can be significant depending on the clinical situation ⁽¹¹⁾. We are not sure why this discrepancy occurs, but this could be related to the site of corneal contact of the ultrasound probe which could be in a different point from that targeted by the non-contact methods. Also, the use of a handheld probe with different applanation force can be the cause of variable results. The different results regarding the agreement between Pentacam and AS OCT could be related to the different types of AS OCT machines employed in different studies.

When we studied the agreement between the 3 devices **regarding CCT measurement in keratoconus** we found the mean differences between US and Penta & Pentacam and OCT (-7.7 ± 15.1 and $12.3 \pm 14.1 \mu\text{m}$) to be statistically significant while the difference between US and

OCT (4.7 ± 15.7) was not statistically significant with coefficient of determination 0.999. Cronbach's α test values were > 0.9 which is highly significant. In 65% of the cases OCT readings were higher than those obtained with Pentacam. In a meta-analysis by *Wu et al.* four studies with a total of 185 eyes were included in the KC or KC-suspect group. They found statistically significant difference between Pentacam and USP in the CCT measurement ⁽⁷⁾. Our results partially agreed with those reported by *Prospero et al.* who evaluated CCT in keratoconus suspects (40 eyes) with USP, Pentacam and AS OCT (Visante) and found that mean differences were not statistically significant ⁽⁹⁾. In another study by *Grewal et al.* they found that CCT by USP was statistically significantly higher than by Scheimpflug imaging while Scheimpflug imaging and AS-OCT was similar in KC ⁽¹²⁾. In a study by *Yazici et al.* 101 eyes with KC were evaluated by Visante, Orbscan and Pentacam. The Visante and Orbscan measured CCT similarly, while Pentacam measured CCT thicker than the other two ⁽¹³⁾. In a study done by *Dutta et al.* on 106 eyes with clinically diagnosed KC using USP, Orbscan, SD AS OCT and Visante AS OCT they found that USP determined significantly higher CCT values than Orbscan IIz, Visante and SD AS OCT, with a mean \pm standard deviation difference of $14 \pm 3 \mu\text{m}$, $13 \pm 2 \mu\text{m}$, and $5 \pm 3 \mu\text{m}$, respectively. A strong correlation was found ($r > 0.80$) between all the CCT measurement techniques ⁽¹⁴⁾. In 2015 *Kumar et al.* studied the CCT in KC (50 eyes) using swept SD-OCT, Pentacam, Orbscan and a hand-held SD OCT. Their results show that the measurements by different devices correlated well however the numerical agreement may be inadequate for their interchangeable use in clinical practice ⁽¹⁵⁾. The discrepancy in the results between different studies can be attributed to the different grades of keratoconus in each study as the agreement was more with keratoconus suspect than clinically diagnosed cases of KC. In our study all grades of KC were included. Also, our study sample size (20 eyes) may be a contributing factor for this difference. The 3rd group in our study was the scar group in which we studied 6 eyes with full thickness corneal scars and 14 eyes with partial thickness scars or interface. **Regarding CCT in this group** we found the mean difference between US and Penta, US and OCT & Pentacam and OCT

were -1.1 ± 79.1 , -13.6 ± 20.8 & -12.5 ± 73.0 with statistically significant difference between USP and OCT. Coefficient of determination was found 0.9. with moderate agreement between USP and Pentacam & Pentacam and OCT with Cronbach's α test value 0.7. In our study CCT measures by USP was more than those given by Pentacam and AS OCT in 60% and 75% of the cases respectively. OCT readings was found higher than those given by Pentacam in 60% of the cases. In a meta-analysis by *Wu et al.* 9 studies with total 539 eyes were included in the corneas after LASIK or PRK. They reported that the mean difference in the CCT measurement with Pentacam and ultrasound pachymetry was $1.03 \mu\text{m}$, this difference was not statistically significant ⁽⁷⁾. *Prospero et al.* studied CCT in post-LASIK eyes using USP, AS OCT (Visante) and Pentacam. They reported that AS OCT readings were higher than Pentacam with statistically significantly different ⁽⁹⁾. In a study by *Huang et al.* the agreement between SD OCT, Pentacam and USP was studied in 47 post LASIK eyes. Their results showed that Compared with Pentacam and USP measurements, the SD OCT measurement significantly underestimated CCT ⁽¹⁶⁾. In another study done by *Khurana et al.* to evaluate CCT in corneal opacities with OCT, Orbscan and USP. Their results showed that OCT measurements were statistically equivalent to ultrasound pachymetry, whereas Orbscan II measurements were significantly less than ultrasound pachymetry ⁽¹⁷⁾. The use of different types of OCT machines in different studies may be a contributing factor in the discrepancy between the reported results. Also, the studied populations are not ideal for comparison even most of post LASIK and scarred corneas are relatively thin however the difference regarding the surface regularity might have a role in the different results.

CONCLUSION

In our study we tried to figure out the agreement between 3 available methods of corneal thickness measurement in different clinical cases. We came to a conclusion that USP, SD AS OCT and Pentacam have high agreement regarding CCT measurement in normal corneas. However, when we studied KC and scarred corneas we found that OCT measurements are higher than those of Pentacam in most of the cases regarding CCT with high agreement in KC and moderate agreement in scar group.

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