Comparison of Central Corneal Thickness Measurement Using Ultrasound Pachymetry and Current Diagnostic Devices in Normal and Keratoconic Eyes

Keratokonuslu ve Normal Gözlerde Ultrason Pakimetri ve Güncel Cihazlarla Kornea Kalınlık Ölçümlerinin Karşılaştırılması

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ABSTRACT

Aim: To compare central corneal thickness (CCT) measurements using four different imaging systems in normal and keratoconic eyes.

Methods: In this retrospective study, a total of 92 eyes of 92 patients (53 normal eyes, 39 keratoconus eyes) were included. Five consecutive measurements were taken with optical low-coherence reflectometry (OLCR), Scheimpflug-Placido Topographer, spectral domain optical coherence tomography (SD-OCT), and ultrasound pachymetry (USP).

Results: In normal eyes, mean OLCR, Scheimpflug-Placido Topographer, SD-OCT, and USP CCT measurements were 520.76±4.31 µm, 519.96±4.33 µm, 522.40±4.20 µm, and 528.89±4.11 µm respectively. There was a statistically significant difference in the CCT measurements between the OLCR and USP and the Scheimpflug-Placido Topographer and USP (p=0.003, p=0.01 respectively). All four modalities of CCT measurements correlated closely with each other, with Pearson correlation coefficients ranging from 0.957 to 0.983. In keratoconic eyes, average OLCR, Scheimpflug-Placido Topographer, SD-OCT, and USP CCT measurements were 449.93±5.77 µm, 455.48±5.79 µm, 457.21±5.61 µm, and 465.87±5.49 µm respectively. In keratoconic eyes, OLCR measurements were thinner than those of USP by a mean of 15.93 µm, of SD-OCT by an average of 7.27 µm (p<0.001, and p=0.007 respectively). All 4 modalities of CCT measurements correlated closely with each other, with Pearson correlation coefficients ranging from 0.872 to 0.932.

Conclusion: Scheimpflug-Placido Topographer and SD-OCT measurements showed good agreement with ultrasound pachymetry in normal and keratoconic eyes. However, OLCR measurements were thinner than the other three devices in keratoconic eyes. Scheimpflug-Placido Topographer, USP, SD-OCT, and OLCR should not be used interchangeably in keratoconic eyes.

Key words: Central corneal thickness, optical low-coherence reflectometry, pachymetry, scheimpflug-placido topographer, spectral domain optical coherence tomography.

ÖZ

Amaç: Keratokonuslu ve normal gözlerde dört farklı görüntüleme cihazı ile santral kornea kalınlık (SKK) ölçümlerinin karşılaştırılması.

Metod: Retrospektif çalışmamıza 92 hastanın (53 normal göz, 39 kerakonuslu göz) 92 gözü dahil edildi. Optik düşük koheranslı reflektometre (ODKR), scheimpflug-placido topografi (SPT), spektral domain optik koherens tomografi (SD-OKT) ve ultrason pakimetri (UP) cihazları ile ardışık beş ölçüm alındı.

Bulgular: Normal gözlerde ortalama SKK değerleri ODKR, scheimpflug-placido topografi, SD-OKT ve UP cihazları ile sırasıyla 520,76±4,31 µm, 519,96±4,33 µm, 522,40±4,20 µm ve 528,89±4,11 µm idi. Santral kornea kalınlığı ölçümleri değerlendirildiğinde

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ODKR ile UP ve SPT ile UP arasında istatistiksel olarak anlamlı fark saptandı (p=0,003, p=0,01 sırasıyla). Tüm cihazların SKK ölçüm değerleri yakın korelasyon göstermekteydi (Pearson Korelasyon değerleri 0,957 -0,983). Keratokonuslu gözlerde ortalama SKK değerleri ODKR, scheimpflug-placido topografi, SD-OKT ve UP cihazları ile sırasıyla; 449,93±5,77 µm, 455,48±5,79 µm, 457,21±5,61 µm ve 465,87±5.49 µm idi. Keratokonuslu gözlerde, ODKR ölçüm değerleri UP'den ortalama 15,93 µm ve SD-OKT'den ortalama 7,27 µm daha ince olduğu görüldü (p<0,001 ve p=0,007 sırasıyla). Tüm cihazların SKK ölçüm değerleri yakın korelasyon göstermekteydi (Pearson Korelasyon değerleri 0,872 -0,932).

Sonuç: Normal ve keratokonuslu gözlerde SPT ve SD-OKT ölçüm değerleri UP değerleri ile iyi uyum göstermekteydi. Ancak, keratokonuslu gözlerde ODKR ölçüm değerleri diğer üç cihaz ile karşılaştırıldığında daha ince olduğu bulundu. Scheimpflug-placido topografi, UP,SD-OKT ve ODKR keratonuslu gözlerde alternatif olarak kullanılmamalıdır.

Anahtar kelimeler: Santral kornea kalınlığı, optik düşük koheranslı reflektometre,pakimetri, scheimpflug-placido topografi, spektral domain optik koherens tomografi.

INTRODUCTION

Keratoconus is characterized by progressive corneal thinning, steepening and distortion of the cornea.[1] The use of imaging systems always has been important in diagnosing and monitoring keratoconus.[2] Along with corneal topography, serial measurement of corneal thickness (CCT) with high accuracy plays a main role in the assessment of keratoconus progression. It is particularly important to identify early reduction of corneal thickness in progressive keratoconus in patients who could be considered for new available treatment methods such as collagen cross-linking.[3]

Various techniques are available to measure corneal thickness, of which ultrasound pachymetry has been regarded as the gold standard. However, a few limitations, such as relatively high interoperator variability, the need for topical anesthesia, and direct contact of the probe with the cornea, have resulted in a search for noninvasive methods.[4] Recently several sophisticated devices are available for the determination of corneal thickness, such as confocal biomicroscopy,[5] ultrasound biomicroscopy,[6] scanning laser topography,[7] partial coherence laser interferometry,[8] Scheimpflug imaging,[9, 10] optical coherence tomography (OCT),[8, 11, 12] OLCR,[13, 14] and specular microscopy (SM)[6].

Recently two studies have compared corneal thickness measured by OLCR, Scheimpflug-Placido Topographer, SD-OCT, and USP by assessing the CCT measurement in healthy subjects.[15, 16] However, to the best of our knowledge, no study has conducted this comparison analysis with these four devices in patients with keratoconus. In this study, we evaluated the level of CCT values measured by OLCR, Scheimpflug-Placido Topographer, SD-OCT, and USP in normal and keratoconic eyes.

PATIENTS AND METHODS

In this retrospective study, a total of 92 eyes of 92 patients (53 normal eyes, 39 keratoconus eyes) were included in the study. Subjects with negative medical history and with no signs of previous or present ocular disease and refractive errors less than ±2 diopter spherical or cylinderic value included in normal eyes. The clinical diagnosis of keratoconus was based on topographic findings as well as biomicroscopic signs of keratoconus. All eyes had early to moderate keratoconus (grade I to II according to Amsler–Krumeich's classification). Patients with keratoconus were excluded from participation if they had a history of ophthalmic surgery, or significant ophthalmic disease other than keratoconus.

All measurements of the CCT were conducted by a single investigator (M.U.) at the same location. Each subject underwent four different methods of measurements sequentially using the following instruments: LenStar LS900 (OLCR; Haag-Streit AG, Koeniz, Switzerland), Sirius Scheimpflug-Placido Topographer (Costruzione Strumenti Oftalmici, Florence, Italy) Spectralis (SD-OCT, Heidelberg Engineering, Germany) and Pacline (USP, Optikon). Consecutive five CCT measurements were obtained from each subject using four different instruments. All measurements were taken at the same time of day (between 10:00 a.m. and 4:00 p.m.) and at least 2 h after wakeup time to avoid the effects of diurnal variation in corneal thickness. All studies adhered to the tenets of the Declaration of Helsinki, and all subjects have given informed consent for participation in this study. The project protocol was approved by the Senate Committee on the Ethics of Research on Human Beings of the Erciyes University.

Noncontact pachymetry examinations were performed as described in the literature.[2, 9] Subjects were positioned on the headrest and instructed to look straight ahead into the built-in fixation targets within each device. After proper alignment, they were asked to blink just before each measurement was taken. Following each acquisition, subjects were then instructed to take their head off the chin rest, blink, and return to the examination position. The device was moved backward and realigned for the next scan.

After completing the noncontact examination, USP was performed. The cornea was first anesthetized with a drop of 0.5% topical proparacaine hydrochloride (Alcaine; Alcon, Belgium). The subject was asked to look straight ahead to a fixation target, and the probe was applied perpendicularly to the central corneal surface. After a measurement was taken, the subject was instructed to blink and a repeated measurement was obtained. The ultrasound probe was sterilized with alcohol after each subject.

Statistical Analysis

All data were analyzed using SPSS software (version 16.0 SPSS, Inc). The descriptive statistics were presented as mean ± standard deviation (SD). Repeated-measures ANOVA was conducted to compare the mean CCT values for the three instruments. Bland–Altman analysis was performed to assess the limits of agreement between different pairings of the four devices. Finally, a Pearson correlation coefficient test was performed to compare the mean CCT values for the all instruments. A p value less than 0.05 was considered statistically significant. Repeatability was assessed using intraclass correlation coefficients (ICCs).

RESULTS

A total of 92 eyes of 92 patients were included (53 normal eyes, 39 keratoconus eyes). The mean age was 28.1±8.9 years (range 18–36 years) for normal subjects and 25.8±7.7 years (range 17–32 years) for keratoconus patients.

Comparison of mean CCT

Table 1 lists corneal thickness measurements obtained using four different devices for the 2 groups. In normal eyes, mean OLCR, Scheimpflug-Placido Topographer, SD-OCT, and USP CCT measurements were 520.76±4.31 μm, 519.96±4.33 μm, 522.40±4.20 μm, and 528.89±4.11 μm respectively. There was a statistically significant difference in the CCT measurements between the OLCR and USP and the Scheimpflug-Placido Topographer and USP (p=0.003, p=0.01; respectively), (Table 2). All 4 modalities of CCT measurements correlated closely with each other, with Pearson correlation coefficients ranging from 0.957 to 0.983. In keratoconic eyes, average OLCR, Scheimpflug-Placido Topographer, SD-OCT, and USP CCT measurements were 449.93±5.77 μm, 455.48±5.79 μm, 457.21±5.61 μm, and 465.87±5.49 μm respectively. In keratoconic eyes, OLCR measurements were thinner than those of USP by a mean of 15.93 μm, of SD-OCT by an average of 7.27 μm (p<0.001, p=0.007; respectively, one-way ANOVA and the Tukey multiple comparisons test). All 4 modalities of CCT measurements correlated closely with each other, with Pearson correlation coefficients ranging from 0.872 to 0.932. Among other measurements than those by OLCR, there was no statistically significant difference (Table 2).

***Table 1:** Descriptive statistics for central corneal thickness measurements in normal and keratoconic eyes.*

			95% Confidence Interval	
		Mean±SD(μm)	Lower Bound	Upper Bound
Normal Eyes	*OLCR*	520.76±4.31	512.19	529.33
	SPT	519.96±4.33	511.35	528.58
	SD-OCT	522.40±4.20	514.06	530.75
	USP	528.89±4.11	520.73	537.06
Keratoconic Eyes	*OLCR*	449.93±5.77	438.47	461.40
	SPT	455.48±5.79	443.96	467.00
	SD-OCT	457.21±5.61	446.05	468.36
	USP	465.87±5.49	454.95	476.79

OLCR : Optical low-coherence reflectometry, SPT: Scheimpflug-Placido Topographer, USP: Ultrasound pachymetry and SD-OCT: Spectral domain optical coherence tomography

***Table 2:** Mean Difference, SD, and 95% Confidence Interval in Comparison of Corneal Thickness Measurements Between Devices in Normal and Keratoconic Eyes*

	Mean Difference ±SD(μm)	P	95% Confidence Interval for Difference	
			Lower	Upper
Normal Eyes				
OLCR and SPT	0.79±2.09	1.00	-4.84	6.43
OLCR and USP	-8.13±2.26	0.003*	-14.25	-2.01
OLCR and SD-OCT	-1.64±1.62	1.00	-6.02	2.73
SPT and USP	-8,93±2,94	0.01*	-16.88	-0.97
SPT and SD-OCT	-2.44±1.40	0.51	-6.22	1.34
USP and SD-OCT	6.49±2,65	0.09	-0.67	13.65
Keratoconic Eyes				
OLCR and SPT	-5.54±2.79	0.30	-13.08	1.99
OLCR and USP	-15.93±3.03	<0.001*	-24.12	-7.75
OLCR and SD-OCT	-7.27±2.17	0.007*	-13.13	-1.41
SPT and USP	-10.39±3.94	0.059	-21.03	0.24
SPT and SD-OCT	-1.72±1.87	1.00	-6.78	3.33
USP and SD-OCT	8.66±3.55	0.1	-0.91	18.25

OLCR : Optical low-coherence reflectometry, SPT: Scheimpflug-Placido Topographer, USP: Ultrasound pachymetry and SD-OCT: Spectral domain optical coherence tomography

*1-way ANOVA and the Tukey multiple comparisons test, P value, 0.05 was considered statistically significant.

Agreement between the instruments

Figures 1 and 2 show the Bland–Altman plots of CCT measurements in normal and keratoconic eyes respectively. Scheimpflug-Placido Topographer, OLCR, and SD-OCT measurements showed good agreement with ultrasound pachymetry data, with a relatively small mean difference of approximately 10 μm in normal eyes. Scheimpflug-Placido Topographer and SD-OCT measurements showed good agreement with ultrasound pachymetry data with mean differences of approximately 10 μm in keratoconic eyes; however, mean differences between OLCR and USP measurements were 15.93 μm, and the limits of agreement between

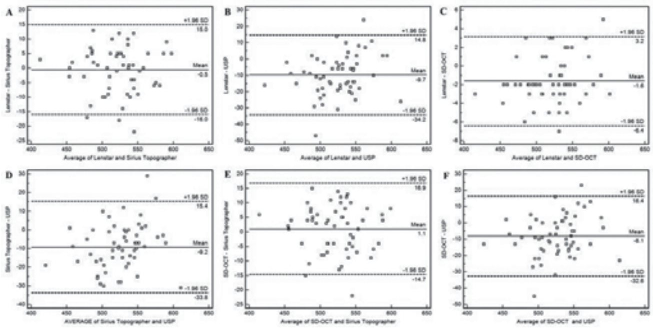

***Figure 1:** Bland Altman plots comparing CCT in normal eyes between LenStar (OLCR) and Sirius Topographer (Scheimpfl ug-Placido topographer) (A), LenStar and USP (B), LenStar and SDOCT (C), Sirius Topographer and USP (D), Sirius Topographer and SD-OCT (E), and SD-OCT and USP (F). The 95% limits of agreement are shown with dashed lines, and the solid line represents the difference between these measurements.*

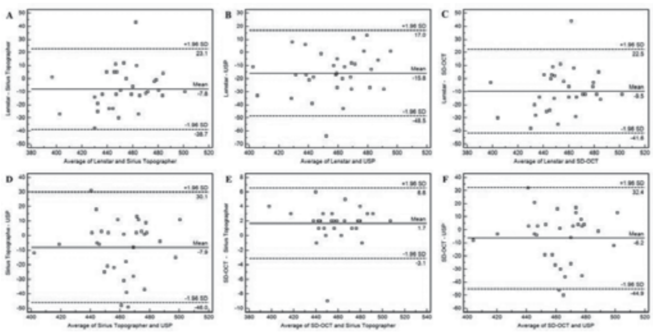

***Figure 2:** Bland Altman plots comparing CCT in keratoconic eyes between LenStar (OLCR) and Sirius Topographer (Scheimpfl ug-Placido topographer) (A), LenStar and USP (B), LenStar and SDOCT (C), Sirius Topographer and USP (D), Sirius Topographer and SD-OCT (E), and SD-OCT and USP (F). The 95% limits of agreement are shown with dashed lines, and the solid line represents the difference between these measurements.*

2 methods were -24.12 to −7.75 µm, thus with a range of 31.87 µm, which was widest among all comparisons.

Intraobserver repeatability of central corneal thickness measurements

Agreement of successive measurements performed during the same visit was excellent for all devices in normal eyes (ICC 0.98 for OLCR, 0.99 for Scheimpflug-Placido Topographer, 0.98 for SD-OCT, and 0.95 for USP) and in keratoconic eyes (ICC 0.97 for OLCR, 0.98 for Scheimpflug-Placido Topographer, 0.98 for SD-OCT, and 0.96 for USP).

DISCUSSION

The ability to obtain accurate CCT measurement is becoming increasingly important in clinical practice in screening for or diagnosing keratoconus and monitoring its progression.

Currently, several devices are available and these instruments rely on different assumptions and technical principles to measure these values. Although numerous studies have been performed to compare different pachymetry methods, to our knowledge, there has been no study comparing USP with OLCR, Scheimpflug-Placido Topographer, and SD-OCT, in patients with keratoconus. So, it is not clear whether the results of these systems match well and can be used interchangeably.

In addition to the new devices that are being introduced, the available imaging systems and their softwares are being improved and updated continuously. Each time a patient is examined with a new device, the common question "How does the new data compare to previous ones?" arises. Furthermore, new patients with previous imaging results with devices that are currently not available are common in daily practice. Therefore, studies of comparison of the data of different imaging systems become important.

In this study OLCR, Scheimpflug-Placido Topographer, and SD-OCT measurements showed good agreement with ultrasound pachymetry data, with a relatively small mean difference of approximately 10 µm in normal eyes. Scheimpflug-Placido Topographer and OLCR showed high correlation with USP, but underestimated CCT by about 8.13 µm and 8.93 respectively, compared with USP (p=0.003, p=0.01; respectively). Scheimpflug-Placido Topographer and SD-OCT measurements showed good agreement with ultrasound pachymetry data in keratoconic eyes; however OLCR measurements were thinner than those of USP by a mean of 15.93 µm, of SD-OCT by an average of 7.27 µm (p<0.001,p=0.007; respectively).

The differences between corneal thickness measurements with USP and SD-OCT are the likely result of different locations of respective reflective interfaces in the cornea. As compared with USP, OCT systems provide better measurement centration and perpendicularity, which could be due to the automatic detection of the anterior and posterior corneal boundaries by the OCT systems.[17] We found that CCT measured by SD-OCT was 6.49µm thinner than USP innormal eyes. This finding is in agreement with the previously published studies.[18, 19] As compared with normal corneas, keratoconus corneas have a prolate shape with steeper central curvature and relatively flatter peripheral curves. Also, the corneal refractive index might change due to corneal histopathological abnormalities in keratoconus. Therefore, it would be necessary to carefully assess the accuracy of the measurement results for keratoconic corneas. Rabinowitz et al.[20] have questioned the value of USP in keratoconus corneas because of the high false-negative and false-positive rates compared with other methods. Grewal et al.[2] studied corneal thickness measurements in normal and keratoconus eyes using Fourier-domain OCT. The authors reported a mean difference of 4.6 mm in CCT measurements between OCT and USP in keratoconus eyes that is slightly less than what we found in the present study (8.66 µm). Fukuda et al.[21] did not find any significant differences in CCT measurements with swept-source OCT, slit scanning topography and USP. The difference in our results and the results of the study by Fukuda et al. may be attributed to different models of OCT machines used in both studies.

To our knowledge, there are few studies comparing combined Scheimpflug-Placido disk system and USP. Results of the studies comparing Scheimpflug-Placido disk system with USP are contradictory. Huang et al.[22] have demonstrated that the CCT measurements obtained with Sirius topography showed good agreement with USP pachymetry and they have expressed that CCT measurements can be used interchangeably in normal and post-LASIK eyes. Bayhan et al.[15] and Simsek et al.[16] reported that Scheimpflug-Placido disk system significantly underestimated the corneal thickness compared with USP in normal eyes.

Ucakhan et al.[14] reported a comparison of CCT with Scheimpflug-Placido topographer, SM and USP measurements in normal and keratoconic corneas. According to their results, Scheimpflug-Placido topographer had better reproducibility than UP and SM in moderate keratoconic eyes. They found a very high correlation between the Scheimpflug-Placido topographer and USP measurements in mild and severe keratoconus. Cınar et al.[23] reported a comparison of CCT with Scheimpflug-Placido topographer, SM, OLCR, and USP measurements in keratoconic eyes. According to SM measurements, the central cornea is thicker in all keratoconic eyes, and it is thinner according to OLCR. They have exppressed that CCT measurements can not be used interrchangeably in keratoconic eyes.

Results of the studies comparing OLCR with USP are contradictory. Shammas et al.[24] reported that precision of the measurements obtained by OLCR was extremely high. The CCT measurements obtained by OLCR have been correlated with the results of USP but mild underestimation was found in terms of CCT measurements obtained by OLCR.[25] Tai [26] and Beutelspacher[27] reported that OLCR and USP provide comparable results. In another study, Cınar et al.[23] reported that US biometry and OLCR should not be used interchangeably for biometric measurements in keratoconus patients.

Overall, pairwise comparisons of all devices showed significantly good correlations in normal as well as in keratoconic eyes. We found that the CCT measurement by OLCR was comparable to that by Scheimpflug-Placido Topographer (with a mean difference of only 0.79 µm) in normal eyes. The Bland Altman plots show that the 95% LoA between them ranged from -16.0 µm to 15.0 µm, meaning that Scheimpflug-Placido Topographer measurements could be as much as –16.0 µm lower or 15.0 µm higher than the OLCR values. The CCT measurement by OLCR was also comparable to that by SD-OCT (with a mean difference of only -1.64 µm) in normal eyes. Bland Altman plots show that the 95% LoA between them ranged from -6.4 µm to 3.2 µm. In keratoconic eyes, we found that the CCT measurements by Scheimpflug-Placido Topographer was comparable to that by SD-OCT (with a mean difference of only 1.72 µm). Bland Altman plots show that the 95% LoA between them ranged from -3.1 µm to 6.6 µm.

Chen et al.[19] assessed the repeatability of measurements between Scheimpflug-Placido Topographer and OLCR biometer. They reported that both devices had excellent repeatability for all parameters assessed, including CCT. Their results indicated that they can be used interchangeably. Jorge et al.[28] reported that CCT measured by Scheimpflug-Placido Topographer and USP methods showed good agreement between repeated measurements obtained in the same subjects (repeatability) with either instrument. However, the CCT value obtained with either technology should not be used interchangeably. Bayhan et al.[15] assessed the repeatability of measurements between Scheimpflug-Placido Topographer, OLCR, SD-OCT (RTVue) and USP. They demonstrated that all devices had high and comparable repeatability in healthy population, though RTVue performed the best. In our study, all devices had excellent repeatability in normal and keratoconic eyes.

There may be several reasons to explain the discrepancy between OLCR and ultrasound pachymetric values in keratoconic eyes. Because OLCR uses the effect of time-domain interferometric or coherent superposition of light waves to measure ocular distances in the eye. The reflections of the different structures within the human eye such as the cornea, lens, and retina are interferometrically superimposed on the reflections of the reference arms. Another consideration includes the shape factor. As compared with normal corneas, keratoconus corneas have a prolate shape, with steeper central curvature and relatively flatter peripheral curves. These algorithms may not properly apply to the corneas with nonphysiological conditions, such as keratoconic eyes. Actually it is unclear whether ultrasound precisely shows the true corneal thickness, so it is important to note that we only evaluated the similarities and differences between the measurements, as the true CCT is not known.

In conclusion, Scheimpflug-Placido Topographer and SD-OCT measurements showed good agreement with ultrasound pachymetry in normal and keratoconic eyes. However, OLCR measurements were thinner than the other three devices in keratoconic eyes. Scheimpflug-Placido Topographer, USP, SD-OCT, and LenStar should not be used interchangeably in keratoconic eyes.

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