

ORİJİNAL ARAŞTIRMA ORIGINAL RESEARCH

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# Reliability of Optical Devices in Terms of Measurements of Corneal Parameters in Cross Linked Keratoconic Eyes: Cross-Sectional Study

## Çapraz Bağlama Yapılmış Keratokonik Gözlerde Optik Cihazların Kornea Parametrelerinin Ölçümleri Açısından Güvenilirliği: Kesitsel Çalışma

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**ABSTRACT Objective:** To determine the reliability and agreement of different optical devices in terms of keratometry and pachymetry measurements in cross-linked (CXL) keratoconic eyes. **Material and Methods:** Thirty-eight CXL-treated keratoconic eyes were evaluated. Three repeated measurements were performed with Topcon KR-1 autorefractokeratometry, Sirius topography, Nidek AL-scan optical biometry and RTVue anterior segment optical coherence tomography (AS-OCT). The devices were compared in terms of pachymetry and keratometric values. Limits of agreement (LoA) between the devices were detected using Bland-Altman analysis. Intra-examiner reliability was obtained using the intraclass correlation coefficient (ICC). **Results:** While the mean central corneal thickness (CCT) and minimum corneal thickness (MCT) measured in AS-OCT were  $456.37 \pm 41.52 \mu\text{m}$  and  $431.89 \pm 43.37 \mu\text{m}$ , respectively, these values were  $432.40 \pm 48.97 \mu\text{m}$  and  $415.67 \pm 47.69 \mu\text{m}$  in topography ( $p < 0.001$ ). The 95% LoA between the devices were  $-21.7$  to  $69.7 \mu\text{m}$  for CCT and  $-17.7$  to  $50.1 \mu\text{m}$  for MCT. Intra-examiner reliability was excellent for both devices in relation to the CCT and MCT measurements ( $\text{ICC} > 0.97$ ). When devices were compared in terms of the keratometric values and corneal astigmatism measurements, there was a significant difference among devices except between autorefractokeratometry and optical biometry ( $p < 0.05$ ; for all). The lowest LoA among the devices was found to be 3.3 D for steep keratometry and 2.9 D for flat keratometry and 2.3 D for corneal astigmatism. Intra-examiner reliability was excellent in all three devices in terms of the keratometric measurements ( $\text{ICC} > 0.99$ ). **Conclusion:** Pachymetry and keratometry can be performed independently in each device with excellent reliability in CXL-treated keratoconic eyes. However, we consider that measurements made with different devices cannot be used interchangeably in these eyes.

**ÖZET Amaç:** Çapraz bağlama yapılmış [cross-linked (CXL)] keratokonik gözlerde, farklı optik cihazların keratometri ve pakimetri ölçümleri açısından güvenilirliğini ve uyumluluğunu belirlemek. **Gereç ve Yöntemler:** CXL ile tedavi edilen keratokonuslu 38 göz değerlendirildi. Topcon KR-1 otorefraktokeratometri, Sirius topografi, Nidek AL-scan optik biyometri ve RTVue ön segment optik koherens tomografi (ÖS-OKT) ile üçer ardışık ölçüm yapıldı. Cihazlar pakimetri ve keratometrik değerler açısından karşılaştırıldı. Cihazlar arasındaki uyum sınırları [limits of agreement (LoA)], Bland-Altman analizi kullanılarak tespit edildi. Sınıf içi güvenilirlik, sınıf içi korelasyon katsayısı [intraclass correlation coefficient (ICC)] kullanılarak elde edildi. **Bulgular:** ÖS-OKT'de ölçülen ortalama santral kornea kalınlığı (SKK) ve minimum kornea kalınlığı (MKK) sırasıyla  $456,37 \pm 41,52 \mu\text{m}$  ve  $431,89 \pm 43,37 \mu\text{m}$  iken, topografide bu değerler  $432,40 \pm 48,97 \mu\text{m}$  ve  $415,67 \pm 47,69 \mu\text{m}$  idi ( $p < 0,001$ ). Cihazlar arasındaki %95 LoA, SKK için  $-21,7$  ile  $69,7 \mu\text{m}$  ve MKK için  $-17,7$  ile  $50,1 \mu\text{m}$  idi. Sınıf içi güvenilirlik, SKK ve MKK ölçümleri açısından her iki cihaz için de mükemmeldi ( $\text{ICC} > 0,97$ ). Cihazlar, keratometrik değerler ve korneal astigmatizma ölçümleri açısından karşılaştırıldığında, otorefraktokeratometri ve optik biyometri dışında cihazlar arasında anlamlı fark vardı (tümü için;  $p < 0,05$ ). Cihazlar arasında en düşük LoA, dik keratometri için 3,3 D ve düz keratometri için 2,9 D ve kornea astigmatizma için 2,3 D olarak bulundu. Her üç cihazda da keratometrik ölçümler açısından sınıf içi güvenilirlik mükemmeldi ( $\text{ICC} > 0,99$ ). **Sonuç:** Pakimetri ve keratometri, CXL ile tedavi edilen keratokonik gözlerde mükemmel güvenilirlikle her cihazda bağımsız olarak gerçekleştirilebilir. Ancak farklı cihazlarla yapılan ölçümlerin, bu gözlerde birbirinin yerine kullanılamayacağını düşünmekteyiz.

**Keywords:** Crosslinking; keratoconus; pachymetry; keratometry; reliability

**Anahtar Kelimeler:** Çapraz bağlama; keratokonus; pakimetri; keratometri; güvenilirlik

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Keratoconus (KC) is a corneal ectasia in which progressive corneal straightening and thinning occurs.<sup>1</sup> Corneal crosslinking (CXL) is the only effective therapeutic approach currently available to stop or slow this steepening and thinning.<sup>2</sup> However, different studies have shown that the disease progresses in 1.5-23% of patients despite CXL treatment.<sup>3,4</sup> Both pachymetry and keratometry are widely used to evaluate the effectiveness of CXL in documenting disease progression or stabilization.<sup>5</sup> Therefore, it is important to examine these parameters reliably and accurately in CXL-treated corneas. There is also a close relationship between changes in keratometry and visual quality. In addition, even if disease progression is stopped with CXL, most patients will need contact lenses for good vision rehabilitation. In order to select the contact lens to be tried in a KC patient and to monitor the effects of this lens on the anterior segment structures, anterior segment parameters should be reliably monitored in CXL-treated corneas.<sup>6,7</sup>

With the advancing technologies in the last few decades, the cornea can be imaged with many different methods based on different studying principles.<sup>8,9</sup> Therefore, it is important to determine the optimal method for the measurement of corneal parameters, such as keratometry and central corneal thickness (CCT) to obtain more reliable values to be also used in the follow-up and grading of the disease.<sup>10</sup> Although the most commonly used method to measure the CCT is ultrasonic pachymetry, it has major disadvantages, such as being dependent on the user, the lack of light providing fixation, the probe positioned obliquely to the cornea, corneal compression, and measurement deviations due to dryness during the measurement, and it is also an invasive procedure that requires topical anesthesia.<sup>11,12</sup> Therefore, many sophisticated devices, especially optical coherence tomography and Scheimpflug measurement methods have been developed and used in clinical practice to evaluate anterior segment parameters non-invasively.<sup>13</sup> Various studies have been conducted to evaluate the reliability of corneal parameters in normal eyes and those with KC.<sup>11,13,14</sup> However, to our knowledge, the reliability and agreement of anterior segment parameter measurements

performed with different imaging technologies in the CXL-treated keratoconic eyes have not previously been compared.

Although corneal haze decreases over time after CXL, it cannot return to the preoperative level.<sup>15</sup> This changes not only the appearance of the cornea but also light distribution and the focal refractive index.<sup>16,17</sup> It has been suggested that this could potentially prevent the reliable scanning of the cornea by changing the reflection of light waves from the cornea.<sup>18</sup> The aim of this cross-sectional study was to evaluate the agreement and intra-examiner reliability of cornea imaging systems based on various optical principles in relation to keratometry and pachymetry measurements in CXL-applied keratoconic eyes.

## MATERIAL AND METHODS

### SUBJECTS

Patients who underwent CXL due to progressive KC within the last 2 years without intraoperative or postoperative complications were included in this study. In the literature, changes in corneal parameters occur in the past 6 months have been evaluated in order to detect the progression in KC patients who underwent CXL.<sup>3</sup> Patients who underwent CXL in the last 6 months were not included in the study, as the progression after CXL may be difficult to determine before 6 months, and therefore measurements after 6 months are more important in terms of progression. The eyes were stratified according to the Amsler-Krumeich classification for the severity of KC.<sup>19</sup> Since KC is an asymmetric disorder, if CXL was applied to both eyes of the patient, they were both included in the study. The study was conducted according to the principles of the Declaration of Helsinki, after obtaining approval from the Kafkas University Faculty of Medicine Ethics Committee (Approval number: 80576354-050-99/266) and informed consent from all patients. Patients with any corneal disease other than KC, severe corneal scarring or a history of hydrops, those who had undergone corneal surgery other than CXL, those who had required a second CXL, those who had used contact lens or had a history of

intraocular surgery and dry eye were excluded from the study.

## STUDY PROTOCOL

During the routine follow-up of the patients, an ophthalmologist measured distant visual acuities corrected by subjective refraction and performed a routine biomicroscopic examination. Within the scope of the study, corneal data were obtained with the Topcon KR-1 (Topcon Corporation, Tokyo, Japan) autorefractokeratometer, Sirius topography (Costruzione Strumenti Ophthalmic, Florence, Italy) and Nidek AL-scan optical biometry (AL-Scan, NIDEK CO, Aichi, Japan), and RTVue (Optovue Inc., Fremont, California, USA) anterior segment optical coherence tomography (AS-OCT). The patients were asked to make a full blink immediately before each measurement to allow the tear film to be evenly distributed. They were told to lean back after each measurement. Five minutes were waited between the measurements of different devices. All the measurements were made at the same period of the day (between 10 a.m.-3 p.m.) during the same visit, at least 2 hours after waking to minimize any daily variation.<sup>20</sup> The measurements were made while bringing the devices into focus, and the patient's eye was aligned along the visual axis with a central fixation light. Three consecutive measurements were obtained for each device in a dim room. All the measurements were obtained by the same examiner (S.N.) experienced in the use of all 4 devices.

The agreement of average keratometric values obtained from autorefractokeratometry, topography and optical biometry were compared. The agreement between topography and AS-OCT to measure CCT and the minimum corneal thickness (MCT) were also compared. In our study, CCT data in optical biometry were not used because it cannot provide CCT measurements in many patients, especially those with advanced KC. The average of the three measurements was used to compare the pachymetry and keratometry parameters between the devices.

## DEVICES

AS-OCT images were acquired using RTVue OCT based on spectral domain OCT system with a

cornea adapter module. The system operates at 830 nm wavelength and has an axial scan rate of 26,000 per second. The depth resolution of the device is 5 µm in tissue. Anterior segment images were taken using the corneal module and wide-angle (long lens) adapter lens. CCT and MCT were recorded from the pachymetric map obtained from these images.

The Sirius anterior segment analysis system is a topography device that includes a 360-degree rotating Scheimpflug camera and a 22-ring Placido disc to view the cornea and other anterior segment structures. It can obtain 25 radial sections of the anterior chamber structures in less than a second. 475 nanometer ultraviolet-free light is used to measure 35,632 points for the anterior corneal surface and 30,000 points for the posterior cornea. Then, a pachymetric map is reconstructed using these points on the anterior and posterior corneal surface. The device is capable to measure the keratometry values of the central corneal area with a diameter of 3.0 mm.

Nidek AL-Scan is an optical biometry device that measures axial length and anterior segment parameters using the principle of partial coherence interferometry. The device detects a ring image projected onto the patient's cornea with a photodetector and measures the radius of steepest and flattest corneal curvature over 2.4 and 3.3 mm. The device has a 3D automatic eye tracking system that prevents measurement deviation caused by eye misalignment. In our study, keratometry values taken over the central 3.3 mm of the cornea were used.

With the autorefractokeratometer, the patient's automatic refraction error can be obtained quickly, as well as keratometric values. The Topcon KR-1 automatic keratometer can analyze the corneal shape and curvature in depth. The device can accurately determine refraction and keratometry simultaneously using the Rotary prism measuring system and Placido rings. For keratometry, infrared-illuminated target mires and an infrared photodetector are used to measure image size and calculate the radius of curvature. The device measures the radius of curvature at steep and flat meridians over an area of 3.0 mm diameter of the central cornea.

## STATISTICAL ANALYSIS

The data were analyzed using the Statistical Package for the Social Sciences (SPSS, IBM, USA) v. 24. Uncertainty for the reliability of the results for 3 consecutive measurements in our sample size was calculated using the model defined in the literature.<sup>21</sup> The sample size in the present study offered uncertainty (level of confidence) within 15%. Normality of data distribution was evaluated. Descriptive statistics are presented as mean±standard deviation (SD) and 95% confidence interval of the mean. Measurements made by various devices were evaluated using the repeated measures analysis of variance (ANOVA). Paired evaluations were performed with the Bonferroni adjustment for multiple comparisons. The relationship between the measurements made using different methods was evaluated with Pearson's correlation coefficients. The Bland-Altman plots were used to evaluate the agreement between the different measurement methods. Using these plots, the 95% limits of agreement (LoA) were defined as the mean±1.96 SD of the difference between the results given by 2 measurement techniques. Reliability, which expresses the degree of consistency between repeated measures, was evaluated using the intraclass correlation coefficient (ICC).<sup>22</sup> The ICC ranges from 0 to 1, where values 0.50 and less mean poor reliability, values between 0.50 and 0.75 mean

moderate reliability, values between 0.75 and 0.90 mean good reliability, and values 0.90 and more mean excellent reliability.<sup>23</sup> A p value less than 0.05 was considered statistically significant.

## RESULTS

Thirty-eight eyes of 29 (15 females, 14 males) patients who underwent CXL due to KC were included in the study. KC was at Stage-1 in 24 eyes, Stage-2 in 7 eyes, Stage-3 in 6 eyes, and Stage-4 in 1 eye. The mean age of the patients was 21.17±4.03 years. Mean central and minimum corneal thickness, steep and flat keratometry and corneal astigmatism values and 95% confidence intervals are summarized in Table 1. The variations between devices in terms of these investigated values are presented in Table 2. While the mean CCT and MCT measured in AS-OCT were 456.37±41.52 and 431.89±43.37 µm, respectively, these values were 432.40±48.97 and 415.67±47.69 µm in topography. AS-OCT measured CCT as approximately 23.97 µm thicker than topography, and MCT as 16.21 µm thicker than topography (p<0.001). However, there was a closely correlation between the devices in terms of CCT and MCT (r=0.880, p<0.001 and r=0.932, p<0.001, respectively).

The Bland-Altman analysis was performed for the differences between AS-OCT and topography.

**TABLE 1:** Descriptive statistics for the corneal thickness and keratometric values.

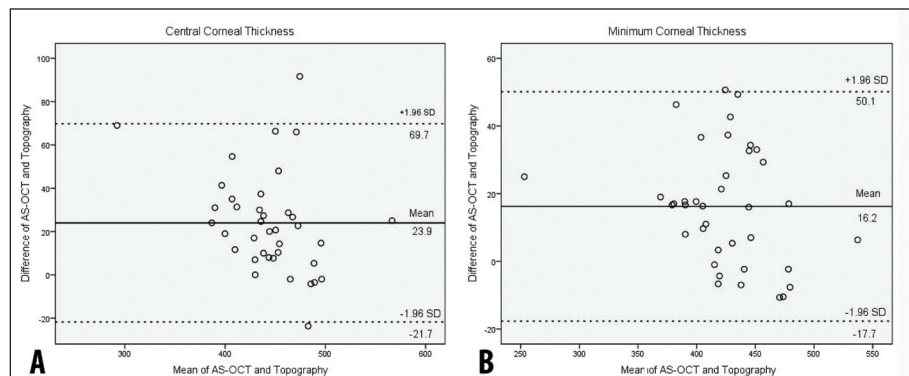
Devices	Measurements	Mean±SD	95% CI
AS-OCT	CCT (µm)	456.37±41.52	442.72-470.02
	MCT (µm)	431.89±43.37	417.63-446.14
Topography	CCT (µm)	432.40±48.97	416.30-448.50
	MCT (µm)	415.67±47.69	399.99-431.35
	Steep keratometry (D)	47.88±3.05	46.88-48.89
	Flat keratometry (D)	44.85±2.32	44.09-45.62
	Corneal astigmatism (D)	3.03±1.63	2.49-3.56
Optical biometry	Steep keratometry (D)	48.86±3.54	47.70-50.03
	Flat keratometry (D)	45.42±2.59	44.57-46.27
	Corneal astigmatism (D)	3.44±1.80	2.84-4.03
Autorefractokeratometry	Steep keratometry (D)	49.03±4.02	47.70-50.35
	Flat keratometry (D)	45.45±2.95	44.48-46.42
	Corneal astigmatism (D)	3.57±1.99	2.91-4.22

SD: Standard deviation; CI: Confidence interval; AS-OCT: Anterior segment optical coherence tomography; CCT: Central corneal thickness; MCT: Minimum corneal thickness; D: Diopter.

**TABLE 2:** Inter-device comparisons in terms of corneal thickness, and keratometric values.

Measurements	Comparisons	Mean difference		95% CI of mean difference		Pearson correlation	
		Mean±SD	p value	Lower-Upper	r value	p value	
CCT (µm)	AS-OCT-topography	23.97±23.35	<0.001	16.29-31.65	0.880	<0.001	
MCT (µm)	AS-OCT-topography	16.21±17.31	<0.001	10.52-21.90	0.932	<0.001	
Steep keratometry (D)	Autorefractokeratometry-optical biometry	0.16±0.96	0.908	-0.23-0.55	0.975	<0.001	
	Autorefractokeratometry-topography	1.14±1.49	<0.001	0.53-1.75	0.947	<0.001	
	Optical biometry-topography	0.97±0.85	<0.001	0.62-1.32	0.977	<0.001	
Flat keratometry (D)	Autorefractokeratometry-optical biometry	0.03±0.74	1.0	-0.26-0.33	0.973	<0.001	
	Autorefractokeratometry-topography	0.60±1.02	0.003	0.18-1.01	0.952	<0.001	
	Optical biometry-topography	0.56±0.77	<0.001	0.25-0.88	0.956	<0.001	
Corneal astigmatism (D)	Autorefractokeratometry-optical biometry	0.13±0.59	0.547	-0.11-0.37	0.956	<0.001	
	Autorefractokeratometry-topography	0.54±0.92	0.003	0.16-0.91	0.887	<0.001	
	Optical biometry-topography	0.41±0.61	0.001	0.16-0.66	0.941	<0.001	

SD: Standard deviation; CI: Confidence interval; CCT: Central corneal thickness; MCT: Minimum corneal thickness; AS-OCT: Anterior segment optical coherence tomography.



**FIGURE 1:** Bland-Altman plots of inter-device differences and 95% limits of agreement for central (A) and minimum (B) corneal thickness. SD: Standard deviation; AS-OCT: Anterior segment optical coherence tomography.

Figure 1 shows Bland-Altman plots of inter-device differences and 95% LoA for CCT and MCT.

The 95% LoA between AS-OCT and topography were -21.7 to 69.7 µm for CCT and -17.7 to 50.1 µm for MCT. Reliability analysis for each parameter is presented in Table 3. Concerning reliability, there was an excellent agreement between the consecutive measurements in terms of CCT and MCT performed by the same practitioner using both devices during the same visit, with ICC ranging from 0.979 to 0.996.

When devices were compared in terms of the keratometric values and corneal astigmatism measurements, there was a significant difference among devices except between autorefractokeratometry and optical biometry ( $p < 0.05$ ; for all). There was no sta-

tistically significant difference between autorefractokeratometry and optical biometry devices in terms of measured steep and flat keratometry and corneal astigmatism values ( $p > 0.05$ ; for all). Keratometric values and corneal astigmatism were measured to be the lowest by topography device and highest by autorefractokeratometer. The keratometric values and corneal astigmatism in all three devices were closely correlated, and Pearson's correlation coefficients varied between 0.887 and 0.977 ( $p < 0.001$ ; for all).

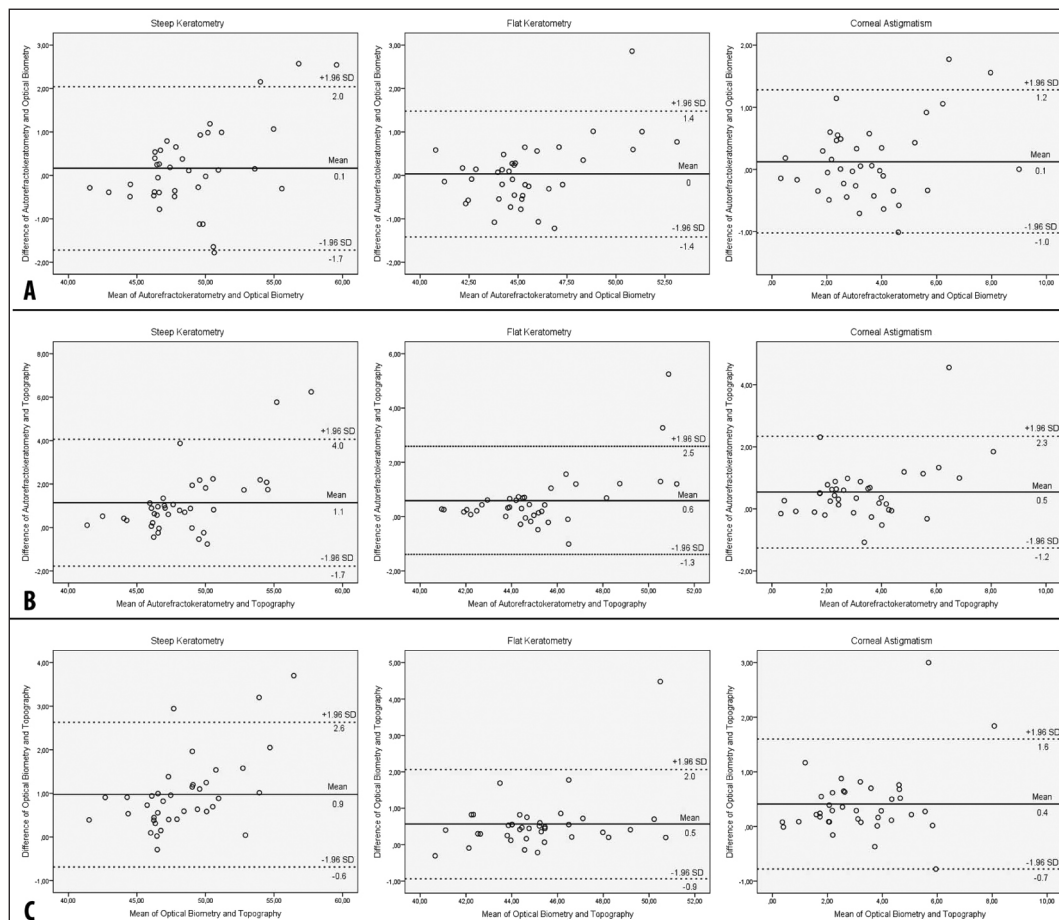
Figure 2 shows Bland-Altman plots of inter-device differences and 95% LoA for steep and flat keratometric values and corneal astigmatism. When the lowest LoA among the devices was investigated, it was found to be 3.3 D for steep keratometry and 2.9



**TABLE 3:** Intra-examiner reliability of each method for corneal thickness, and keratometric values.

Devices	Measurement	ICC	95% CI Lower-Upper	p value
AS-OCT	CCT ( $\mu\text{m}$ )	0.985	0.974-0.992	<0.001
	MCT ( $\mu\text{m}$ )	0.996	0.994-0.998	<0.001
Topography	CCT ( $\mu\text{m}$ )	0.995	0.992-0.997	<0.001
	MCT ( $\mu\text{m}$ )	0.979	0.965-0.989	<0.001
	Steep keratometry (D)	0.998	0.996-0.999	<0.001
	Flat keratometry (D)	0.997	0.994-0.998	<0.001
	Corneal astigmatism (D)	0.998	0.996-0.999	<0.001
Optical biometry	Steep keratometry (D)	0.999	0.999-1.0	<0.001
	Flat keratometry (D)	0.999	0.999-1.0	<0.001
	Corneal astigmatism (D)	0.998	0.997-0.999	<0.001
Autorefractokeratometry	Steep keratometry (D)	0.997	0.995-0.998	<0.001
	Flat keratometry (D)	0.997	0.995-0.998	<0.001
	Corneal astigmatism (D)	0.994	0.989-0.997	<0.001

SD: Standard deviation; CI: Confidence interval; AS-OCT: Anterior segment optical coherence tomography; CCT: Central corneal thickness; MCT: Minimum corneal thickness; D: Diopter.

**FIGURE 2:** Bland-Altman plots comparing average keratometry between autorefractokeratometry and topography (A), autorefractokeratometry and optical biometry (B), topography and optical biometry (C). SD: Standard deviation.

D for flat keratometry and 2.3 D for corneal astigmatism.

When the devices were evaluated in terms of reliability, it was found that the consecutive keratometric values or corneal astigmatism measurements showed a perfect agreement using each device (ICC: 0.994-0.999).

## DISCUSSION

Since progression may occur in KC after CXL treatment or additional treatments may be needed, it is extremely important to reliably evaluate corneal parameters.<sup>3</sup> Therefore, in this study, we investigated the reliability of corneal parameters, such as the keratometry and pachymetry measurements of different devices in patients with KC who underwent CXL treatment. In this respect, consistency between consecutive measurements is one of the main parameters in evaluating the reliability of the use of devices in diagnosis, treatment and follow-up processes.<sup>11,13</sup> We determined that both AS-OCT and topography had high reliability in terms of the CCT and MCT measurements in the same KC population treated with CXL. Although there are no data in the literature on the reliability of these methods in patients that have undergone CXL, they have been reported to measure CCT with high reliability in healthy individuals.<sup>11,24</sup>

Although there was a correlation between the devices in terms of pachymetry measurements, AS-OCT measured CCT as approximately 23.97  $\mu\text{m}$  thicker than topography, and MCT as 16.21  $\mu\text{m}$  thicker than topography. The Bland Altman analysis also revealed that LoA were 91.5  $\mu\text{m}$  for CCT and 67.8  $\mu\text{m}$  for MCT. Antonios et al. found that postoperative AS-OCT measured CCT thicker than the topography in individuals who had undergone CXL, which is in agreement with our study.<sup>18</sup> Bayhan et al. reported that in terms of the CCT of healthy individuals, comparable results were obtained from the topography and AS-OCT devices used in our study.<sup>11</sup> In contrast, in our study, the mean difference between the devices and LoA in CXL-treated corneas were clinically significant for a sensitive patient group, such as KC. Therefore, we consider that these two methods cannot be used interchangeably in the meas-

urement of CCT or MCT. It has previously been suggested that different devices can measure pachymetry differently because they use different technological imaging principles.<sup>24</sup> It has also been considered that the tear film layer may be effective in the pachymetry differences between Scheimpflug imaging and AS-OCT techniques.<sup>25</sup> These mechanisms can also explain the results of our study.

Patients with KC who have undergone CXL may potentially need intracorneal ring segment implantation or photorefractive keratectomy.<sup>26,27</sup> In addition to pachymetry, it is necessary to obtain an accurate keratometric measurement for accurate planning and follow-up. Studies have been conducted to investigate the reliability of keratometry measurements in healthy individuals, eyes with cataracts, and patients with KC.<sup>28-30</sup> However, the disadvantage of these studies is that CXL-treated eyes were not presented. It has been reported that the keratometry values measured by topography (Sirius) and optical biometry (Nidek) in patients with cataracts and in the healthy population are compatible, and therefore these two devices could be used interchangeably.<sup>28,29</sup>

In our study, there was a significant difference among devices except between autorefractokeratometry and optical biometry in terms of keratometric values and corneal astigmatism measurements ( $p < 0.05$ ; for all). Although there was no statistically significant difference between autorefractokeratometry and optical biometry devices in terms of measured steep and flat keratometry and corneal astigmatism values their LoA values had a very wide range (2.3-3.76 D). Therefore, we think that the devices used in our study cannot be used interchangeably in terms of keratometric values. These variable results between devices may be due to the measurement deviations caused by the changes in corneal optical quality and the distribution of reflected light waves, depending on the residual haze remaining after CXL or the differences in the response to this treatment. In addition, posterior astigmatism and asymmetrical cone placement may have caused variation in the keratometry measurements of different devices. In addition, as Hashemi et al. suggested, the low number of analyzed points due to irregular cornea may have led to variation between the devices.<sup>10</sup> It has been reported in the

literature that 95% LoA is a better indicator when evaluating agreement between devices.<sup>31</sup> In our study when the lowest LoA among the devices was investigated, it was found to be 3.3 D for steep keratometry and 2.9 D for flat keratometry and 2.3 D for corneal astigmatism. For keratometric values, LoA between devices being lower than 0.50 D is considered to indicate a perfect agreement. It has been reported that a LoA value of 1 D or higher is clinically significant.<sup>30,32</sup> Therefore, the devices evaluated in our study cannot be used interchangeably in CXL-treated eyes.

In the literature, it has been found that optical biometry and topography devices used in our study can measure anterior segment parameters with high repeatability in patients with KC and in healthy individuals.<sup>11,33</sup> We found that these two devices and the autorefractokeratometer had high reliability in CXL-treated eyes. Consistent with our results, Hashemi et al previously stated that CXL did not affect the reliability of the measurement of corneal parameters using the Pentacam HR (OCULUS Optikgeräte GmbH, Wetzlar, Germany) topography device.<sup>34</sup> It has been reported that the stage of KC may affect the reliability of the measurements.<sup>35</sup> However, since both our study and Hashemi et al. study did not compare patients at different stages with each other, there is a need for studies examining patients with KC at different stages who underwent CXL. In addition, we believe that studies investigating inter-examiner reliability of optical devices, which is an important parameter in the reliability of optical devices in KC patients who have undergone CXL, and which were not evaluated in our study, will make significant contributions to the literature.

Although our study is the first to determine the reliability of important corneal parameters, such as keratometric values, CCT and MCT with different devices in the CXL-treated KC population, it has certain limitations. The first limitation concerns the cross-sectional design. Second, since only non-contact optical devices were evaluated in our study, ultrasound was not evaluated due to its invasive nature. In addition to CCT, it is also important to monitor MCT in the follow-up of ectasia. However, it may not be practical and reliable to determine

MCT using ultrasound. Third, our study needs to be supported by studies evaluating KC patients who underwent CXL as well as KC patients who were not treated with CXL and healthy individuals in order to more clearly reveal the relationship between the agreement of measurements and CXL. Fourth, larger series studies are needed to lower the uncertainty for the reliability in the results.

## CONCLUSION

Pachymetry and keratometry can be measured with non-contact optical devices with excellent reliability in CXL-treated eyes. Therefore, we consider that when used independently, each optical device reliably measures pachymetry or keratometry after CXL. With regard to the agreement between the devices, AS-OCT provided thicker measurements for CCT and MCT than topography in these patients. Due to the low level of agreement between the keratometry values measured by autorefractokeratometry, topography and optical biometry, we think the measurements performed with these devices cannot be interchangeably used in CXL-treated keratoconic eyes.

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## Conflict of Interest

*No conflicts of interest between the authors and / or family members of the scientific and medical committee members or members of the potential conflicts of interest, counseling, expertise, working conditions, share holding and similar situations in any firm.*

## Authorship Contributions

**Idea/Concept:** Ersin Muhafiz, Erdinç Bozkurt; **Design:** Ersin Muhafiz, Şerif Nizamoğulları; **Control/Supervision:** Ersin Muhafiz, Erdinç Bozkurt, Şerif Nizamoğulları; **Data Collection and/or Processing:** Ersin Muhafiz, Erdinç Bozkurt, Şerif Nizamoğulları; **Analysis and/or Interpretation:** Ersin Muhafiz, Erdinç Bozkurt, Şerif Nizamoğulları; **Literature Review:** Ersin Muhafiz, Erdinç Bozkurt; **Writing the Article:** Ersin Muhafiz, Erdinç Bozkurt, Şerif Nizamoğulları; **Critical Review:** Ersin Muhafiz, Erdinç Bozkurt, Şerif Nizamoğulları.



## REFERENCES

- Rabinowitz YS. Keratoconus. *Surv Ophthalmol*. 1998;42(4):297-319. [[Crossref](#)] [[PubMed](#)]
- Wollensak G, Spoerl E, Seiler T. Riboflavin/ultraviolet-a-induced collagen crosslinking for the treatment of keratoconus. *Am J Ophthalmol*. 2003;135(5):620-7. [[Crossref](#)] [[PubMed](#)]
- Akkaya Turhan S, Aydın FO, Tokar E. Clinical results of repeated corneal collagen cross-linking in progressive keratoconus. *Cornea*. 2020;39(1):84-7. [[Crossref](#)] [[PubMed](#)]
- Soeters N, Wisse RP, Godefröij DA, Imhof SM, Tahzib NG. Transepithelial versus epithelium-off corneal cross-linking for the treatment of progressive keratoconus: a randomized controlled trial. *Am J Ophthalmol*. 2015;159(5): 821-8.e3. [[Crossref](#)] [[PubMed](#)]
- Shetty R, Pahuja NK, Nuijts RM, Ajani A, Jayadev C, Sharma C, et al. Current protocols of corneal collagen cross-linking: visual, refractive, and tomographic outcomes. *Am J Ophthalmol*. 2015;160(2):243-9. [[Crossref](#)] [[PubMed](#)]
- Mandathara PS, Kalaiselvan P, Rathil VM, Murthy SI, Taneja M, Sangwan VS. Contact lens fitting after corneal collagen cross-linking. *Oman J Ophthalmol*. 2019;12(3):177-80. [[Crossref](#)] [[PubMed](#)] [[PMC](#)]
- Berjandy F, Nabovati P, Hashemi H, Yekta A, Ostadimoghaddam H, Sardari S, et al. Predicting initial base curve of the rigid contact lenses according to Javal keratometry findings in patients with keratoconus. *Cont Lens Anterior Eye*. 2021;44(3):101340. [[Crossref](#)] [[PubMed](#)]
- Çelebi ARC, Mirza GE. Comparison of spectral domain optical coherence tomography and ultrasonic pachymetry for assessment of central corneal thickness. *Türk J Ophthalmol*. 2014;44(4):259-62. [[Link](#)]
- Büyük K, Bozkurt B, Kaniş Ü, Özkağın A, Okudan S. Comparison of central corneal thickness measurements in normal and keratoconic eyes using ultrasonic pachymetry and OCULUS Pentacam [Normal ve keratoconuslu gözlerde ultrasonik paki metri ve OCULUS Pentacam ile ölçülen santral kornea kalınlıklarının karşılaştırılması]. *Türk J Ophthalmol*. 2011;41(2):104-7. [[Crossref](#)]
- Hashemi H, Yekta A, Khabazkhoob M. Effect of keratoconus grades on repeatability of keratometry readings: Comparison of 5 devices. *J Cataract Refract Surg*. 2015;41(5):1065-72. [[Crossref](#)] [[PubMed](#)]
- Bayhan HA, Aslan Bayhan S, Can I. Comparison of central corneal thickness measurements with three new optical devices and a standard ultrasonic pachymeter. *Int J Ophthalmol*. 2014;7(2):302-8. [[PubMed](#)] [[PMC](#)]
- Nemeth G, Tsorbatzoglou A, Kertesz K, Vajas A, Berta A, Módos L Jr. Comparison of central corneal thickness measurements with a new optical device and a standard ultrasonic pachymeter. *J Cataract Refract Surg*. 2006; 32(3):460-3. [[Crossref](#)] [[PubMed](#)]
- Viswanathan D, Kumar NL, Males JJ, Graham SL. Comparative analysis of corneal measurements obtained from a Scheimpflug camera and an integrated Placido-optical coherence tomography device in normal and keratoconic eyes. *Acta Ophthalmol*. 2015;93(6): e488-94. [[Crossref](#)] [[PubMed](#)]
- Tiryaki Demir S, Odaş M, Oba ME, Burcu Dirim A, Can E, Kara O. Ultrasonik pakimetre ve Orbscan II korneal topografi santral kornea kalınlık ölçümlerinin karşılaştırılması ve ultrasonik pakimetrenin tekrarlanabilirliğinin değerlendirilmesi [Comparison of central corneal thickness measurements by ultrasonic pachymetry and Orbscan II corneal topography and evaluation of ultrasonic pachymetry repeatability]. *Türk J Ophthalmol*. 2014;44(4):263-7. [[Crossref](#)]
- Greenstein SA, Fry KL, Bhatt J, Hersh PS. Natural history of corneal haze after collagen crosslinking for keratoconus and corneal ectasia: Scheimpflug and biomicroscopic analysis. *J Cataract Refract Surg*. 2010;36(12): 2105-14. [[Crossref](#)] [[PubMed](#)]
- Pahuja N, Shetty R, Subbiah P, Nagaraja H, Nuijts RM, Jayadev C. Corneal densitometry: Repeatability in eyes with keratoconus and post-collagen cross-linking. *Cornea*. 2016; 35(6):833-7. [[Crossref](#)] [[PubMed](#)]
- Rocha KM, Perez-Straizota CE, Stulting RD, Randleman JB. Epithelial and stromal remodeling after corneal collagen cross-linking evaluated by spectral-domain OCT. *J Refract Surg*. 2014;30(2):122-7. Erratum in: *J Refract Surg*. 2014;30(3):171. Rocha, Karoline Maia [corrected to Rocha, Karoline Maia]. [[Crossref](#)] [[PubMed](#)]
- Antonios R, Fattah MA, Maalouf F, Abiad B, Awwad ST. Central corneal thickness after cross-linking using high-definition optical coherence tomography, ultrasound, and dual Scheimpflug tomography: A comparative study over one year. *Am J Ophthalmol*. 2016; 167:38-47. [[Crossref](#)] [[PubMed](#)]
- Krumeich JH, Daniel J, Knülle A. Live-epikeratophakia for keratoconus. *J Cataract Refract Surg*. 1998;24(4):456-63. [[Crossref](#)] [[PubMed](#)]
- Read SA, Collins MJ. Diurnal variation of corneal shape and thickness. *Optom Vis Sci*. 2009;86(3): 170-80. [[Crossref](#)] [[PubMed](#)]
- McAlinden C, Khadka J, Pesudovs K. Precision (repeatability and reproducibility) studies and sample-size calculation. *J Cataract Refract Surg*. 2015; 41(12):2598-604. [[Crossref](#)] [[PubMed](#)]
- Ateş C, Öztuna D, Genç Y. Sağlık araştırmalarında sınıf içi korelasyon kat sayısının kullanımı [The use of intraclass correlation coefficient (ICC) in medical research: Review]. *Türkiye Klinikleri J Biostat*. 2009;1(2):59-64. [[Link](#)]
- McGraw KO, Wong SP. Forming inferences about some intraclass correlation coefficients. *Psychol Meth*. 1996;1(1):30-46. [[Crossref](#)]
- Doğan M, Ertan E. Comparison of central corneal thickness measurements with standard ultrasonic pachymetry and optical devices. *Clin Exp Optom*. 2019;102(2):126-30. [[Crossref](#)] [[PubMed](#)]
- Milla M, Pi-ero DP, Amparo F, Alió JL. Pachymetric measurements with a new Scheimpflug photography-based system: intraobserver repeatability and agreement with optical coherence tomography pachymetry. *J Cataract Refract Surg*. 2011;37(2): 310-6. [[Crossref](#)] [[PubMed](#)]
- Shaheen MS, Shalaby Bardan A, Pi-ero DP, Ezzeldin H, El-Kateb M, Helaly H, et al. Wave front-guided photorefractive keratectomy using a high-resolution aberrometer after corneal collagen cross-linking in keratoconus. *Cornea*. 2016;35(7): 946-53. [[Crossref](#)] [[PubMed](#)]
- Pi-ero DP, Alió JL. Intracorneal ring segments in ectatic corneal disease - a review. *Clin Exp Ophthalmol*. 2010;38(2):154-67. [[Crossref](#)] [[PubMed](#)]
- Duman R, Çetinkaya E, Duman R, Dogan M, Sabaner MC. Comparison of anterior segment measurements using Sirius Topographer® and Nidek Axial Length-Scan® with assessing repeatability in patients with cataracts. *Indian J Ophthalmol*. 2018; 66(3):402-6. [[Crossref](#)] [[PubMed](#)] [[PMC](#)]
- Çağlar Ç, Kocamış Sİ, Demir E, Durmuş M. Comparison of the measurements of a novel optical biometry: Nidek AL-Scan with Sirius and a ultrasound biometry. *Int Ophthalmol*. 2017;37(3):491-8. [[Crossref](#)] [[PubMed](#)]
- Altinel MG, Uslu H. Agreement of keratometric readings measured using rotating Scheimpflug imaging, auto-refractometer, and biograph in eyes with keratoconus. *Int Ophthalmol*. 2021;41(5):1659-69. [[Crossref](#)] [[PubMed](#)]
- Bland JM, Altman DG. Statistical methods for assessing agreement between two methods of clinical measurement. *Lancet*. 1986;1(8476):307-10. [[Crossref](#)] [[PubMed](#)]

32. Hua Y, Xu Z, Qiu W, Wu Q. Precision (repeatability and reproducibility) and agreement of corneal power measurements obtained by topcon KR-1W and iTrace. PLoS One. 2016;11(1):e0147086. [[Crossref](#)] [[PubMed](#)] [[PMC](#)]
33. Yağcı R, Güler E, Kulak AE, Erdoğan BD, Balcı M, Hepşen İF. Repeatability and reproducibility of a new optical biometer in normal and keratoconic eyes. J Cataract Refract Surg. 2015;41(1):171-7. [[Crossref](#)] [[PubMed](#)]
34. Hashemi H, Mehravaran S, Asgari S. The effect of corneal cross-linking on the anterior and posterior parameters of the cornea: A prospective repeatability study. Rom J Ophthalmol. 2019;63(1):68-74. [[Crossref](#)] [[PubMed](#)] [[PMC](#)]
35. Tunç U, Akbaş YB, Yıldırım Y, Kepez Yıldız B, Kırız A, Demirok A. Repeatability and reliability of measurements obtained by the combined Scheimpflug and Placido-disk tomography in different stages of keratoconus. Eye (Lond). 2021; 35(8):2213-20. [[Crossref](#)] [[PubMed](#)] [[PMC](#)]