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ARTICLE

# Repeatability and reliability of measurements obtained by the combined Scheimpflug and Placido-disk tomography in different stages of keratoconus

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## Abstract

**Objective** The objective of this study is to evaluate the repeatability and reliability of corneal parameters in different stages of keratoconus patients using a combined Scheimpflug–Placido disc analysis system.

**Materials and methods** In this prospective study, three consecutive measurements were performed by the same observer using Scheimpflug–Placido disc anterior segment analysis device in keratoconus patients. Flattest and steepest simulated keratometry and corneal volume, corneal aberrations, thinnest corneal thickness, symmetry index, keratoconus vertex and Baiocchi–Calossi–Versaci index were recorded. Keratoconic eyes were divided into four stages using the Amsler–Krumeich classification. Repeatability was evaluated using within the subject standard deviation, repeatability index (Ri) and coefficient of variation; reliability was evaluated by intraclass correlation coefficient (ICC). Pearson correlation coefficients were used to assess the correlation between the parameters evaluated.

**Results** Two hundred sixty-one eyes of 261 keratoconus patients were included in the study. The repeatability for all corneal curvature parameters decreased as the keratoconus severity increased, and there is a positive correlation between keratometry of the apex and corneal curvature parameters ($p < 0.05$) except mean simulated keratometry. The corneal aberrations were repeatable in all keratoconus subgroups (Ri < 0.34 µm). There are also positive correlations between keratometry of apex and corneal aberrations ($p < 0.05$) except total high-order root mean square and spherical aberration. The reliability was excellent (ICC > 0.90) for all indices except keratoconus vertex back.

**Conclusion** The parameters used in the diagnosis and follow-up of keratoconus in the Sirius corneal tomography system may differ more than expected at stages 3 and 4 of the disease. Awareness of this situation may be helpful in planning follow-up and treatment.

## Introduction

Keratoconus is an asymmetrical corneal disease, in which corneal thinning and irregularity cause irregular astigmatism and visual impairment [1]. One of the most sensitive methods for early diagnosis and progression of keratoconus is anterior segment analysis with corneal tomography devices [2]. Differences in these parameters are used to follow disease progression [3, 4].

The Sirius® (Costruzione Strumenti Oftalmici, Florence, Italy) device, which includes Scheimpflug tomography and Placido-disc topography, provides a detailed evaluation of the anterior segment and cornea. It is frequently used to detect keratoconus diagnosis and progression [5].

The repeatability and reliability of the tomography parameters are very important for diagnosis and progression analysis of keratoconus. The repeatability and reliability of the parameters of different corneal tomography devices on healthy people and keratoconus cases have been shown previously [6–9]. In the literature, there are studies on the repeatability and reliability of measurements obtained with Sirius tomography device in keratoconus patients [6, 9]. In the present study, we aimed to investigate and compare the reliability and reproducibility of these measurements in patients with keratoconus at different stages.

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## Patients and methods

This prospective study was conducted at a tertiary eye care centre in İstanbul, Turkey under the approval of the hospital management and the local ethics committee. All subjects provided written informed consent in accordance with the Declaration of Helsinki.

We studied patients who were referred to the cornea unit with the diagnosis of keratoconus. In subjects diagnosed with bilateral keratoconus, the eye for study was selected randomly. The ocular findings that defined keratoconus were a distortion of red reflex on retinoscopy, characteristic keratoconus signs on corneal tomography (e.g., asymmetric bowtie pattern with or without skewed axes, posterior and anterior elevation, inferior–superior asymmetry elevation) and at least one keratoconus sign on slit lamp examination (conical protrusion of cornea, stromal thinning, Fleischer ring, Vogt striae, anterior corneal scarring). The exclusion criteria were previous ocular surgery, cross-linking history, corneal hydrops and extensive corneal scarring. Keratoconic eyes were divided into four stages using the Amsler–Krumeich classification. With G-power software (version 3.1, Franz Faul, Kiel University, Kiel, Germany), the power was assessed for each test using sample size, type 1 error, effect size, correlation between repeated measures and number of measurements [10].

### Measurement system and procedure

The Sirius system is a common device that combines a monochromatic 360-degree rotating Scheimpflug camera and a Placido disk-based corneal topographer. This system allows measurement of 35,632 points of the anterior corneal surface and 30,000 points of the posterior corneal surface in a high-resolution mode in <1 s. It acquires a series of 25 Scheimpflug images (meridians) and one Placido top-view image and fully analyses the cornea and anterior segment for tangential and axial curvature data of anterior and posterior corneal surfaces, the global refractive power of the cornea, corneal wavefront analysis, corneal pachymetry maps and a biometric estimation of various structures.

A single experienced technician (SD) performed all tests. Measurements with the Sirius system (version 2.0) were performed according to the manufacturer's guidelines. All measurements were taken between 9 and 12 a.m. to minimise diurnal variation. Measurements were performed under scotopic conditions, while the device was brought into focus. The subject's eye was aligned along the visual axis with a central fixation light, and when the instrument showed a green light the acquisition was taken. Three measurements were taken with an interval of 5 min. Before each measurement, the subjects were advised to recline and reposition their heads. The device was then realigned, and subjects were instructed to blink completely to provide a smooth tear film on the corneal surface. The measurement quality was determined according to the acquisition quality section, where the Scheimpflug images (clearness and coverage), keratoscopy results (centration and coverage), and eye fixation were evaluated. Measurements with an unsatisfactory acquisition were excluded.

### Analysed parameters

The following anterior segment parameters were analysed: keratometry of the apex ($K_{apex}$), simulated keratometry of the flattest meridian (SimK1) averaging the axial curvature from the fourth to the eight Placido ring, simulated keratometry of the steepest meridian (SimK2) averaging the axial curvature from the fourth to the eight Placido ring, mean simulated keratometry ($SimK_{avg}$) averaging the axial curvature from the fourth to the eight Placido ring, corneal volume (Cvol) at 10.0 mm zone, thinnest corneal thickness (TCT) at 6.0 mm zone. Keratoconus screening parameters were also evaluated: symmetry index of frontal surface curvature map (SIf), keratoconus vertex front (KVf), Baiocchi–Calossi–Versaci index of front (BCVf), symmetry index of back surface curvature map (SIb), keratoconus vertex back (KVb), Baiocchi–Calossi–Versaci index of back (BCVb). Corneal aberrometry parameters were analysed: astigmatism, coma, trefoil, primary spherical aberration and total high-order root mean square (RMS) at 4.0 mm zone.

### Statistical analysis

Statistical analysis used SPSS for Windows software (version 22.0, SPSS, Inc.). The normality of the data was confirmed using the Kolmogorov–Smirnov test.

Repeatability is the variation between the repeated measurements under the same conditions, such as examiner, device, etc. The parameters used to evaluate the repeatability of the anterior segment measurements were within-subject standard deviation of three consecutive measurements ($S_w$), repeatability index (Ri) and the coefficient of variation (CoV). The $S_w$ enables the measurement error size.

The Ri, also known as test-retest variability, is defined as the difference between two measurements for the same subject and is expected to be $<2.77 \times S_w$ for 95% of pairs of observation. A lower Ri implies better repeatability. Repeatability is acceptable if the magnitude of the Ri for the studied parameter is smaller than the mean values. The CoV is defined as the SD of the measurements divided by its mean value and is represented as a percentage. The CoV was calculated for each participant and each parameter. The meaning of all CoV values is defined as the CoV of the

specific parameter. A lower CoV leads to a smaller variation in the measurement. The CoV value was not calculated for parameters with both positive values and negative values.

Reliability is defined as the degree of consistency of measurements and evaluated with intraclass correlation coefficient (ICC). ICC is an analysis of the variance-based type of correlation that measures the relative homogeneity within groups (between the repeated measurements) as a ratio to the total variation. The ICC will approach 1.0 when there is no variance within repeated measurements. ICC values of <0.50 are indicative of poor reliability, and values between 0.50 and 0.75 indicate moderate reliability. Values of 0.75 and 0.90 indicate good reliability and values > 0.90 indicate excellent reliability. Pearson correlation coefficients were used to assess the correlation between mean $K_{apex}$ and the repeatability parameters evaluated.

## Results

We analysed 261 eyes of 261 patients with a mean age of 27 ± 6.82 (range, 15–48). One hundred eight patients (41%) were female, 153 patients (58%) were male. There were 56 eyes (21%) in stage 1, 77 eyes (30%) in stage 2, 38 eyes (14%) in stage 3 and 90 eyes (34%) in stage 4 according to the Amsler–Krumeich classification. Coverage and centration are predictive values for the quality of measurements and were 83.6 ± 4.5 and 90.7 ± 3.6, respectively. Patient demographics of whole cohorts, coverage and centration values are given in Table 1.

Table 2 shows the mean deviation, repeatability and reliability of the curvature and volume of cornea in keratoconus patients. The $S_w$ values for $K_{apex}$, SimK1, SimK2 and $SimK_{avg}$ ranged between 0.22 and 0.59 D for all keratoconus patients. The $S_w$ values were 0.69 D or less for the keratoconus subgroups. The CoV values for $K_{apex}$, SimK1, SimK2 and $SimK_{avg}$ were 1.0% or less except Cvol value (CoV = 1.12%). Furthermore, the $S_w$ and CoV of SimK1 and SimK2 values were less (better) than all keratoconus subgroups. The most repeatable measurements were from stages 1 and 2 keratoconus subgroups. The $S_w$, Ri and CoV for all parameters increased as the keratoconus severity increased. The reliability of all parameters in all keratoconus subgroups was excellent (ICC ≥ 0.900) except for the $K_{apex}$ value for stage 3 keratoconus subgroups (ICC = 0.695).

The mean deviation, repeatability and reliability of the keratoconus screening parameters (KVf, KVb, BCVf, BCVb, TCT, Slf and Slb) are shown in Table 3. The $S_w$ values for KVf, BCVf, BCVb, SIf and SIb were 0.94 or less. The highest $S_w$ values in all parameters belonged to KVb and TCT (4.48 and 4.68 µm, respectively). Both values were obtained in stage 4 keratoconus subgroups. A Ri value lower than 2.60 was obtained for KVf, BCVf, BCVb, SIf and SIb. When evaluated on all keratoconus subgroups, the highest Ri value belonged to KVb and TCT (12.4 and 12.9 µm, respectively). The lowest CoV values belonged to BCVb and TCT in all parameters (0.98% and 0.75%, respectively). The remaining CoV parameters ranged between 4.24 and 7.79%. The reliability of all parameters was excellent (ICC > 0.900) for all keratoconus patients. The lowest ICC value was obtained from a KVb value in stage 1 keratoconus subgroup (ICC = 0.776).

Table 4 shows the mean deviation, repeatability and reliability of the total corneal aberrations in keratoconus patients. The highest $S_w$ and Ri values belong to astigmatism in stage 4 keratoconus subgroup (0.12 and 0.36, respectively). The highest CoV value belongs to trefoil aberration in stage 4 keratoconus subgroup (14.78%). The CoV was not calculated for spherical aberration because measured values contained both negative and positive

**Table 1** Patient demographics of whole cohorts, coverage and centration values.

| | Stage 1 ($n = 56$) | Stage 2 ($n = 77$) | Stage 3 ($n = 38$) | Stage 4 ($n = 90$) | Total ($n = 261$) |
|---|---|---|---|---|---|
| Age | | | | | |
| Min/max | 18/37 | 16/44 | 17/38 | 15/48 | 15/48 |
| Mean ± SD | 26.53 ± 6.03 | 27.25 ± 7.12 | 26.84 ± 5.89 | 27.13 ± 7.54 | 27 ± 6.82 |
| Sex | | | | | |
| Female (*n*, %) | 22 (40.7%) | 36 (46.1%) | 20 (52.6%) | 30 (33.3%) | 108 (41.2%) |
| Male (*n*, %) | 34 (59.2%) | 41 (53.8%) | 18 (47.3%) | 60 (66.6%) | 153 (58.7%) |
| Coverage | | | | | |
| Min/max | 75/93 | 71/93 | 75/90 | 72/95 | 71/95 |
| Mean ± SD | 82.7 ± 4.5 | 83.82 ± 4.2 | 82.6 ± 4.9 | 84.07 ± 6.8 | 83.6 ± 4.5 |
| Centration | | | | | |
| Min/max | 82/96 | 82/98 | 75/90 | 81/97 | 81/98 |
| Mean ± SD | 91.3 ± 3.9 | 90.5 ± 3.4 | 90.9 ± 3.5 | 90.7 ± 3.8 | 90.7 ± 3.6 |

**Table 2** The mean deviation, repeatability and reliability of the curvature and volume of cornea in keratoconus patients.

| Parameters and group | Mean ± SD | $S_w$ | Ri | CoV (%) | ICC | 95% confidence interval |
|---|---|---|---|---|---|---|
| $K_{apex}$ (D) | 53.46 ± 6.08 | 0.44 | 1.23 | 0.80 | 0.989 | 0.985–0.992 |
| Stage 1 | 46.31 ± 1.41 | 0.25 | 0.71 | 0.55 | 0.979 | 0.960–0.989 |
| Stage 2 | 50.53 ± 1.34 | 0.35 | 0.98 | 0.70 | 0.965 | 0.940–0.980 |
| Stage 3 | 53.80 ± 0.62 | 0.45 | 1.27 | 0.85 | 0.695 | 0.344–0.873 |
| Stage 4 | 60.31 ± 4.27 | 0.63 | 1.74 | 1.02 | 0.985 | 0.975–0.991 |
| SimK1 (D) | 45.28 ± 2.94 | 0.22 | 0.61 | 0.48 | 0.989 | 0.985–0.992 |
| Stage 1 | 42.87 ± 1.38 | 0.16 | 0.45 | 0.38 | 0.992 | 0.986–0.996 |
| Stage 2 | 44.17 ± 1.61 | 0.16 | 0.44 | 0.36 | 0.995 | 0.991–0.997 |
| Stage 3 | 45.24 ± 1.97 | 0.28 | 0.78 | 0.63 | 0.991 | 0.980–0.996 |
| Stage 4 | 47.76 ± 3.08 | 0.28 | 0.78 | 0.59 | 0.994 | 0.990–0.996 |
| SimK2 (D) | 48.31 ± 4.18 | 0.23 | 0.65 | 0.48 | 0.995 | 0.993–0.996 |
| Stage 1 | 44.34 ± 1.46 | 0.16 | 0.45 | 0.36 | 0.993 | 0.987–0.997 |
| Stage 2 | 46.84 ± 1.52 | 0.19 | 0.52 | 0.40 | 0.992 | 0.986–0.996 |
| Stage 3 | 47.37 ± 2.00 | 0.29 | 0.81 | 0.62 | 0.990 | 0.979–0.996 |
| Stage 4 | 52.39 ± 4.21 | 0.29 | 0.81 | 0.57 | 0.998 | 0.996–0.999 |
| $SimK_{avg}$ (D) | 46.63 ± 3.51 | 0.30 | 0.85 | 0.62 | 0.906 | 0.877–0.930 |
| Stage 1 | 43.63 ± 1.33 | 0.16 | 0.44 | 0.36 | 0.992 | 0.985–0.996 |
| Stage 2 | 45.45 ± 1.37 | 0.16 | 0.46 | 0.36 | 0.992 | 0.987–0.996 |
| Stage 3 | 46.28 ± 1.97 | 0.27 | 0.76 | 0.60 | 0.991 | 0.981–0.996 |
| Stage 4 | 50.11 ± 3.51 | 0.53 | 1.48 | 1.03 | 0.908 | 0.850–0.947 |
| Cvol ($mm^3$) | 54.19 ± 4.33 | 0.59 | 1.64 | 1.12 | 0.950 | 0.934–0.963 |
| Stage 1 | 54.63 ± 3.38 | 0.36 | 0.99 | 0.67 | 0.995 | 0.990–0.997 |
| Stage 2 | 54.24 ± 3.63 | 0.69 | 1.92 | 1.33 | 0.949 | 0.912–0.971 |
| Stage 3 | 54.61 ± 3.96 | 0.54 | 1.50 | 1.00 | 0.992 | 0.983–0.997 |
| Stage 4 | 54.34 ± 5.51 | 0.67 | 1.87 | 1.26 | 0.991 | 0.986–0.995 |

*SD* standard deviation, $S_w$ within-subject standard deviation, *Ri* repeatability index, *CoV* coefficient of variation, *ICC* intraclass correlation coefficient, $K_{apex}$ keratometry of apex, *SimK1* simulated keratometry of flattest, *SimK2* simulated keratometry, $SimK_{avg}$ mean simulated keratometry, *Cvol* corneal volume.

values. The reliability of all parameters was excellent (ICC > 0.900) for all keratoconus subgroups.

The correlation between mean $K_{apex}$ and repeatability parameters ($S_w$, Ri and CoV) for all measurements are shown in Table 5. There is a positive correlation between mean $K_{apex}$ and corneal curvature repeatability parameters except for the $SimK_{avg}$. Also, there is a positive correlation between mean $K_{apex}$ and the Ri value of keratoconus screening repeatability parameters except for the KVb. Although there is positive correlation in corneal aberration parameters only for astigmatism, coma and trefoil, there is not positive correlation for total RMS and spherical aberration.

## Discussion

Keratoconus can be detected at any stage in clinical practice and may cause permanent vision loss in advanced stages. Corneal tomography measurements are crucial for the diagnosis and follow-up. These data should be repeatable and reliable for clinicians to manage the disease appropriately.

The repeatability and reliability of corneal tomographic parameters used for keratoconus progression have been evaluated in many studies. However, studies comparing different stages of the disease, especially over a large series, are rare. One of the most commonly used commercially available systems is the Sirius system. There are many studies on the repeatability and reliability of various corneal tomography devices [7, 8, 11, 12]. The current study is one of the few studies to evaluate keratoconus cases over different stages by using the Sirius system [13–15]. In addition, our study offers a larger number of patients than previous studies that used a Scheimpflug-based imaging system.

Staging of keratoconus is important for follow-up and treatment. Many studies have used keratoconus classifications systems. The Amsler–Krumeich classification is one of the earliest classifications and has been used in many studies because of its simplicity and convenience [16]. Thus, we used this system to stage keratoconic eyes.

**Table 3** The mean deviation, repeatability and reliability of the keratoconus screening parameters.

| Parameters and groups | Mean ± SD | $S_w$ | Ri | CoV (%) | ICC | 95% confidence interval |
|---|---|---|---|---|---|---|
| KVf (μm) | 24.72 ± 15.72 | 0.94 | 2.60 | 4.24 | 0.985 | 0.980–0.989 |
| Stage 1 | 8.42 ± 3.95 | 0.57 | 1.59 | 6.52 | 0.979 | 0.889–0.989 |
| Stage 2 | 16.69 ± 5.40 | 0.58 | 1.62 | 3.85 | 0.995 | 0.991–0.997 |
| Stage 3 | 24.22 ± 7.38 | 0.70 | 1.96 | 3.24 | 0.996 | 0.991–0.998 |
| Stage 4 | 42.03 ± 11.84 | 1.57 | 4.35 | 3.57 | 0.978 | 0.963–0.987 |
| KVb (μm) | 61.42 ± 39.46 | 3.25 | 9.01 | 5.64 | 0.952 | 0.936–0.964 |
| Stage 1 | 21.25 ± 9.82 | 2.71 | 7.50 | 9.14 | 0.776 | 0.580–0.889 |
| Stage 2 | 42.36 ± 19.18 | 2.79 | 7.74 | 6.53 | 0.946 | 0.908–0.970 |
| Stage 3 | 61.66 ± 19.39 | 2.09 | 5.79 | 3.30 | 0.992 | 0.984–0.997 |
| Stage 4 | 102. 91 ± 31.01 | 4.48 | 12.4 | 3.69 | 0.954 | 0.924–0.973 |
| BCVf (D) | 2.38 ± 1.64 | 0.11 | 0.32 | 7.77 | 0.985 | 0.980–0.989 |
| Stage 1 | 0.80 ± 0.46 | 0.07 | 0.19 | 14.38 | 0.976 | 0.956–0.988 |
| Stage 2 | 1.70 ± 0.71 | 0.06 | 0.18 | 4.57 | 0.996 | 0.993–0.998 |
| Stage 3 | 2.48 ± 0.78 | 0.13 | 0.36 | 6.21 | 0.984 | 0.965–0.993 |
| Stage 4 | 3.91 ± 1.65 | 0.18 | 0.50 | 7.15 | 0.989 | 0.982–0.993 |
| BCVb (D) | 2.55 ± 1.72 | 0.13 | 0.38 | 8.83 | 0.977 | 0.970–0.983 |
| Stage 1 | 0.87 ± 0.55 | 0.04 | 0.13 | 10.27 | 0.994 | 0.989–0.997 |
| Stage 2 | 1.82 ± 0.94 | 0.10 | 0.28 | 10.37 | 0.989 | 0.982–0.994 |
| Stage 3 | 2.86 ± 0.79 | 0.11 | 0.31 | 4.02 | 0.988 | 0.975–0.995 |
| Stage 4 | 4.10 ± 1.66 | 0.23 | 0.64 | 8.77 | 0.980 | 0.968–0.988 |
| TCT (μm) | 449.03 ± 51.18 | 3.25 | 9.01 | 0.75 | 0.995 | 0.993–0.996 |
| Stage 1 | 479.03 ± 38.22 | 2.56 | 7.09 | 0.54 | 0.998 | 0.996–0.999 |
| Stage 2 | 465.02 ± 43.64 | 2.62 | 7.28 | 0.56 | 0.998 | 0.997–0.999 |
| Stage 3 | 451.19 ± 40.38 | 2.29 | 6.36 | 0.50 | 0.999 | 0.997–0.999 |
| Stage 4 | 416.89 ± 51.70 | 4.68 | 12.96 | 1.15 | 0.988 | 0.980–0.993 |
| SIf (D) | 4.25 ± 3.41 | 0.22 | 0.61 | 5.87 | 0.996 | 0.986–0.992 |
| Stage 1 | 1.59 ± 0.94 | 0.10 | 0.28 | 6.01 | 0.995 | 0.990–0.997 |
| Stage 2 | 3.18 ± 1.88 | 0.16 | 0.45 | 4.94 | 0.996 | 0.993–0.998 |
| Stage 3 | 5.13 ± 1.69 | 0.29 | 0.81 | 6.04 | 0.974 | 0.944–0.989 |
| Stage 4 | 6.48 ± 4.37 | 0.32 | 0.89 | 6.52 | 0.996 | 0.993–0.998 |
| SIb (D) | 1.22 ± 0.85 | 0.07 | 0.20 | 7.79 | 0.979 | 0.972–0.985 |
| Stage 1 | 0.53 ± 0.33 | 0.02 | 0.07 | 8.66 | 0.996 | 0.992–0.998 |
| Stage 2 | 0.96 ± 0.53 | 0.06 | 0.17 | 10.15 | 0.986 | 0.976–0.992 |
| Stage 3 | 1.52 ± 0.50 | 0.06 | 0.17 | 4.57 | 0.990 | 0.978–0.996 |
| Stage 4 | 1.72 ± 1.02 | 0.11 | 0.31 | 6.57 | 0.990 | 0.984–0.994 |

*SD* standard deviation, $S_w$ within-subject standard deviation, *Ri* repeatability index, *CoV* coefficient of variation, *ICC* intraclass correlation coefficient, *KVf* keratoconus vertex front, *KVb* keratoconus vertex back, *BCVf* Baiocchi–Calossi–Versaci index of front, *BCVb* Baiocchi–Calossi–Versaci index of back, *TCT* thinnest corneal thickness, *Slf* symmetry index of frontal surface curvature map, *Slb* symmetry index of back surface curvature map.

The repeatability and reliability of $K_{apex}$ were excellent in all keratoconus patients. The $S_w$ and Ri values of $K_{apex}$ were 0.44 and 1.23 D, respectively. The ICC value was more than 0.90 for all keratoconus patients. These results are similar to Prakash et al.'s study [11]. The Ri obtained for $K_{apex}$ were 1.74 D in eyes with stage 4 keratoconus, 1.27 D in eyes with stage 3 keratoconus, 0.98 D in eyes with stage 2 keratoconus and 0.71 D in eyes with stage 1 keratoconus. The results show that while the repeatability was excellent in keratoconus subgroups, the $K_{apex}$ measurements are less repeatable in stages 3 and 4 keratoconus than stages 1 and 2 keratoconus. Also, we detected a positive correlation between mean $K_{apex}$ and the repeatability parameters of $K_{apex}$.

Guilbert et al. [17] reported that the repeatability limits analysed by using Orbscan II topographer (Bausch & Lomb) were as high as 1.73 D in eyes with advanced keratoconus, 1.11 D in eyes with mild keratoconus and 0.61 D

**Table 4** The mean deviation, repeatability and reliability of the total corneal aberrations in keratoconus patients.

| Aberration type and groups[a] | Mean ± SD | $S_w$ | Ri | CoV (%) | ICC | 95% confidence interval |
|---|---|---|---|---|---|---|
| Total RMS (μm) | 0.62 ± 0.38 | 0.02 | 0.06 | 5.41 | 0.998 | 0.996–0.999 |
| Stage 1 | 0.24 ± 0.14 | 0.01 | 0.05 | 8.70 | 0.992 | 0.949–0.999 |
| Stage 2 | 0.46 ± 0.21 | 0.01 | 0.05 | 5.17 | 0.996 | 0.972–0.999 |
| Stage 3 | 0.60 ± 0.19 | 0.03 | 0.08 | 5.30 | 0.989 | 0.929–0.999 |
| Stage 4 | 1.18 ± 0.12 | 0.03 | 0.08 | 2.47 | 0.978 | 0.855–0.999 |
| Astigmatism (μm) | 1.19 ± 0.91 | 0.06 | 0.18 | 5.57 | 0.997 | 0.993–0.999 |
| Stage 1 | 0.73 ± 0.68 | 0.04 | 0.12 | 8.50 | 0.997 | 0.981–0.999 |
| Stage 2 | 1.20 ± 0.71 | 0.03 | 0.08 | 3.95 | 0.999 | 0.994–0.999 |
| Stage 3 | 1.70 ± 0.48 | 0.06 | 0.18 | 4.14 | 0.994 | 0.962–0.999 |
| Stage 4 | 2.33 ± 0.55 | 0.12 | 0.34 | 5.70 | 0.981 | 0.981–0.999 |
| Coma (μm) | 0.50 ± 0.32 | 0.02 | 0.06 | 6.47 | 0.998 | 0.996–0.999 |
| Stage 1 | 0.15 ± 0.13 | 0.01 | 0.03 | 10.53 | 0.998 | 0.987–0.999 |
| Stage 2 | 0.33 ± 0.19 | 0.01 | 0.05 | 7.03 | 0.996 | 0.976–0.999 |
| Stage 3 | 0.49 ± 0.17 | 0.02 | 0.07 | 6.07 | 0.989 | 0.928–0.999 |
| Stage 4 | 1.05 ± 0.07 | 0.03 | 0.09 | 3.34 | 0.926 | 0.908–0.995 |
| Trefoil (μm) | 0.26 ± 0.14 | 0.03 | 0.10 | 14.08 | 0.964 | 0.918–0.986 |
| Stage 1 | 0.14 ± 0.06 | 0.02 | 0.06 | 8.08 | 0.946 | 0.889–0.996 |
| Stage 2 | 0.24 ± 0.08 | 0.02 | 0.08 | 11.73 | 0.961 | 0.918–0.997 |
| Stage 3 | 0.23 ± 0.11 | 0.04 | 0.12 | 14.71 | 0.972 | 0.928–0.998 |
| Stage 4 | 0.42 ± 0.14 | 0.04 | 0.16 | 14.78 | 0.925 | 0.898–0.995 |
| Spherical (μm) | −0.007 ± 0.11 | 0.014 | 0.041 | –[b] | 0.995 | 0.993–0.996 |
| Stage 1 | –0.029 ± 0.04 | 0.006 | 0.018 | – | 0.989 | 0.927–0.998 |
| Stage 2 | –0.063 ± 0.06 | 0.006 | 0.018 | – | 0.996 | 0.974–0.998 |
| Stage 3 | –0.069 ± 0.02 | 0.020 | 0.057 | – | 0.962 | 0.912–0.997 |
| Stage 4 | 0.132 ± 0.13 | 0.025 | 0.070 | – | 0.981 | 0.874–0.998 |

*SD* standard deviation, $S_w$ within-subject standard deviation, *Ri* repeatability index, *CoV* coefficient of variation, *ICC* intraclass correlation coefficient, *RMS* root mean square.

[a]All parameters obtained at total corneal 4 mm zone.

[b]The CoV was not calculated for spherical aberration because measured values contained both negative and positive values.

in normal eyes. Another previous study used the Pentacam HR (Oculus Optikgeräte GmbH) and showed that the $K_{max}$ value was 1.34 D in advanced keratoconus groups [7]. These results are similar to our results for the $K_{apex}$ value of advanced keratoconus. These results further indicated that changes > 1 D for $K_{apex}$ are likely to arise from a measurement error change especially in advanced keratoconus patients.

One of the most accepted criteria for keratoconus progression is a more than 1 D increase in $K_{apex}$ [18]. In order to obviate this variability in $K_{apex}$ value, the cut-off value for progression determination might be increased, more than one measurement in each control might be taken and new parameters for detecting the keratoconus progression might be added. Prakash et al. [11] recommended that the $K_{apex}$ value increases more than 1.24 D for keratoconus progression criteria. Therefore, interpreting the $K_{apex}$ value with the additional corneal data might be more useful, despite the fact that keratometric measurements are effective and highly repeatable in keratoconus screening.

In this study, the CoV values for SimK1, SimK2 and $SimK_{avg}$ were <0.62%, and the ICC values were 0.90 or more in all keratoconus patients. This means that SimK1, SimK2 and $SimK_{avg}$ values are repeatable and reliable. Savini et al. [19] obtained a CoV of 0.34% and an ICC more than 0.99 for mean simulated *K* in keratoconus patients which including 13 cases. These results are similar to our results. In addition, an increase of more than 1–1.5 D of SimK2 and an increase of more than 0.75 D of $SimK_{avg}$ are important for keratoconus progression analysis [6, 20]. We found <1 D of Ri values for SimK2 in all keratoconus subgroups. The measurement error change of Ri is below the progression limit value for SimK2. However, the Ri values of $SimK_{avg}$ for stages 3 and 4 keratoconus are above 0.75 D (0.76 and 1.48 D, respectively). Therefore, for the Sirius device, SimK2 might be used for progression analysis in all stages of keratoconus, but $SimK_{avg}$ can cause false positive predictions for stages 3 and 4 keratoconus.

The repeatability (CoV ≤ 1.26%) and reliability (ICC ≥ 0.90) were excellent for Cvol in all keratoconus subgroups. In a previous study, the CoV and ICC for Cvol measurements were 1.1% and 0.972%, respectively [11]. The CoV value reported there was similar to our study. However, in this study, these parameters were not compared between keratoconus stages. Here, the repeatability of stages 1 and 3 was better than stages 2 and 4 keratoconus.

The TCT is important for keratoconus diagnosis and progression analysis. In this study, the repeatability

**Table 5** The correlation between mean $K_{apex}$ and repeatability parameters for all measurements.

| Parameters | Correlation Pearson coefficient | | |
|---|---|---|---|
| Mean $K_{apex}$ correlation with | $S_w$ | Ri | CoV |
| $K_{apex}$ (D) | 0.369* | 0.369* | 0.239* |
| SimK1 (D) | 0.260* | 0.260* | 0.216* |
| SimK2 (D) | 0.361* | 0.361* | 0.273* |
| $SimK_{avg}$ (D) | 0.134 | 0.134 | 0.130 |
| Cvol ($mm^3$) | 0.327* | 0.327* | 0.306* |
| KVf (μm) | 0.428* | 0.428* | −0.275 |
| KVb (μm) | 0.091 | 0.091 | −0.214 |
| BCVf (D) | 0.410* | 0.410* | −0.081 |
| BCVb (D) | 0.536* | 0.536* | 0.023 |
| TCT (μm) | 0.342* | 0.342* | 0.363* |
| Slf (D) | 0.329* | 0.329* | −0.036 |
| Slb (D) | 0.380* | 0.380* | 0.008 |
| Total RMS (μm) | 0.219 | 0.219 | −0.268 |
| Astigmatism (μm) | 0.406* | 0.406* | 0.015 |
| Coma (μm) | 0.475* | 0.475* | −0.187 |
| Trefoil (μm) | 0.412* | 0.412* | −0.034 |
| Spheric (μm) | 0.182 | 0.182 | – |

$S_w$ within-subject standard deviation, *Ri* repeatability index, *CoV* coefficient of variation, $K_{apex}$ keratometry of apex, *SimK1* simulated keratometry of flattest, *SimK2* simulated keratometry, $SimK_{avg}$ mean simulated keratometry, *Cvol* corneal volume, *KVf* keratoconus vertex front, *KVb* keratoconus vertex back, *BCVf* Baiocchi–Calossi–Versaci index of front, *BCVb* Baiocchi–Calossi–Versaci index of back, *TCT* thinnest corneal thickness, *Slf* symmetry index of frontal surface curvature map, *Slb* symmetry index of back surface curvature map.

*Significantly positive Pearson correlation coefficient ($p < 0.05$).

(CoV ≤ 1.15%) and reliability (ICC ≥ 0.988) of TCT were excellent in all keratoconus subgroups. The Ri value of TCT ranged between 7.09 and 12.9 μm. The greatest Ri value in keratoconus subgroups was obtained for stages 2 and 4 keratoconus (7.28 and 12.9 μm, respectively). A previous study with Pentacam HR (Oculus Optikgeräte GmbH) showed that the Rİ of TCT was 15 μm at stage 1, 13.73 μm at stage 2 and 17.15 μm at stage 3 [15]. In other studies regarding the repeatability of TCT measurement showed that the Ri values of TCT ranged between 6.45 and 9.3 μm [9, 11, 19]. Only one study has been reported that the Ri value of TCT was 24.6 μm [6]. In all studies, the CoV value of TCT ranged between 2.1 and 0.50%, and the ICC value of TCT was more than 0.90. These results were observed in accordance with our results. In the literature, a decrease in corneal thickness 2–5% or more than 30 μm is recommended as progression criteria [11, 13, 21, 22]. Although there was a positive correlation between mean Kapex and Ri and Cov values of TCT in our study, the higher Ri value of TCT is 12.9 μm. Therefore, this variability can be accepted to follow-up the keratoconus progression analysis.

The reliability of keratoconus screening parameters (KVf, KVb, SIf, SIb, BCVf and BCVb) was excellent (ICC ≥ 0.90) in this study. Prakash et al. [11] indicated that the reliability of KVf, KVb, Slf and Slb was excellent (ICC ≥ 0.966). Previous studies showed that the reliability of BCV was similarly excellent (ICC ≥ 0.971), and the Ri of the BCVf and BCVb values were 0.094 and 0.193, respectively [8, 9, 11]. The Ri of BCV parameters that we obtained were higher than these values (0.32 and 0.38, respectively). This difference may be caused by the fact that the number of stages 3 and 4 keratoconus patients in our study was higher than these studies. In the current study, there was a positive correlation between mean $K_{apex}$ and Ri values of keratoconus screening parameters except for the KVb.

Previous studies indicated that corneal wavefront aberrations are good indicators for early detection and grading of keratoconus [23, 24]. Bayhan et al. [8] analysed the repeatability and reliability of the Sirius system for anterior and posterior aberrations over 6.0 mm pupil by taking three readings. They reported that the highest Ri value belonged to anterior and posterior total higher-order aberrations (HOAs) (0.2 μm), and the ICC values of corneal aberrations (astigmatism, coma, trefoil and total HOAs) ranged between 0.833 and 0.988. In our study, we observed that the highest Ri value of corneal aberrations was obtained from astigmatism (0.18 μm), and the reliability (ICC > 0.900) was excellent for all keratoconus subgroups. These differences may be explained by the higher number of advanced keratoconus patients in our study. The Ri value of spherical aberration was 0.08 μm in keratoconus patients reported by Savini et al. [19] based on analysis by Sirius system. This result was similar to ours for stage 4 keratoconus subgroups (0.07 μm). In these studies, corneal aberrations were not classified according to keratoconus stages. On the other side, in our study, we observed that the repeatability of corneal aberrations may be varied according to keratoconus stages. Furthermore, there was a positive correlation between mean $K_{apex}$ and Ri values of astigmatism, coma and trefoil aberrations. We thought that the stage of keratoconus patients included in the study may change the repeatability of corneal aberrations. This may be the reason for the discordance between values obtained in our study and the others.

This study used tomographic parameters from the Sirius device in patients with keratoconus at different stages. The main limitations of our study were that no comparison was made with different devices. Refractive status and visual acuity levels of the cases and their relationship with tomographic parameters were not evaluated. Future study will focus on larger cohorts and comparisons.

In conclusion, the parameters used in the diagnosis and follow-up of keratoconus in the Sirius corneal tomography system may differ more than expected at stages 3 and 4 of

the disease. Awareness of this situation may be helpful in planning follow-up and treatment.

## Summary

### What was known before

- The repeatability and reliability of the tomography parameters are very important for diagnosis and progression analysis of keratoconus.
- The repeatability and reliability of the parameters of different corneal tomography devices on healthy people and keratoconus cases have been shown previously.

### What this study adds

- The parameters used in the diagnosis and follow-up of keratoconus in the Sirius corneal tomography system may differ more than expected at stages 3 and 4 of the disease.
- Awareness of this situation may be helpful in planning follow-up and treatment.

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## Compliance with ethical standards

**Conflict of interest** The authors declare that they have no conflict of interest.

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