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Comparison of Keratoconus Cone Location of Different Topo/tomographical Parameters

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Running head: Keratoconus cone location on different maps

Abstract

Purpose: To compare the corneal cone location on different maps and instruments and their agreements with elevation maps.

Methods: In 90 left eyes with bilateral keratoconus, the apex of cone location was determined based on the maximum simulated keratometry (Kmax) location on the anterior sagittal curvature map by Pentacam HR, the maximum curvature on the mean curvature map by ATLAS 9000, most elevated point of the island of positive elevation relative to the best fit sphere on the front and back corneal elevation maps by Pentacam HR, and thinnest point on the thickness map by Pentacam HR and Orbscan, and the thinnest points on pachymetry and epithelial thickness maps by RTVue OCT.

Results: There was a significant difference among the location on different maps along the x- and y- axes ($p < 0.001$). The lowest agreement with the cone apex on both front and back elevation maps was for the anterior sagittal curvature map and the highest agreement for the Pentacam thickness map. The majority of keratoconus cone apexes were displaced in the inferotemporal direction on the different maps except for the epithelial thickness maps.

Conclusions: Despite the variability between different devices and methods; the thickness map on the Pentacam HR showed the highest correlation with the front and back elevation maps, while the RTVue epithelial thickness map showed the poorest correlation. Based on this study, epithelial thickness maps and anterior curvature maps should be utilized with caution to determine the location of the cone.

Keywords: Keratoconus, Cone location, Elevation map, Curvature map, Pachymetry map

Introduction

Keratoconus, the most common primary corneal ectasia, is characterized by a progressive structural weakening resulting in corneal thinning and protrusion, irregular astigmatism leading to a decrease in both quality and quantity of vision.[1, 2] The disease is typically bilateral, but often highly asymmetric, and commonly presents in the teens to early twenties and slows or stabilizes after the fourth decade of life.[3]

Determining the center or apex of the cone has significant clinical applications, including evaluation of keratoconus progression, proper contact lens fitting, and in the surgical management where treatments, such as intracorneal ring segments (ICRS), deep anterior lamellar keratoplasty (DALK), and corneal cross-linking (CXL) are typically centered over the cone apex.[4-6]

The corneal cone in keratoconus is characterized by its location, volume (extent) and height.[7] The cone apex, or tip, is applied to the most elevated point in the island of positive elevation with a spherical reference sphere taken from the central 8.0 mm optical zone and its decentration refers to the distance between the apex of the cornea and apex of the cone.

There is still confusion or disagreement in how the cone apex is located or described. These different criteria include the point of maximum curvature on the axial (sagittal),[8] local (tangential),[9] or mean curvature maps,[10] the location of the corneal thinnest point in the pachymetry map, the location of the thinnest epithelial point on the epithelial thickness map,[11] or the point of maximal elevation in the "island of positive elevation" seen on both anterior and posterior elevation maps with a best-fit-sphere (BFS) reference surface.[12, 13]

The present study was designed to compare the apex of the keratoconus cone using different imaging systems Atlas 9000 topographer (Humphrey, Carl Zeiss Meditec, Jena, Germany), Oculus Pentacam (Oculus GmbH, Wetzlar, Germany), Orbscan (Bausch & Lomb, Rochester, NY, USA), RTVue optical coherence tomography (OCT) (Optovue, Inc., Fremont, CA, USA) and different maps/displays (sagittal and mean curvature maps, corneal thickness maps, epithelial thickness maps, and anterior and posterior elevation maps).

Materials and Methods

Ninety left eyes of 90 patients with bilateral definite keratoconus were included in this study. The diagnosis of keratoconus was confirmed by an experienced corneal specialist (MRS). Diagnosis was based on slit-lamp findings (e.g. Fleischer ring, Vogt striae), abnormal topographic patterns on the sagittal (axial) front curvature map, abnormal anterior and posterior values on the front and back elevation maps, distortion of the retinoscopic reflex and a final "D" value at least 2.7 on Belin-Ambrósio enhanced ectasia display printout (BAD-D).[14] Patients with a history of contact lens wear, ocular diseases, ocular trauma and corneal hydrops/ scar, ocular surgery, atopy and history of CXL or insertion of intrastromal corneal rings were excluded from the study. In addition, patients suspected to pellucid marginal degeneration (PMD) with against-the-rule astigmatism, flattening in the vertical meridian and claw or kissing-bird patterns on the sagittal curvature map; abnormal anterior and posterior elevation values on the elevation maps and the classic inferior band of thinning on the pachymetry map were excluded from the study.[15] The study was approved by the ethics committee of Mashhad University of Medical Sciences (Code No: 970183) and followed the tenets of the Helsinki principles.

All patients were imaged by an experienced ophthalmic technician with the following; Placido disk-based topography using ATLAS 9000 (Humphrey Atlas, Carl Zeiss Meditec, Jena, Germany), Scheimpflug tomography using Pentacam HR (Oculus Optikgeräte, Wetzlar, Germany), slit-scanning tomography using Orbscan (Bausch & Lomb, Rochester, NY, USA) and optical coherence tomography using the RTVue XR OCT Avanti (Optovue, Inc., Fremont, CA, USA). Pentacam images with “”OK”” quality specification and OCT images with a signal strength index of at least 30 were considered for analysis.[16] Also, during corneal imaging using the Orbscan and ATLAS systems, the operator emphasized the stability of patients' fixation on the fixation target and the precise adjustment of the device on the cornea.

All corneal imaging was performed between 16:00 and 20:00 during a single visit. The order of the tests was randomized and the results were not viewed at the time of capture to minimize the chance of bias.

The apex of keratoconus cone was determined by the following; the point of maximum simulated keratometry (Kmax) on anterior sagittal curvature map provided by Pentacam HR, the location of maximum curvature on the mean curvature map by ATLAS 9000 corneal topographer, the most elevated point in the island of positive elevation relative to the best fit sphere on the front and back corneal elevation maps by Pentacam HR, the thinnest point on the thickness map by Pentacam HR, Orbscan, and RTVue OCT, and the thinnest point on the epithelial thickness map by RTVue OCT. The apex location was recorded in an X/Y coordinate grid relative to the corneal apex.

Keratoconus severity was classified by CLEK (collaborative longitudinal evaluation of keratoconus) study criterion based on the steep keratometry reading into mild (<45 D), moderate (45-52 D) and severe (>52 D) stages.[17]

Data were analyzed in SPSS.22 software (IBM Inc., Chicago, Illinois, USA). The Kolmogorov-Smirnov test was used to assess the normality of quantitative data distribution. As the data was significantly different from a normal distribution, the Freedman test (within-subject ANOVA analysis) was used to compare the mean location of the desired points along the x- and y-axes on different maps and the Dunn-Bonferroni post hoc tests for pairwise comparison. With this statistic, the study was 95% powered to detect an effect size of 0.15. Correlation of the apex location on the front and back elevation maps separately along the x- and y-axes as referenced[13] with the location on the other maps were assessed using the Pearson (or Spearman) correlation test. Intraclass correlation coefficients (ICC) were used to assess the agreement of cone apex on the elevation map with other maps. An ICC more than 0.950 was considered strong for the comparison purposes.[18, 19 20] The limits of agreement (LoA) were determined as the mean difference ±1.96SD of the mean differences. A p-value of less than 0.05 was considered significant statistically in all tests.

Results

Of the 90 left eyes evaluated in this study, 46 eyes (51.1 %) were female. The mean age of subjects was 26±6.6 years with a range of 13 to 45 years. The mean apex of keratoconus cone along the x- and y-axes on the different maps provided by different devices are presented in Table 1.

Table 1:

There was a statistically significant difference in the location along the x- ($X^2(7) = 53.565$, $p< 0.001$) and y- ($X^2(7) = 120.511$, $p< 0.001$) axes on different maps using Friedman test.

Pairwise comparisons were used to determine the location on which maps have statistically significant difference from which on other maps separately along the x- and y- axes. The adjusted p-values of pairwise comparisons using Dunn-Bonferroni post hoc tests are shown in Table 2.

Table 2:

The location of cone coordinates on the anterior curvature maps (mean and sagittal) showed significant difference with the cone coordinates along the y-axis on all maps provided by different devices ($p<0.05$). The cone coordinates on the corneal thickness maps compared to the elevation maps on both corneal surfaces had insignificant differences along the y-axis for both Pentacam and RTVue OCT, and along the x-axis and both x/y axes and for the Orbscan thickness map with the front and back surface elevation maps, respectively. The thinnest epithelial point location by RTVue OCT had the poorest correlation with nearly half of the epithelial thickness maps suggesting a superior cone location.

Comparison of the location cone along the x- and y-axes on the front and back elevation maps as referenced with the locations on the other maps are illustrated in Tables 3 and 4, respectively. (Tables 3 & 4)

The mean differences, agreement and correlation of the cone location coordinates on the front elevation map with the curvature, pachymetry and epithelial thickness maps are presented in Table 3.

Table 3:

The least mean difference and the highest agreement with the location on the front elevation map along the x-axis were related to the Pentacam thinnest point (±0.18) and most elevated point in the island of positive elevation on the back elevation map (±0.22), while the lowest agreement was seen for the Kmax location on the sagittal curvature map (±1.63). The strongest agreement was related to the Pentacam thinnest point and the back most elevated point in the island of positive elevation. Also, there was a significant correlation between the locations on the front elevation map with other maps using the Spearman correlation test. ($p < 0.05$)

Along the y- axis, the cone location on the front elevation map showed the lowest mean differences and highest correlation with the Pentacam's thickness map (0.01±0.08 mm) in addition to the most elevated point in the island of positive elevation on the back elevation map (-0.01±0.07 mm). The highest mean difference and the lowest correlation was found for the epithelial thickness map by RTVue OCT.

Table 4 shows the mean differences, agreement and correlation of the cone location along the x- and y- axis on the back elevation map with other maps.

Table 4:

Using the island of positive elevation on the back elevation map as reference, apart from the front elevation map, the highest agreement along the x- and y- axes was for the thinnest point on the Pentacam thickness map, while the lowest agreement and correlation was related for the thinnest point on the epithelial thickness map provided by the RTVue OCT.

The Kmax location on the anterior sagittal curvature map provided by Pentacam HR showed the lowest agreement with the cone location on both front and back elevation maps, and in increasing order of agreement for the location of maximum curvature on the mean curvature map by ATLAS 9000 corneal topographer, the thinnest points on the RTVue OCT's epithelial and pachymetry maps, the thinnest point location on the Orbscan thickness map and the highest agreement for the thinnest point location on the Pentacam thickness map.

The keratoconus cone locations on various maps provided by different devices are presented in Table 5.

Table 5:

Except for the sagittal curvature map (based on the Kmax position) and epithelial thickness map (based on the thinnest point location), the majority of keratoconus cone apexes were displaced in the inferotemporal direction. Contrary to accepted knowledge, epithelial thickness maps depicted the cone apex in the supratemporal and superonasal quadrants directions in 37.8% and 7.8% of cases.

The mean keratmetry reading in different keratoconus stages was 42.69±1.20, 46.43±1.64 and 54.38±2.81 D for mild (n= 27 eyes), moderate (n= 29 eyes), and severe (n= 34 eyes) stages, respectively. Re-analysis of data in different stages of keratoconus classified by CLEK criterion did not show considerable change in the previous results.

The mean final "D" value on BAD-D printout was 7.07±2.97 (range 3.08 to 19.87) in all eyes and 4.59±1.15, 6.38±1.18, 9.64±3.05 in mild, moderate and severer keratoconus.

Discussion

The cone apex is considered as an important factor in clinical decision making and predicting the outcome of various interventions. Reports of more corneal flattening, better visual outcomes and improved corneal biomechanical behavior following the CXL or combined topography-guided photorefractive keratectomy and CXL or customized CXL in the keratoconus eyes and other ectatic conditions with the central cones compared to the peripheral cones determined on both anterior sagittal and tangential curvature maps refer to the importance of precisely defining the location of the cones.[21-23] This keratoconus cone location effect highlights the importance of comparing the cone apex on various maps provided by different devices.

The cone location is considered as a critical factor in selecting the type of corneal rings for the corneal reshaping and providing the best possible visual outcomes. In cases of central cones, using a complete intrastromal corneal ring such as Myoring (Dioptex, Gmbh, Linz, Austria),[24] or two symmetrical ICRSs such as Keraring segments (Mediphacos, Belo Horiztone, Brazil)[25] are likely to produce maximum flattening effect.[26]

Predicting the visual benefits after rigid gas-permeable contact lens prescription in keratoconus is another indication of cone location assessment. The cone locations closer to the geometric center of the cornea is expected to be associated with a better improvement in corrected visual acuity and post fitting stability and centration. Greater improvement was reported in visual acuity in the keratoconus eyes with central cone defined on the anterior tangential curvature topographic map by Sirius corneal tomographer (Costrozione Strumenti Oftalmici, Scandicci Fi, Italy).[27]

This present study showed variability between devices and methods in determining the cone coordinates. The most elevated point in the island of positive elevation on both front and back elevation maps showed better agreement with the thinnest point location on the thickness maps than the maximum keratometry on the curvature maps. The highest agreement with the elevation map in locating the cone apex was related to the thinnest point on the thickness map provided by Pentacam HR. According to the highest frequency of cone location in the inferotemporal direction on the elevation map, the Pentacam thickness map showed the highest similarity with this map and the epithelial thickness map by RTVue OCT showed the lowest similarity with the elevation maps.

Some studies have proposed the priority of elevation maps in determining cone location.[13] In a study by Nunez and Blanco (2008) on 23 eyes with keratoconus, they compared the cone location on the back elevation map and the mean power keratometric map by Orbscan and reported the superiority of the back elevation map on the mean curvature keratometric map in determining the cone location.[28] In line with their results, the present study showed a lower agreement of the anterior curvature (mean and sagittal) maps compared to the corneal thickness maps with the elevation maps provided by Pentacam HR. Although it appears that one reason for the low agreement of the curvature map, especially with the back elevation map, can be attributed to the role of corneal epithelial remodeling effect, which tends to largely mask corneal irregularities and masquerade the stromal forward bulging through its resurfacing ability especially in the early stages of keratoconus. Therefore, sometimes changes in corneal regularity may be indiscoverable by corneal topography, especially in some topographic maps that are not very sensitive to mild irregularitie;[29] however, the present findings in over half our patients of a superior location for the area of maximal epithelial thinning, as opposed to over the apex of the cone, raises some questions on the applicability of epithelial thickness maps.

Demirbas in evaluation of the topography pattern and location of the cone apex on the elevation map by the PAR Corneal Topography System (PAR-CTS) and the anterior sagittal curvature map by the Tomey Topographic Modeling System (TMS-1) reported that the cone apex was present in the inferotemporal quadrant in 65% of corneas evaluated with the PAR-CTS and had a statistically significant difference with the apex location in the sagittal curvature map; while 20% of corneas that showed an apex on the sagittal curvature map had a normal pattern with no a detectable cone apex on the elevation mode display. They concluded that the apex location on the elevation map has a better diagnostic specificity than the regional difference of curvatures on the sagittal curvature map.[13] In confirming their findings, the current study showed no considerable agreement between the elevation and sagittal/mean curvature maps in locating the apex of the cone. Also, in the majority of cases, the apex was found in the inferotemporal zone (approximately 95%) on the elevation map, while this quadrant contained only 17.8% of the cone apex on the sagittal curvature map and the most cases were in the inferonasal quadrant (71.1%). On the other hand, the mean curvature map by atlas corneal topographer showed more similarity in the position of the cone with the elevation maps by Pentacam HR than the sagittal curvature map by the Pentacam HR.

Our findings suggest that using the maximum simulated keratometry (Kmax) on the anterior sagittal curvature map and/or the epithelial thickness map is not a suitable option for locating the cone apex, in spite of the fact that Kmax and anterior curvature maps are commonly used for that purpose.[6]

Tang et al. (2005) in comparing of cone coordinates on the sagittal, tangential and mean curvature maps in both keratoconus and pellucid marginal degeneration reported the precision of the mean curvature map in quantifying the apical cone location in both groups.[30] Although, the present findings showed more agreement of the mean curvature with the elevation maps than the sagittal curvature; however, the Pentacam thickness map had more accuracy than the mean curvature map provided by Atlas. Contrary to their study, the current study only investigated keratoconus eyes.

Keratoconus cone apex was displaced in the inferotemporal direction for the majority of eyes on all maps except for the anterior sagittal curvature map and epithelial thickness maps. These findings are in line with the Ertan's study which reported the apex of the cone on the temporal direction and especially in the inferior quadrant in a higher age group.[31]

A limitation of the current study was our sole use of the sagittal curvature map, while it has been claimed that the tangential curvature map determines the cone location better than the sagittal map.[32, 33]

Conclusion

Despite the variability between various devices and different methods in defining the x and y coordinates of the cone apex; however, the thinnest point (cone) location on the thickness maps showed better agreement with the cone apex on the elevation maps as reference than the maximum keratometry on the curvature maps. The highest agreement was related to the thinnest point on the thickness map provided by Pentacam HR. Also, disease severity classified by the CLEK criterion showed no change in agreement between findings obtained in the apical cone position on different maps with the locations on the elevation maps. Displacement of the cone was mostly seen in the inferotemporal direction on the elevation maps. The thickness map on the Pentacam HR showed the highest correlation with the front and back elevation maps, while the RTVue epithelial thickness map showed the poorest correlation. Although there are potential reasons, such as epithelial remodeling and the different alignments/acquisition techniques used of various devices to locate the keratoconus cone. Based on this study, the use of epithelial thickness maps and the sagittal curvature maps should be utilized with caution to determine the keratoconus cone location.

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(Ethic code: 970183)

Disclosure statement

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Table 1: Mean and SD of absolute values and the cone location along the x- and y- axes in millimeters on the front/back elevation, anterior sagittal/mean curvature and pachymetry/epithelial thickness maps by different devices. (n=90 eyes)

Variables	**Mean±SD**

	(95% CI)		
	Absolute Value	Coordinate	
		X-axis	Y-axis
Pentacam Sagittal Curvature (Kmax)	53.31±8.26 (51.58 to 55.04)	-0.13±0.50 (-0.23 to -0.03)	-0.94±0.97 (-1.14 to -0.74)
Atlas Mean Curvature (Kmax)	51.26±6.91 (49.81 to 52.71)	0.04±0.76 (-0.12 to 0.20)	-0.91±0.60 (-1.03 to -0.78)
Pentacam TP	457.74±48.10 (447.67 to 467.82)	0.17±0.57 (0.05 to 0.29)	-0.51±0.25 (-0.56 to -0.45)
Orbscan TP	454.63±57.46 (442.60 to 466.67)	0.17±0.66 (0.03 to 0.31)	-0.66±0.37 (-0.74 to -0.58)
OCT TP	456.77±46.92 (446.94 to 466.59)	0.06±0.59 (-0.06 to 0.18)	-0.66±0.36 (-0.73 to -0.58)
OCT Epi TP	45.06±4.72 (44.07 to 46.04)	0.08±1.31 (-0.19 to 0.35)	0.27±1.88 (-0.12 to 0.66)
Pentacam Front Elevation	20.46±11.87 (17.80 to 23.10)	0.23±0.58 (0.11 to 0.35)	-0.52±0.27 (-0.57 to -0.46)
Pentacam Back Elevation	83.83±22.58 (38.81 to 48.86)	0.25±0.58 (0.13 to 0.37)	-0.52±0.27 (-0.58 to -0.47)

(Kmax: Maximum keratometry, TP: Corneal thinnest point, OCT: Optical coherence tomography, Epi: Epithelium)

Table 2: Pairwise comparisons of the apex of keratoconus location along the x- and y-axes on the front/back elevation, anterior sagittal/mean curvature and pachymetry/epithelial thickness maps by different devices. (n=90 eyes)

Variables	**Pentacam Sagittal Curvature (Kmax)**		**Atlas Mean Curvature (Kmax)**		**Pentacam TP**		**Orbscan TP**		**OCT TP**		**OCT Epi TP**		**Pentacam Front Elevation**	
	X	**Y**	**X**	**Y**	**X**	**Y**	**X**	**Y**	**X**	**Y**	**X**	**Y**	**X**	**Y**

Atlas MC	1.0	1.0	-	-	-	-	-	-	-	-	-	-	-	-
Pentacam TP	1.0	<0.001	1.0	<0.001	-	-	-	-	-	-	-	-	-	-
Orbscan TP	0.043	0.020	1.0	0.041	1.0	0.005	-	-	-	-	-	-	-	-
OCT TP	1.0	0.012	1.0	0.025	1.0	0.005	1.0	1.0	-	-			-	-
OCT Epi TP	0.137	<0.001	1.0	<0.001	1.0	1.0	1.0	0.018	1.0	0.030	-	-	-	-
Pentacam Front Elevation	<0.001	<0.001	0.005	<0.001	0.010	1.0	1.0	0.046	0.007	0.073	0.401	1.0	-	-
Pentacam Back Elevation	<0.001	<0.001	0.001	<0.001	0.002	1.0	0.368	0.217	0.001	0.232	0.130	1.0	1.0	1.0

(Kmax: Maximum keratometry, TP: Corneal thinnest point, OCT: Optical coherence tomography, Epi: Epithelium)

Table 3: Mean difference, 95% limits of agreement and correlation of the cone coordinates along the x and y axes on the front elevation map with the curvature, pachymetry and epithelial thickness maps by different devices. (n= 90 eyes)

Apical cone location on the front elevation map with different maps		**Mean difference±SD (95%CI)**	**95% LoA (1.96 × SD of differences)**	**ICC**	**Correlation**
Pentacam Sagittal curvature (Kmax)	**X-axis**	-0.36±0.83 (-0.53 to -1.17)	-1.99, 1.27 (±1.63)	-0.357 p= 0.959	-0.256 p= 0.015
	Y-axis	-0.42±0.85 (-0.60 to -0.24)	-2.08, 1.24 (±1.66)	0.400 p= 0.002	0.637 p< 0.001
Atlas Mean Curvature (Kmax)	**X-axis**	-0.19±0.57 (-0.31 to -0.07)	-1.31, 0.93 (±1.12)	0.766 p< 0.001	0.740 p< 0.001

	Y-axis	-0.39±0.55 (-0.51 to -0.27)	-1.47, 0.69 (±1.08)	0.354 p= 0.003	0.518 p< 0.001
Pentacam TP	**X-axis**	-0.06±0.09 (-0.08 to -0.04)	-0.24, 0.13 (±0.18)	0.990 p< 0.001	0.962 p< 0.001
	Y-axis	0.01±0.08 (-0.01 to 0.03)	-0.15, 0.17 (±0.16)	0.973 p< 0.001	0.937 p< 0.001
Orbscan TP	**X-axis**	-0.06±0.36 (-0.14 to 0.04)	-0.77, 0.65 (±0.71)	0.905 p< 0.001	0.768 p< 0.001
	Y-axis	-0.14±0.35 (-0.22 to -0.07)	-0.83, 0.55 (±0.69)	0.523 p< 0.001	0.419 p< 0.001
OCT TP	**X-axis**	-0.17±0.35 (-0.24 to -0.10)	-0.86, 0.52 (±0.69)	0.882 p< 0.001	0.722 p< 0.001
	Y-axis	-0.14±0.33 (-0.20 to -0.07)	-0.79, 0.51 (±0.65)	0.632 p< 0.001	0.461 p< 0.001
OCT Epi TP	**X-axis**	-0.15±0.14 (-0.39 to 0.09)	-0.42, 0.12 (±0.27)	0.535 p< 0.001	0.488 p< 0.001
	Y-axis	0.79±1.92 (0.39 to 1.19)	-2.97, 4.55 (±3.76)	-0.054 p= 0.613	0.034 0.747
Pentacam Back Elevation	**X-axis**	0.01±0.11 (-0.01 to 0.04)	-0.23, 0.21 (±0.22)	0.990 p< 0.001	0.982 p< 0.001
	Y-axis	-0.01±0.07 (-0.02 to 0.01)	-0.15, 0.13 (±0.14)	0.984 p< 0.001	0.966 p< 0.001

(LoA: Limits of agreement, Kmax: Maximum keratometry, TP: Corneal thinnest point, OCT: Optical coherence tomography, 95%CI: 95% Confidence interval, ICC: Intra-class correlation coefficient)

Table 4: Mean difference, 95% limits of agreement and correlation of the apex of cone along the x and y axes on the back elevation map with the curvature, pachymetry and epithelial thickness maps by different devices. (n= 90 eyes)

Apical cone location on the back elevation map with different maps		**Mean difference±SD (95%CI)**	**95% LoA (1.96 × SD of differences)**	**ICC**	**Correlation**
Pentacam Sagittal curvature (Kmax)	**X-axis**	-0.38±0.82 (-0.55 to -0.20)	-1.98, 1.22 (±1.60)	-0.310 p= 0.942	-0.248 p= 0.018
	Y-axis	-0.42±0.85 (-0.59 to -0.24)	-2.09, 1.25 (±1.67)	0.398 p= 0.003	0.625 p< 0.001
Atlas Mean Curvature (Kmax)	**X-axis**	-0.21±0.57 (-0.33 to -0.09)	-1.32, 0.91 (±1.12)	0.760 p< 0.001	0.732 p< 0.001
	Y-axis	-0.38±0.55 (-0.50 to -0.27)	-1.46, 0.70 (±1.08)	0.363 p= 0.002	0.529 p< 0.001
Pentacam TP	**X-axis**	-0.08±0.14 (-0.11 to -0.05)	-0.35, 0.139 (±0.27)	0.981 p< 0.001	0.955 p< 0.001
	Y-axis	0.02±0.08 (-0.00 to 0.03)	-0.158, 0.08 (±0.16)	0.972 p< 0.001	0.941 p< 0.001
Orbscan TP	**X-axis**	-0.09±0.37 (-0.15 to 0.00)	-0.81, 0.63 (±0.72)	0.905 p< 0.001	0.764 p< 0.001
	Y-axis	-0.14± 0.37 (-0.21 to -0.06)	-0.86, 0.58 (±0.72)	0.494 p< 0.001	0.373 p< 0.001

OCT TP	**X-axis**	-0.19±0.35 (-0.26 to -0.11)	-0.86, 0.53 (±0.67)	0.901 p< 0.001	0.766 p< 0.001
	Y-axis	-0.13±0.32 (-0.20 to -0.07)	-0.76, 0.50 (±0.63)	0.628 p< 0.001	0.456 p< 0.001
OCT Epi TP	**X-axis**	-0.17±1.15 (-0.41 to 0.07)	-2.42, 2.08 (±2.25)	0.515 p< 0.001	0.479 p< 0.001
	Y-axis	0.80±1.94 (0.39 to 1.20)	-4.60, 3.00 (±3.80)	-0.081 p= 0.664	-0.001 p= 0.994
Pentacam Front Elevation	**X-axis**	-0.01±0.11 (-0.04 to 0.01)	-0.23, 0.21 (±0.22)	0.990 p< 0.001	0.982 p< 0.001
	Y-axis	0.01±0.07 (-0.01 to 0.02)	-0.15, 0.13 (±0.14)	0.984 p< 0.001	0.966 p< 0.001

(LoA: Limits of agreement, Kmax: Maximum keratometry, TP: Corneal thinnest point, OCT: Optical coherence tomography, 95% CI: 95% Confidence interval, ICC: Intra-class correlation coefficient)

Table 5: Frequency distribution of the cone location on the front/back elevation, anterior sagittal/mean curvature and pachymetry/epithelial thickness maps by different devices. (n=90 eyes)

Apical Cone Location / Map	n (%)								Total
	I	IN	IT	N	S	SN	ST	T	
Pentacam Front Elevation	0	2 (2.2)	85 (94.4)	1 (1.1)	0	0	0	2 (2.2)	90 (100)
Pentacam Back Elevation	0	1 (1.1)	87 (96.7)	1 (1.1)	0	0	0	1 (1.1)	
Pentacam Sagittal Curvature (Kmax)	5 (5.6)	64 (71.1)	16 (17.8)	0	0	1 (1.1)	4 (4.4)	0	
Pentacam Thickness	1 (1.1)	0	87 (96.7)	0	1 (1.1)	0	1 (1.1)	0	
OCT Epi Thickness	0	9 (10)	40 (44.4)	0	0	7 (7.8)	34 (37.8)	0	
OCT Pachymetry	0	10 (11.1)	79 (87.8)	0	0	0	1 (1.1)	0	
Atlas Mean Curvature (Kmax)	6 (6.7)	8	74 (82.2)	0	0	1 (1.1)	1 (1.1)	0	
Orbscan Thickness	3 (3.3)	5 (5.6)	79 (87.8)	0	0	0	3 (3.3)	0	

(I: Inferior, IN: Inferonasal, IT: Inferotemporal, N: Nasal, S: Superior, SN: Superanasal, ST: Superatemporal, T: Temporal, n: Number of the eyes)