Research Square

Preprints are preliminary reports that have not undergone peer review.
They should not be considered conclusive, used to inform clinical practice,
or referenced by the media as validated information.

Impact of tear film osmolarity in keratometric interchangeability: a prospective bivariate vector analysis of three contemporary imaging devices

Tyll Jandewerth
Goethe-University
Klemens P. Kaiser
Goethe-University
Elias Golschan
Goethe-University
Petra Davidova
Goethe-University
Thomas Kohnen
Kohnen@em.uni-frankfurt.de
Goethe-University

Research Article

Keywords: Tear film osmolarity, interchangeability, keratometry, vector analysis

Posted Date: July 29th, 2026

DOI: https://doi.org/10.21203/rs.3.rs-10467160/v1

License: This work is licensed under a Creative Commons Attribution 4.0 International License.
Read Full License

Additional Declarations: Competing interest reported. KPK: Lecturing for Oculus and he received an ESCRS Peter Barry Fellowship Grant. TK: Consultant, Research and Lecturing for Alcon, Oculus, Schwind, Staar. Consultant and Lecturing for Tarsus, Ziemer. Research and Lecturing for Teleon Surgical. Consulting for Abbvie, Geuder, LensGen, Santen, Stadapharm, Thieme, Zeiss Meditec. Lecturing for Allergan, Bausch & Lomb, Johnson & Johnson, MedUpdate, streamedup. All conflicts of interest are outside of the submitted work. All other authors have no financial interests to declare.

Abstract

Background

To assess the interchangeability of keratometry and astigmatism measurements from three ophthalmic imaging devices using bivariate vector analysis depending on tear film osmolarity.

Methods

In this prospective study, 3 repeated measurements were performed with the IOLMaster 700 (IOLM), Pentacam AXL (PC), and Galilei G6 (G6) in 97 eyes of 97 patients. Patients were stratified by tear film osmolarity into four groups (≤ 299, 300–309, 310–319, ≥ 320 mOsm/L). Interchangeability was evaluated using pairwise difference vector (DV) analysis, Bland-Altman limits of agreement (LoA), intraclass correlation coefficients (ICC), and bivariate vector analysis of Cartesian X and Y components.

Results

Mean DV magnitude was smallest for difference between IOLMaster 700 and Pentacam (IOLM-PC) (0.775 diopter (D)), followed by IOLM-G6 (0.932 D) and PC-G6 (0.945 D). The proportion of eyes below the 1.5 D threshold was significantly higher for IOLM-PC (89.7%) than for IOLM-G6 (78.4%, adj. p = 0.046) and PC-G6 (79.4%, adj. p = 0.046). Bland-Altman LoA were wide across all pairs (± 0.87 to ± 0.98 D). ICC for the X component ranged from 0.770 to 0.830; the PC-G6 Y component showed notably lower agreement (ICC = 0.591). In eyes with borderline osmolarity (300–309 mOsm/L), G6 exhibited a systematic horizontal bias of + 0.23 D relative to both other devices.

Conclusion

None of the three device pairs met interchangeability criteria for toric IOL planning. IOLM and PC showed the closest agreement. Tear film osmolarity selectively modulated inter-device discordance, most prominently at 300–309 mOsm/L osmolarity levels, underscoring the importance of device consistency prior to toric IOL surgery.

Trial registration

The study was registered at the German Clinical Trial Register (ID DRKS00040992)

BACKGROUND

According to the subcommittee of the International Dry Eye Workshop, dry eye disease (DED) can be defined as a “multifactorial disease of the tears and ocular surface that results in symptoms of discomfort, visual disturbance, and tear film instability with potential damage to the ocular surface” and can be “accompanied by increased osmolarity of the tear film and subacute inflammation of the ocular surface”. (1) Recent studies have shown that, additionally, DED can be defined with the characteristics of an inflammatory disease that has many features in common with autoimmune diseases. (2, 3) DED was

postulated to affect approximately 11–30% of individuals in western countries (4–6) and is associated with a substantial impact on visual acuity, quality of life, work productivity, and carries a physical and psychological burden. (7–9) Nevertheless, the impact on diagnostic approaches, e.g. on surgical planning of refractive and cataract procedures or on diagnosis of corneal ectatic diseases, must not be underestimated, too, and is subject of current research. (10–12)

For all those diagnostic approaches available, accurate and precise measurements are essential, since even minor variability may significantly influence clinical decision-making, such as early detection of subtle corneal changes or toric intraocular lens calculation. (13, 14) While repeatability and agreement of these devices have been extensively studied, less is known about factors that may compromise interchangeability between the different devices. (15, 16)

Imaging platforms that are currently available include Scheimpflug-based devices, swept-source optical coherence tomography (SS-OCT) biometers, and hybrid systems that combine both imaging modalities. They provide three-dimensional high-resolution reconstructions of the anterior segment and are used for obtaining reliable measurements of corneal curvature, elevation, and pachymetry, as well as axial length and lens power calculations. As one example of the latest generation of Scheimpflug-based devices, the Pentacam AXL (PC) (Oculus Optikgeräte GmbH, Wetzlar, Germany) integrates corneal tomography with optical biometry, thereby broadening its diagnostic application and impact on surgical planning. (17) Similarly for SS-OCT technology, the IOLMaster 700 (IOLM) (Carl Zeiss Meditec AG, Jena, Germany) as a reference standard in modern cataract surgery planning provides precise measurements of axial length, keratometry, anterior chamber depth, and lens thickness. (18) Combining dual-Scheimpflug tomography with Placido-disc topography and optical biometry, the Galilei G6 (G6) (Ziemer Ophthalmic Systems AG, Port, Switzerland) offers the evaluation of corneal morphology, tomography and ocular dimensions in a single device. (19) Several devices are often considered in the clinical decision-making process and single measurement parameter could be compared to each other.

The present study therefore investigates the interchangeability of corneal keratometry parameters obtained with the IOLMaster 700, the Pentacam AXL, and the Galilei G6 in relation to tear film osmolarity.

METHODS

Study design

This prospective clinical trial was performed at the Department of Ophthalmology, Goethe-University Frankfurt, Germany, between March 2022 and October 2025. The principles of the Declaration of Helsinki were strictly followed, all patients provided informed consent, and the study protocol was approved by the local ethics committee (approval number: 2021 – 433).

Inclusion and exclusion criteria

Patients were included in the study with age ≥ 18 years and otherwise healthy eyes who visited the cataract consultation hour at the Department of Ophthalmology. After they agreed in participating, they were provided with and signed informed consent. Patients were excluded if they had any active ocular pathology that could affect the planned measurements like acute or chronic corneal diseases, any prior intraocular surgery or trauma, any eye drops application 30 minutes before the measurements or contact lens wearing two weeks prior to the study visit.

Measurements

The patients received three repeated measurements on one eye using IOLMaster 700 (Version 1.90.12.05), Pentacam AXL (Version 1.33r03) and the Galilei G6 (Version 2.6.0). The study eye and the sequence of measurements were randomized by drawing a sequence number out of a raffle box. Measurements were performed by a trained and blinded member of the study team. To maintain independent measurements and to avoid repeated measurement bias, the patient was asked to stand up and sit down again after each measurement. All measurements with bad quality feedback (otherwise than “OK”) were excluded and not used for further analysis. For analysis of interchangeability, curvature radii values of the flat and steep meridian of the anterior corneal surface measurements were used. The values were transformed into keratometry values using the same refractive index (n = 1.3375).

Tear film osmolarity was measured with the TearLab Osmolarity System (TearLab Corporation, San Diego, CA, USA) following the initial measurements. After applying the test card to the test pen, the patient was advised to look straight. The tip of the test pen was placed above the temporal lower eyelid in front of the inferior tear film meniscus without pulling it down. The tip of the test pen was lowered down into the tear film meniscus and turned green after successful tear collection. The test pen was then placed back into the test station, and the test result was shown on the test station screen. For classification of tear film osmolarity, the patient collective was divided into four groups depending on the osmolarity values: group 1 (≤ 299 mOsm/L; Osmo1), group 2 (300–309 mOsm/L; Osmo2), group 3 (310–319 mOsm/L, Osmo3) and group 4 (≥ 320 mOsm/L, Osmo4). This classification is based on the grading system of a modified DED severity scale by Sullivan et al. (20)

Statistical Analysis and Sample Size Calculation

To minimize inter-measurement variability, the mean of three consecutive acquisitions was computed and used for all subsequent analyses. Astigmatism measurements were decomposed into Cartesian X and Y components and analyzed using the vector analysis framework of the Wilcoxon-Holladay-Wang-Koch software implemented in R (version 4.3.1; R Foundation for Statistical Computing, Vienna, Austria). (21–23) Astigmatism classification in double-angle plots and the corresponding Cartesian X and Y components are illustrated schematically in Fig. 1. In the double-angle representation, each astigmatism vector is plotted at twice its axis angle, converting the 180° periodicity of astigmatism into a full 360° circle. The X-component (horizontal) represents with-the-rule/against-the-rule astigmatism, and the Y-

component represents oblique astigmatism at 45°/135°. Difference vectors (DV) were computed for all three device pairs (IOLM-PC, IOLM-G6, PC-G6), and the DV magnitude as twice the Euclidean distance between components. Mean DV magnitudes were compared using Wilcoxon signed-rank tests, and proportions of eyes below predefined DV magnitudes thresholds (0.25 to 2.0 D) using McNemar's test. For the bivariate analysis, 95% bootstrap confidence regions were constructed for the mean and median of each pair's X-Y distribution; the corresponding p-value tests whether the centroid is significantly displaced from the origin, indicating systematic inter-device bias. Pairwise centroid comparisons between device pairs used robust bootstrap tests on difference scores, and total variance (sum of marginal variances of X and Y components, in D^2) was compared using the Morgan-Pitman test with HC4 correction. Additionally, Bland-Altman analysis was performed separately for the X and Y components to assess systematic bias and limits of agreement (LoA = mean difference ± 1.96 SD), with 95%-confidence interval (CI) computed for the mean bias and LoA. (24) Proportional bias was evaluated by regression of the difference on the mean. Intraclass correlation coefficients (ICC, two-way mixed-effects model, absolute agreement) were calculated separately for the X and Y components. All analyses were repeated across four tear film osmolarity subgroups. P-values were Holm-adjusted; statistical significance was defined as $p < 0.05$.

The sample size calculation relies on the following assumptions: a significance level of alpha = 0.0125 and a test strength of 80%, a clinically relevant mean difference of 0.5 and a standard deviation of 0.43 diopter for the keratometry readings. Then, a case number of at least 22 patients per group was needed to achieve a test power of 80%. To compensate for a drop-out rate of about 5%, data from at least 23 patients per group and a total of 92 patients should be included in the study.

RESULTS

The study included 97 eyes of 97 patients from which 52 were female (53.61%). Mean age was 64.9 ± 12.1 years (range 25.9 to 90.2 years). Demographic, astigmatism and keratometry data including the different osmolarity groups are shown in Table 1.

Table 1
Patients' demographic, characteristics and keratometry and astigmatism values of the three devices.

Characteristic	**Osmo1 (n = 23)**	**Osmo2 (n = 24)**	**Osmo3 (n = 24)**	**Osmo4 (n = 26)**	***p*-value[a]**
Age (years; mean, 95%-CI)	68.65 ± 9.61 (64.46, 72.77)	66.29 ± 12.18 (−61.21, 71.58)	64.08 ± 11.52 (−59.19, 68.91)	61.04 ± 13.67 (−55.52, 66.56)	0.231
Sex (female; n; %)	14; 60.9%	9; 37.5%	11; 45.8%	18; 69.2%	0.109
Eye (right; n; %)	10; 43.5%	10; 41.7%	10; 41.7%	13; 50%	0.885
Osmolarity (mOsm/l; mean, 95%-CI)	291.70 ± 6.87 (288.72, 294.67)	305.67 ± 3.41 (304.67, 307.11)	314.5 ± 2.77 (313.33, 315.67)	329.24 ± 7.88 (326.19, 332.42)	< 0.001
K_1 (D; mean, 95%-CI)					
IOLMaster 700	43.515 (42.977, 44.053)	42.941 (42.371, 43.512)	43.389 (42.711, 44.066)	43.315 (42.726, 43.904)	0.574X
Pentacam AXL	43.330 (42.746, 43.915)	42.682 (42.119, 43.245)	42.958 (42.259, 43.657)	42.933 (42.295, 43.572)	0.455
Galilei G6	43.318 (42.766, 43.870)	42.713 (42.129, 43.297)	43.017 (42.264, 43.770)	43.053 (42.430, 43.060)	0.599
K_2 (D; mean, 95%-CI)					
IOLMaster 700	44.391 (43.774, 45.008)	43.797 (43.202, 44.392)	44.220 (43.531, 44.910)	44.130 (43.473, 44.786)	0.606
Pentacam AXL	44.149 (43.516, 44.782)	43.472 (42.916, 44.029)	43.721 (43.026, 44.416)	43.740 (43.027, 44.452)	0.435

[a]Kruskal-Wallis-Test, p < 0.05 statistically significant; 95%-CI = 95% confidence interval; D = diopter; K_1 = flat keratometry; K_2 = steep keratometry; K_m = mean keratometry.

Characteristic	Osmo1 (n = 23)	Osmo2 (n = 24)	Osmo3 (n = 24)	Osmo4 (n = 26)	*p*-value[a]
Galilei G6	44.202 (43.582, 44.822)	43.669 (43.094, 44.243)	43.138 (43.138, 44.547)	43.918 (43.226, 44.610)	0.688
K_m (D; mean, 95%-CI)					
IOLMaster 700	43.953 (43.385, 44.521)	43.369 (42.797, 43.941)	43.805 (43.126, 44.483)	43.722 (43.105, 44.339)	0.530
Pentacam AXL	43.740 (43.143, 44.337)	43.078 (42.530, 43.624)	43.340 (42.646, 44.033)	43.337 (42.666, 44.008)	0.471
Galilei G6	43.760 (43.184, 44.336)	43.191 (42.621, 43.761)	43.430 (42.707, 44.153)	43.486 (42.834, 44.138)	0.639
Astigmatism (D; mean, 95%-CI)					
IOLM700	0.876 (0.653, 1.100)	0.855 (0.633, 1.078)	0.832 (0.670, 0.993)	0.815 (0.628, 1.002)	0.992
Pentacam AXL	0.819 (0.576, 1.062)	0.790 (0.558, 1.022)	0.763 (0.624, 0.901)	0.806 (0.632, 0.981)	0.901
Galilei G6	0.883 (0.659, 1.107)	0.956 (0.751, 1.160)	0.825 (0.634, 1.016)	0.865 (0.682, 1.048)	0.845

[a]*Kruskal-Wallis-Test, p < 0.05 statistically significant; 95%-CI = 95% confidence interval; D = diopter; K_1 = flat keratometry; K_2 = steep keratometry; K_m = mean keratometry.*

Difference vector magnitudes

Considering all eyes, mean DV magnitudes was smallest for IOLM-PC (0.775 D), followed by IOLM-G6 (0.932 D) and PC-G6 (0.945 D). Pairwise comparisons of mean DV magnitudes did not reach statistical significance (all adj. p > 0.10). At the 1.5 D threshold, however, significantly more eyes fell below the cutoff for IOLM-PC (89.7%) than for IOLM-G6 (78.4%, adj. p = 0.046) and PC-G6 (79.4%, adj. p = 0.046); no other threshold comparison was significant. Within osmolarity subgroups, DV magnitudes ranking

followed the same pattern, but no pairwise comparison reached significance in any subgroup. An exception was Osmo4, where PC-G6 yielded the lowest mean DV magnitudes (0.634 D), reversing the general rank order.

Bivariate vector analysis

The centroid of the DV distribution (reflecting systematic directional bias) was closest to the origin for IOLM-PC across all groups (full cohort: X = + 0.025 D, Y = -0.018 D). The larger positive X-centroids of IOLM-G6 (+ 0.108 D) and PC-G6 (+ 0.083 D) indicate a consistent rank order IOLM > PC > G6 in horizontal astigmatic power, with G6 recording the least with-the-rule astigmatism of the three devices. This pattern was most pronounced in Osmo2, where the X-centroids of IOLM-G6 (+ 0.228 D) and PC-G6 (+ 0.240 D) were markedly elevated compared to IOLM-PC (-0.011 D), indicating that G6 underestimated horizontal astigmatic power by approximately 0.23 to 0.24 D relative to both other devices - roughly nine-fold larger than in the full cohort. Double angle plots of the full cohort of the 3 pairwise device comparisons are shown in Fig. 2. Each panel displays the X and Y components of the difference vectors (DV) for one device pair. The centroid (mean DV) with its 95%-CI bootstrap confidence region (convex hull) is shown. Displacement of the centroid from the origin indicates systematic directional bias.

In the full cohort, none of the three device pairs showed a bivariate mean significantly displaced from the origin (all mean-based $p > 0.05$), indicating no statistically significant systematic bias. The median-based test was significant for IOLM-PC ($p = 0.046$), reflecting distributional asymmetry rather than a systematic offset, given the near-origin centroid. In Osmo2, the mean-based tests for IOLM-G6 ($p = 0.042$) and PC-G6 ($p = 0.008$) were significant, consistent with the centroid findings. In Osmo1, only the median-based IOLM-PC comparison was significant ($p = 0.032$); all remaining subgroup comparisons were non-significant.

IOLM-PC showed the lowest total variance across all analyses. In the full cohort, total variance was 0.285 D^2 for IOLM-PC, 0.368 D^2 for IOLM-G6, and 0.423 D^2 for PC-G6, with no pairwise differences reaching significant deviation from the null vector (all adjusted $p > 0.17$). In Osmo3, the total variance of PC-G6 (0.664 D^2) was significantly greater than that of IOLM-PC (0.446 D^2; adj. $p = 0.002$), representing an approximately 49% increase in dispersion driven predominantly by the Y-component (0.308 vs. 0.098 D^2). No other variance comparison reached significance in any subgroup.

Bland-Altman Analysis

Bland-Altman analysis was performed separately for the X and Y Cartesian components of the difference vectors (Table 2). Across the full cohort, bias was smallest for IOLM-PC in both components (X: +0.025 D, 95%-CI -0.064 to + 0.114; Y: -0.019 D, 95% CI -0.079 to + 0.042), with neither CI excluding zero. For IOLM-G6, the X-component bias was + 0.108 D (95%-CI + 0.012 to + 0.204), the only instance in the full cohort where the CI excluded zero, confirming a small but statistically significant systematic

offset. LoA were wide across all pairs, ranging from approximately ± 0.87 D (IOLM-PC Y) to ± 0.98 D (PC-G6 X), exceeding the clinically relevant threshold of ± 0.50 D typically applied in toric IOL planning. Bland-Altman plots of the three pairwise comparisons for all eyes are shown in Fig. 3. Each plot displays the difference (first minus second device) against the mean of two devices for the Cartesian X component and Y component.

Table 2
Bland-Altman limits of agreement (LoA) for Cartesian X and Y components of astigmatism difference vectors between device pairs, for all eyes and osmolarity subgroups. Differences computed as first device - second device.

		Cartesian X				Cartesian Y			
Group	Device pair	Bias (D) [95%-CI]	LoA lower (D) [95%-CI]	LoA upper (D) [95%-CI]	SD (D)	Bias (D) [95%-CI]	LoA lower (D) [95%-CI]	LoA upper (D) [95%-CI]	SD (D)
All eyes (n = 97)	**IOLM – PC**	+ 0.025 [-0.064, + 0.114]	-0.839 [-0.992, -0.685]	+ 0.889 [+ 0.735, + 1.043]	0.441	-0.018 [-0.079, + 0.042]	-0.608 [-0.713, -0.503]	+ 0.571 [+ 0.466, + 0.676]	0.301
	IOLM – G6	+ 0.108* [+ 0.012, + 0.204]	-0.823 [-0.989, -0.657]	+ 1.039 [+ 0.873, + 1.205]	0.475	+ 0.022 [-0.054, + 0.098]	-0.716 [-0.847, -0.584]	+ 0.760 [+ 0.629, + 0.892]	0.376
	PC – G6	+ 0.083 [-0.018, + 0.184]	-0.896 [-1.071, -0.722]	+ 1.062 [+ 0.888, + 1.236]	0.500	+ 0.041 [-0.043, + 0.125]	-0.775 [-0.920, -0.629]	+ 0.856 [+ 0.711, + 1.001]	0.416
Osmo1 (n = 23)	**IOLM – PC**	+ 0.039 [-0.155, + 0.234]	-0.841 [-1.178, -0.505]	+ 0.920 [+ 0.584, + 1.257]	0.449	+ 0.031 [-0.121, + 0.183]	-0.659 [-0.922, -0.395]	+ 0.720 [+ 0.457, + 0.984]	0.352
	IOLM – G6	-0.001 [-0.200, + 0.199]	-0.907 [-1.253, -0.560]	+ 0.906 [+ 0.559, + 1.252]	0.462	-0.053 [-0.207, + 0.101]	-0.751 [-1.017, -0.484]	+ 0.644 [+ 0.378, + 0.911]	0.356

*Bias 95% confidence interval (95%-CI) excludes zero, a statistically significant systematic offset ($p < 0.05$). D = diopter; LoA = Limits of Agreement (Bias ± 1.96*SD); SD = standard deviation; 95%-CI shown in brackets.

	PC – G6	-0.040 [-0.249, + 0.169]	-0.988 [-1.351, -0.626]	+ 0.909 [+ 0.546, + 1.271]	0.484	-0.084 [-0.292, + 0.124]	-1.026 [-1.386, -0.666]	+ 0.858 [+ 0.498, + 1.218]	0.481
Osmo2 (n = 24)	**IOLM – PC**	-0.011 [-0.166, + 0.143]	-0.729 [-0.997, -0.461]	+ 0.706 [+ 0.438, + 0.974]	0.366	-0.050 [-0.163, + 0.063]	-0.575 [-0.771, -0.379]	+ 0.475 [+ 0.279, + 0.670]	0.268
	IOLM – G6	+ 0.228* [+ 0.013, + 0.444]	-0.771 [-1.144, -0.398]	+ 1.228 [+ 0.855, + 1.601]	0.510	+ 0.061 [-0.080, + 0.202]	-0.595 [-0.839, -0.350]	+ 0.716 [+ 0.472, + 0.961]	0.334
	PC – G6	+ 0.240 [-0.002, + 0.482]	-0.883 [-1.302, -0.464]	+ 1.362 [+ 0.943, + 1.781]	0.573	+ 0.111 [-0.025, + 0.247]	-0.519 [-0.754, -0.284]	+ 0.741 [+ 0.506, + 0.977]	0.322
Osmo3 (n = 24)	**IOLM – PC**	+ 0.042 [-0.207, + 0.291]	-1.114 [-1.545, -0.683]	+ 1.198 [+ 0.766, + 1.629]	0.590	+ 0.015 [-0.118, + 0.147]	-0.600 [-0.829, -0.370]	+ 0.629 [+ 0.400, + 0.859]	0.314
	IOLM – G6	+ 0.147 [-0.071, + 0.366]	-0.867 [-1.245, -0.488]	+ 1.162 [+ 0.783, + 1.540]	0.518	+ 0.077 [-0.129, + 0.283]	-0.879 [-1.235, -0.522]	+ 1.032 [+ 0.676, + 1.389]	0.487
	PC – G6	+ 0.105 [-0.146, + 0.357]	-1.063 [-1.499, -0.627]	+ 1.274 [+ 0.838, + 1.710]	0.596	+ 0.062 [-0.173, + 0.296]	-1.026 [-1.432, -0.620]	+ 1.150 [+ 0.744, + 1.556]	0.555

*Bias 95% confidence interval (95%-CI) excludes zero, a statistically significant systematic offset ($p < 0.05$). D = diopter; LoA = Limits of Agreement (Bias ± 1.96*SD); SD = standard deviation; 95%-CI shown in brackets.

Osmo4 (n = 26)	**IOLM – PC**	+ 0.031 [-0.111, + 0.173]	-0.657 [-0.903, -0.411]	+ 0.719 [+ 0.473, + 0.965]	0.351	-0.063 [-0.175, + 0.048]	-0.602 [-0.795, -0.410]	+ 0.476 [+ 0.283, + 0.668]	0.275
	IOLM – G6	+ 0.057 [-0.107, + 0.220]	-0.737 [-1.021, -0.454]	+ 0.851 [+ 0.567, + 1.134]	0.405	+ 0.003 [-0.125, + 0.132]	-0.621 [-0.844, -0.398]	+ 0.627 [+ 0.405, + 0.850]	0.318
	PC – G6	+ 0.026 [-0.090, + 0.142]	-0.536 [-0.737, -0.336]	+ 0.588 [+ 0.387, + 0.789]	0.287	+ 0.067 [-0.034, + 0.168]	-0.423 [-0.598, -0.248]	+ 0.557 [+ 0.382, + 0.732]	0.250

*Bias 95% confidence interval (95%-CI) excludes zero, a statistically significant systematic offset ($p < 0.05$). D = diopter; LoA = Limits of Agreement (Bias ± 1.96*SD); SD = standard deviation; 95%-CI shown in brackets.

In the osmolarity subgroups, LoA were broadly comparable to the full cohort, with no subgroup showing substantially narrower agreement. The most pronounced systematic offsets were again observed in Osmo2, where IOLM-G6 (X-bias: +0.228 D, 95% CI + 0.046 to + 0.410) and PC-G6 (X-bias: +0.240 D, 95% CI + 0.063 to + 0.417) both showed CI excluding zero, while IOLM-PC remained unbiased (X-bias: -0.011 D). No significant proportional bias was detected in any osmolarity subgroup.

Intraclass correlation coefficients

ICC were calculated separately for the X and Y Cartesian components for all eyes, as well as for the 4 osmolarity groups separately and are shown in **Table 3**.

Table 3. Intraclass correlation coefficients (ICC) for Cartesian X and Y components of astigmatism measurements between device pairs, stratified by osmolarity group.

Group	Pair	ICC Cartesian X	ICC 95%-CI	ICC Cartesian Y	ICC 95%-CI
All eyes (n = 97)	IOLM-PC	0.830	0.756, 0.883	0.775	0.682, 0.844
	IOLM-G6	0.794	0.704, 0.858	0.714	0.600, 0.799
	PC-G6	0.770	0.675, 0.840	0.591	0.445, 0.706
Osmo1 (n = 23)	IOLM-PC	0.870	0.718, 0.943	0.717	0.438, 0.869
	IOLM-G6	0.860	0.697, 0.938	0.773	0.539, 0.897
	PC-G6	0.848	0.675, 0.933	0.489	0.108, 0.746
Osmo2 (n = 24)	IOLM-PC	0.903	0.790, 0.957	0.835	0.659, 0.925
	IOLM-G6	0.781	0.537, 0.901	0.758	0.521, 0.887
	PC-G6	0.723	0.451, 0.871	0.730	0.473, 0.873
Osmo3 (n = 24)	IOLM-PC	0.644	0.328, 0.829	0.800	0.589, 0.908
	IOLM-G6	0.687	0.407, 0.850	0.656	0.353, 0.835
	PC-G6	0.545	0.193, 0.774	0.502	0.129, 0.750
Osmo4 (n = 26)	IOLM-PC	0.856	0.706, 0.933	0.750	0.522, 0.879
	IOLM-G6	0.819	0.638, 0.914	0.717	0.460, 0.863
	PC-G6	0.909	0.808, 0.958	0.768	0.552, 0.888

95%-CI = 95%-confidence interval (95%-CI); G6 = Galilei G6; IOLM = IOLMaster 700; Osmo1 = osmolarity group 1; Osmo2 = osmolarity group 2; Osmo3 = osmolarity group 3; Osmo4 = osmolarity group 4; PC = Pentacam AXL

DISCUSSION

The present study investigated the interchangeability of astigmatism measurements in eyes with dry eye disease, stratified by tear film osmolarity, obtained with three widely used ophthalmic imaging devices: the IOLMaster 700, Pentacam AXL, and Galilei G6. The central finding of this study is that none of the device pairs met formal interchangeability criteria based on the LoA threshold of ± 0.50 D clinically relevant for toric IOL planning, and that inter-device agreement was selectively modulated by tear film osmolarity rather than uniformly degraded across all osmolarity levels.

Across all analyses, DV magnitude, bivariate centroid analysis, total variance, Bland-Altman LoA, and ICC, the IOLMaster 700 and Pentacam AXL showed the best mutual agreement, while pairs involving the Galilei G6 showed consistently larger discordance. This hierarchy was most apparent in the bivariate centroid analysis and Bland-Altman results, where the X-component bias for IOLM-G6 was the only pair across the full cohort whose 95%-CI excluded zero (+ 0.108 D, 95%-CI + 0.012 to + 0.204), indicating a small but statistically significant systematic underestimation of with-the-rule astigmatism by the Galilei G6 relative to the IOLMaster 700. Previous work has similarly demonstrated discordance between Scheimpflug-based and SS-OCT-based devices: Hoffmann et al. reported DV magnitudes of approximately 0.43 D to 0.70 D between tomographic and refractive astigmatism measurements, with the largest DV observed for the Pentacam. (25) Wang et al. found higher anterior corneal astigmatism values for SS-OCT-based devices compared to a dual Scheimpflug device and a more significantly correlation in with-the-rule astigmatism, against-the-rule astigmatism and oblique astigmatism for the SS-OCT-based device. (26) Another research group reported that measurements obtained with the Pentacam are not directly interchangeable with those acquired using other devices, particularly SS-OCT-based instruments. (27) The LoA values exceeding ± 0.50 D observed in the present study are therefore clinically relevant, as they may affect toric IOL axis selection and power calculation, particularly when the inter-device discordance approaches or exceeds the threshold at which a cylinder correction would change.

A notable finding of the subgroup analysis was the selective deterioration of inter-device agreement in the Osmo2 group (300–309 mOsm/L), where both IOLM-G6 and PC-G6 showed statistically significant systematic horizontal biases of approximately + 0.23 D, while IOLM-PC remained well-aligned. This osmolarity range corresponds to borderline tear film instability according to the classification of Sullivan et al., and may represent a particularly vulnerable state in which tear film irregularities cause differential measurement artifacts depending on the optical principle of the device. (20, 28) The SS-OCT-based IOLMaster 700 and the Scheimpflug-based Pentacam AXL may be less susceptible to tear film surface irregularities at this osmolarity level than the dual-Scheimpflug/Placido-disc system of the Galilei G6, though this hypothesis requires further investigation. In contrast, the highest osmolarity group (Osmo4, ≥ 320 mOsm/L) showed the best inter-device agreement overall, with PC-G6 even yielding the lowest mean DV magnitude (0.634 D), which may reflect the more stable - albeit pathologically reduced - tear film in severely dry eyes. Increased dispersion of PC-G6 differences in Osmo3 (total variance 0.664 vs. 0.446 D^2 for IOLM–PC; adj. p = 0.002) further supports a graded and device-specific influence of tear film quality on measurement variability.

The ICC analysis corroborated the Bland-Altman findings. ICC values for the Cartesian X component ranged from 0.770 to 0.830 across all eyes, indicating good but not excellent agreement. The most clinically concerning finding was the ICC of 0.591 (95%-CI 0.445–0.706) for PC-G6 in the Y component across all eyes, falling below the conventionally accepted threshold of 0.75 for clinical interchangeability. This was further reduced to 0.489 in Osmo1 and 0.502 in Osmo3, suggesting that oblique astigmatism is particularly susceptible to inter-device discordance and that this is not exclusively a function of tear film osmolarity but may also reflect fundamental differences in measurement technology.

Several strengths of the present study merit consideration. First, the three devices investigated (IOLMaster 700, Pentacam AXL, and Galilei G6) represent distinct and complementary optical technologies (swept-source OCT, Scheimpflug tomography, and dual-Scheimpflug/Placido-disc imaging, respectively) that are among the most widely used platforms in contemporary cataract and refractive surgery practice, enhancing the clinical relevance and generalizability of the findings. Second, the prospective study design with randomization of both the study eye and the device measurement sequence minimized selection bias and systematic order effects, ensuring that differences observed between devices reflect true inter-device variability rather than measurement fatigue or tear film depletion artifacts. Third, the use of three consecutive measurements per device with subsequent averaging increased the robustness and reproducibility of the data, reducing the influence of single-measurement outliers on the comparative analysis. Fourth, the application of a comprehensive, multi-layered analytical framework, including DV magnitude analysis, bivariate confidence area testing, Bland-Altman analysis, total variance comparison, and ICC, provided a thorough and methodologically rigorous assessment of interchangeability that goes beyond the pairwise agreement statistics reported in most previous studies. Finally, the stratification by tear film osmolarity using a validated, standardized classification system allowed for a systematic investigation of how a quantifiable, clinically measurable tear film parameter modulates inter-device agreement, a question that has not previously been addressed in this form.

Several limitations of the present study must be acknowledged. First, the sample size of 97 eyes, while meeting the pre-specified power calculation for the primary endpoint, results in subgroup sizes of 23 to 26 eyes, which limits the precision of confidence intervals and the detection of smaller osmolarity-dependent effects. Second, the study population consisted of patients attending a cataract consultation, which may not be representative of all DED subtypes. Third, while three repeated measurements were performed and averaged, the influence of measurement order and blink-related tear film recovery between measurements was not systematically analyzed. Finally, the present study focused on corneal astigmatism measured by keratometry; the relationship between inter-device discordance and postoperative toric IOL outcomes was not assessed and would require a separate prospective trial.

CONCLUSION

This prospective study demonstrates that none of the three investigated device pairs (IOLMaster 700, Pentacam AXL, and Galilei G6) meets formal interchangeability criteria for astigmatism measurement in

eyes with dry eye disease, based on clinically relevant LoA thresholds for toric IOL planning. Across all analytical approaches, the IOLMaster 700 and Pentacam AXL showed the closest mutual agreement, while pairs involving the Galilei G6 exhibited consistently greater discordance. Importantly, inter-device agreement was not uniformly degraded by tear film dysfunction but was selectively and most severely compromised in eyes with borderline tear film osmolarity (300–309 mOsm/L), where the Galilei G6 showed a systematic underestimation of horizontal astigmatic power relative to both other devices. These findings have direct clinical implications: in patients with DED scheduled for toric IOL implantation, measurements from different devices should not be used interchangeably. Preoperative repeated measurements with the same device may reduce measurement variability and improve surgical outcomes in this population.

Abbreviations

CI
95%-confidence interval
D
diopter
DED
dry eye disease
DV
difference vector
G6
Galilei G6
ICC
intraclass correlation coefficients
IOLM
IOLMaster 700
K_1
flat keratometry
K_2
steep keratometry
K_m
mean keratometry
LoA
Bland-Altman limits of agreement
Osmo1
osmolarity group 1
Osmo2
osmolarity group 2
Osmo3

osmolarity group 3
Osmo4
osmolarity group 4
PC
Pentacam AXL
SD
standard deviation
SS-OCT
swept-source optical coherence tomography

Declarations

Ethics approval and consent to participate

All patients provided informed consent, and approval has been granted by the local ethic committee.

Consent for publication

All authors have read and agreed to the published version of the manuscript.

Availability of data and materials

All data generated or analysed during this study are included in this article. Further enquiries can be directed to the corresponding author.

Competing interests

KPK: Lecturing for Oculus and he received an ESCRS Peter Barry Fellowship Grant. TK: Consultant, Research and Lecturing for Alcon, Oculus, Schwind, Staar. Consultant and Lecturing for Tarsus, Ziemer. Research and Lecturing for Teleon Surgical. Consulting for Abbvie, Geuder, LensGen, Santen, Stadapharm, Thieme, Zeiss Meditec. Lecturing for Allergan, Bausch & Lomb, Johnson & Johnson, MedUpdate, streamedup. All conflicts of interest are outside of the submitted work. All other authors have no financial interests to declare.

Funding

No specific funding was received for this study.

Authors´ contributions

T.J., E.G., P.D., T.K., K.P.K

Conceptualization, T.J., K.P.K.; methodology, T.J., K.P.K.; formal analysis, T.J., K.P.K.; investigation, T.J.; data curation, T.J., K.P.K.; writing—original draft preparation, T.J., K.P.K., E.G. and P.D.; writing—review and

editing, T.J., K.P.K., E.G. and P.D.; visualization, T.J., K.P.K.; supervision, T.K.

Acknowledgements

No acknowledgements.

References

1. The definition and classification of dry eye disease: report of the Definition and Classification Subcommittee of the International Dry Eye WorkShop. (2007). Ocul Surf. 2007;5(2):75–92.
2. Stevenson W, Chauhan SK, Dana R. Dry eye disease: an immune-mediated ocular surface disorder. Arch Ophthalmol. 2012;130(1):90–100.
3. Stern ME, Schaumburg CS, Pflugfelder SC. Dry eye as a mucosal autoimmune disease. Int Rev Immunol. 2013;32(1):19–41.
4. Malet F, Le Goff M, Colin J, Schweitzer C, Delyfer MN, Korobelnik JF, et al. Dry eye disease in French elderly subjects: the Alienor Study. Acta Ophthalmol. 2014;92(6):e429–36.
5. Viso E, Rodríguez-Ares MT, Abelenda D, Oubiña B, Gude F. Prevalence of asymptomatic and symptomatic meibomian gland dysfunction in the general population of Spain. Invest Ophthalmol Vis Sci. 2012;53(6):2601–6.
6. Vehof J, Kozareva D, Hysi PG, Hammond CJ. Prevalence and risk factors of dry eye disease in a British female cohort. Br J Ophthalmol. 2014;98(12):1712–7.
7. Stapleton F, Alves M, Bunya VY, Jalbert I, Lekhanont K, Malet F, et al. TFOS DEWS II Epidemiology Report. Ocul Surf. 2017;15(3):334–65.
8. Morthen MK, Magno MS, Utheim TP, Snieder H, Hammond CJ, Vehof J. The physical and mental burden of dry eye disease: A large population-based study investigating the relationship with health-related quality of life and its determinants. Ocul Surf. 2021;21:107–17.
9. van Tilborg MM, Murphy PJ, Evans KS. Impact of Dry Eye Symptoms and Daily Activities in a Modern Office. Optom Vis Sci. 2017;94(6):688–93.
10. Biela K, Winiarczyk M, Gumieniak-Goch B, Mackiewicz J. The Effect of Dry Eye Disease Treatment Prior to Cataract Surgery on Refractive Error Reduction. J Clin Med. 2026;15(4).
11. Coco G, Messmer EM, Starr CE, Pereira-Gomes JA, Lazreg S, Budimlija N, et al. A Practical Approach for Optimizing Ocular Surface Status Before Cataract Surgery to Improve Visual Outcomes and Reduce the Risk of Postoperative Dry Eye. Ophthalmol Ther. 2025;14(11):2697–733.
12. Jiang Y, Chen X, Gao Y, Gao N, Wang H, Feng Y, et al. Impact of tear film stability on corneal refractive power measurement and surgical planning for cataract. Adv Ophthalmol Pract Res. 2025;5(2):100–6.
13. Ramsauer M, Luft N, Vounotrypidis E, Priglinger SG, Mayer WJ. Accuracy of toric intraocular lens power calculation depending on different keratometry values using a novel network based software platform. Front Med (Lausanne). 2024;11:1363286.

14. Kreps EO, Jimenez-Garcia M, Issarti I, Claerhout I, Koppen C, Rozema JJ. Repeatability of the Pentacam HR in Various Grades of Keratoconus. Am J Ophthalmol. 2020;219:154–62.
15. Tariq U, Parveen S, Mahmood Wazir S, Khan TA, Zahid MA, Tariq Bangash M. Comparative Analysis of Keratometric and Pachymetry Values From Corneal Topography Scans: A Comparison Between Pentacam and Galilei. Cureus. 2024;16(6):e61993.
16. Kundu G, Shetty N, Modak D, Kaweri L, Khamar P, Arora V, et al. Repeatability and agreement of a new anterior segment optical coherence tomography with standard devices in normal, keratoconus, and post-refractive eyes. Indian J Ophthalmol. 2025;73(3):325–34.
17. Wan KH, Liao XL, Yu M, Tsui RWY, Chow VWS, Chong KKL, et al. Wavefront aberrometry repeatability and agreement-A comparison between Pentacam AXL Wave, iTrace and OPD-Scan III. Ophthalmic Physiol Opt. 2022;42(6):1326–37.
18. Michael R, Wirkner K, Engel C, Loeffler M, Kirsten T, Rauscher FG. Feasibility and repeatability of ocular biometry measured with IOLMaster 700 in a large population-based study. Ophthalmic Physiol Opt. 2023;43(4):860–73.
19. Moshirfar M, Tenney S, McCabe S, Schmid G. Repeatability and reproducibility of the galilei G6 and its agreement with the pentacam® AXL in optical biometry and corneal tomography. Expert Rev Med Devices. 2022;19(4):375–83.
20. Sullivan BD, Whitmer D, Nichols KK, Tomlinson A, Foulks GN, Geerling G, et al. An objective approach to dry eye disease severity. Invest Ophthalmol Vis Sci. 2010;51(12):6125–30.
21. Kohnen T, Næser K, Holladay JT, Stulting RD, Wang L, Abulafia A, et al. Standards for analyzing astigmatic outcomes: Part I: astigmatism basics. J Cataract Refract Surg. 2025;51(6):440–6.
22. Koch DD, Holladay JT, Naeser K, Abulafia A, Wang L, Stulting RD, et al. Standards for analyzing astigmatic outcomes: Part II: Recommended statistical methods. J Cataract Refract Surg. 2025;51(6):447–55.
23. Koch DD, Kohnen T. Setting standards for astigmatism analysis. J Cataract Refract Surg. 2025;51(6):439.
24. Bland JM, Altman DG. Statistical methods for assessing agreement between two methods of clinical measurement. Lancet. 1986;1(8476):307–10.
25. Hoffmann PC, Abraham M, Hirnschall N, Findl O. Prediction of residual astigmatism after cataract surgery using swept source fourier domain optical coherence tomography. Curr Eye Res. 2014;39(12):1178–86.
26. Wang L, Cao D, Vilar C, Koch DD. Posterior and total corneal astigmatism measured with optical coherence tomography-based biometer and dual Scheimpflug analyzer. J Cataract Refract Surg. 2020;46(12):1652–8.
27. Wang L, Shao X, Fu JL, Hu JJ, Zhou KJ, Li R, et al. Repeatability and Agreement of 4 Biometers Measuring Corneal Astigmatism in Eyes With Irregular Corneal Astigmatism Component. Am J Ophthalmol. 2024;265:200–12.

28. Lemp MA, Bron AJ, Baudouin C, Del Benítez JM, Geffen D, Tauber J, et al. Tear osmolarity in the diagnosis and management of dry eye disease. Am J Ophthalmol. 2011;151(5):792–e81.

Figures

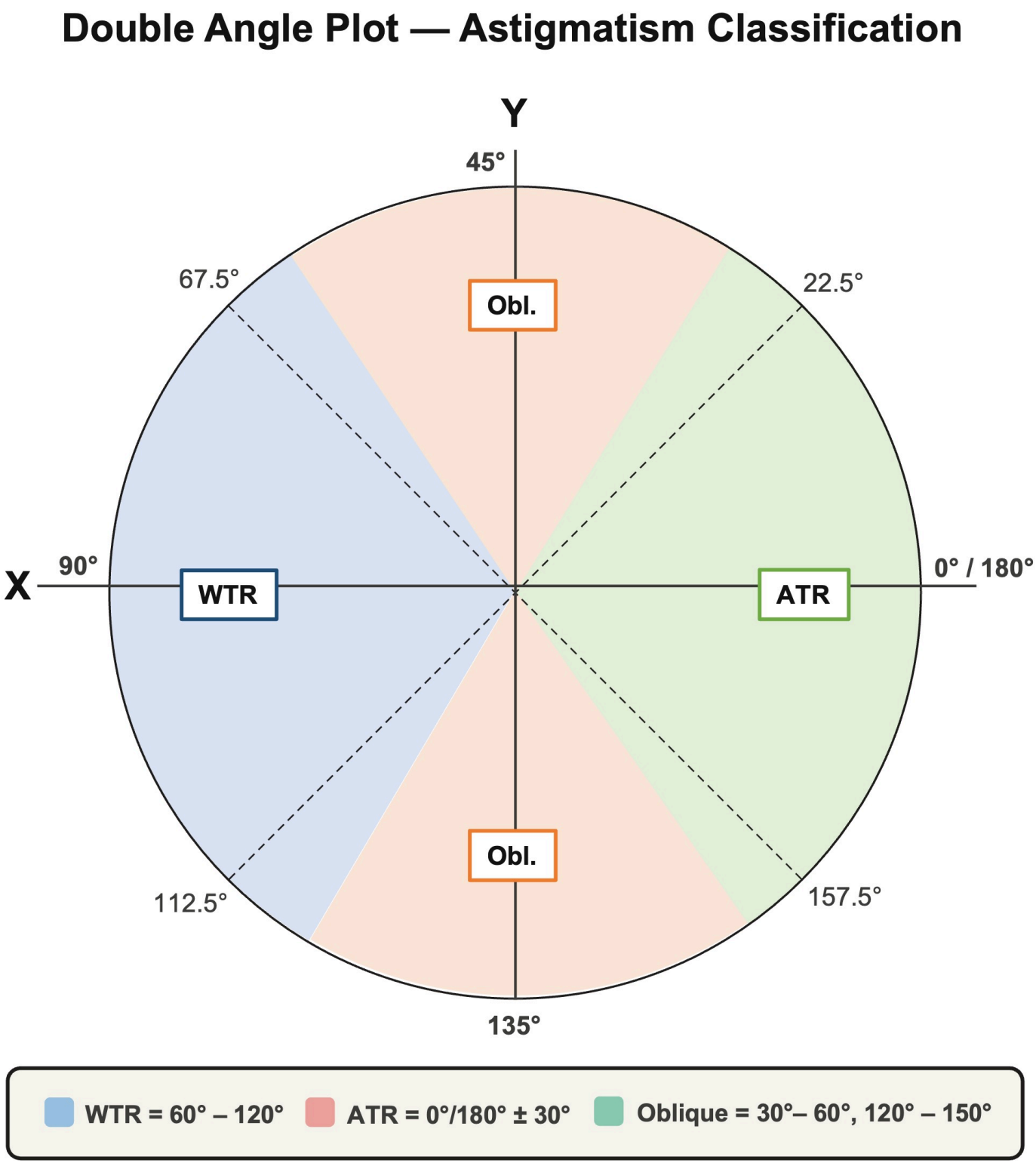


Figure 1

Schematic illustration of astigmatism classification using double-angle plots and the corresponding Cartesian X and Y components.

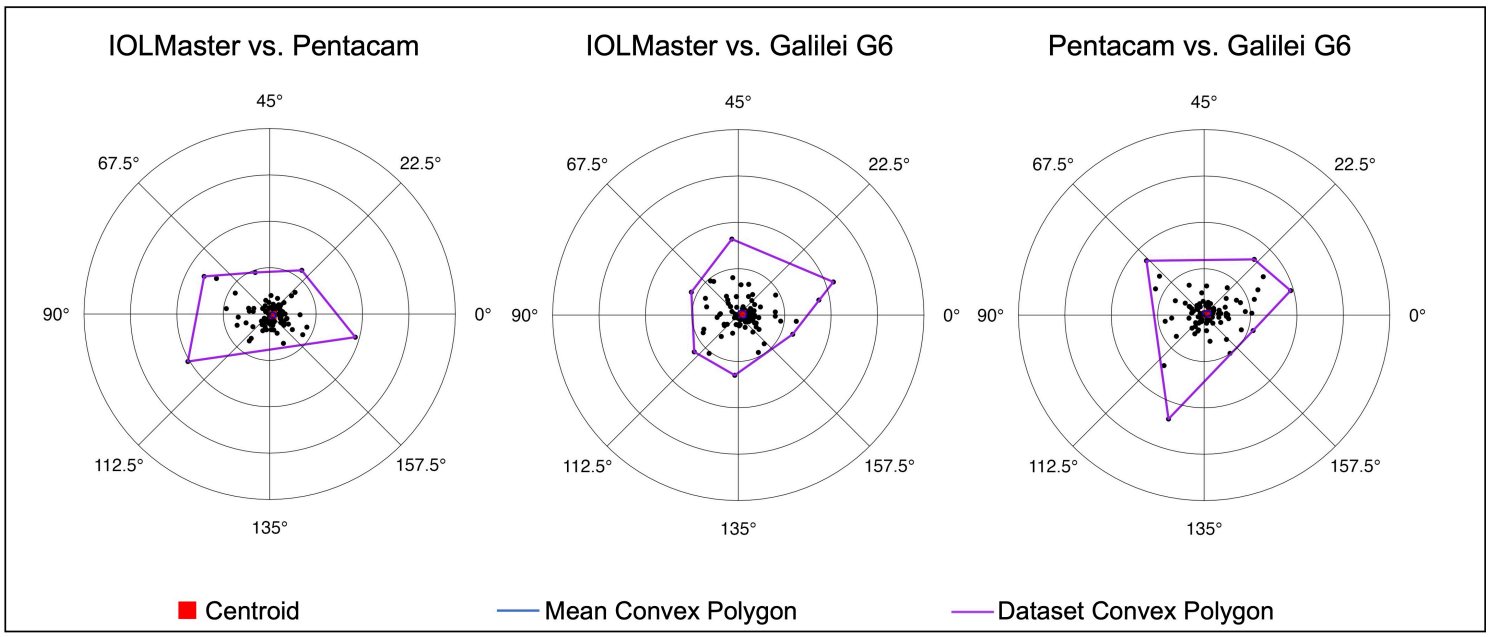


Figure 2

Double-angle plots of pairwise device comparisons for the full cohort (*n*=97).

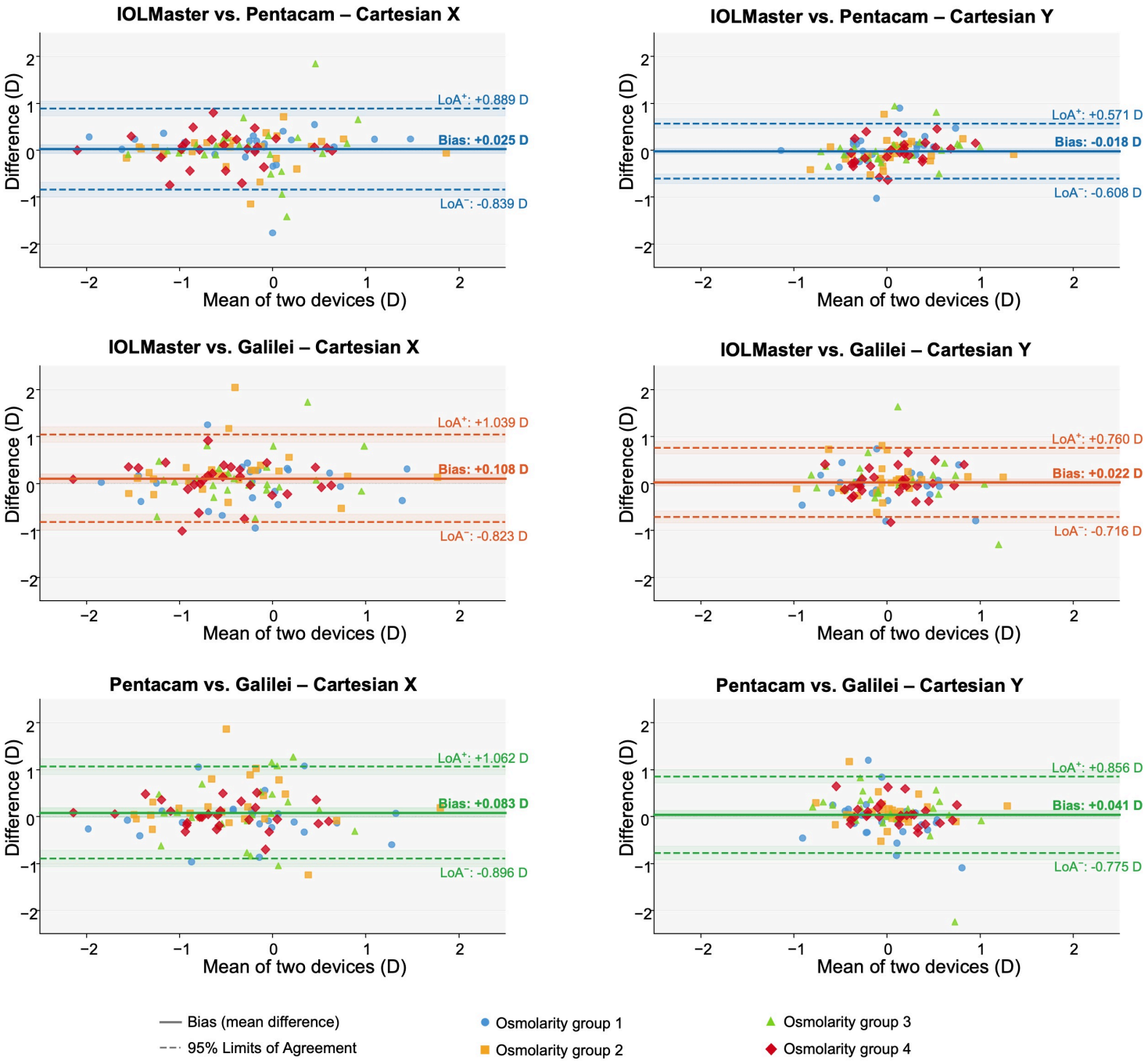


Figure 3

Bland-Altman plots for pairwise astigmatism comparisons across all eyes (n=97).