Comparison of Artemis 2 Ultrasound and Visante Optical Coherence Tomography Corneal Thickness Profiles

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ABSTRACT

PURPOSE: To compare corneal thickness profiles of cross-sections of cornea determined by arc-scanned immersion ultrasound and optical coherence tomography (OCT).

METHODS: Corneas of 28 eyes from 14 participants were scanned in triplicate using the Artemis 2 high-frequency arc-scanned ultrasound system (ArcScan Inc) and the Visante OCT system (Carl Zeiss Meditec). Corneal thickness and reproducibility were compared within 3.5 mm of central cornea in the horizontal plane.

RESULTS: Although highly correlated, Visante central and peripheral corneal thickness values were systematically thinner than Artemis 2 values. Within the central 0.5 mm, the difference was approximately 8 μm, but the difference increased with distance from the center. Reproducibility for each instrument was comparable, measuring <4 μm centrally and increasing peripherally.

CONCLUSIONS: Visante OCT measurements of corneal thickness are thinner than Artemis 2 ultrasound values centrally with an increasing difference with peripheral position. Measurement reproducibility was comparable for the two techniques. [*J Refract Surg*. 2013;29(1):36-41.]

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Corneal imaging and biometric analysis may be performed by ultrasound and optical techniques including Scheimpflug photography, scanning slit systems, and optical coherence tomography (OCT). Contact ultrasound pachymetry (USP) is widely considered the gold standard for measurement of central corneal thickness (CCT). Pachymeters, however, require topical anesthesia and may cause corneal compression and thus affect accuracy.[1,2] Although USP can in principle measure peripheral corneal thickness (PCT), manual positioning is susceptible to problems in reproducibility. Ultrasound biomicroscopy systems using a fluid standoff between the probe and the eye can provide cross-sectional corneal images while avoiding contact. Ultrasound biomicroscopy systems, however, do not provide a fixation target or allow systematic scanning in a series of ordered planes or meridians, limiting reproducibility.[3] The Artemis 2 high-frequency ultrasound system (Arcscan Inc, Morrison, Colorado), however, includes optical monitoring of eye position and a fixation target during scanning. It also utilizes arc-shaped scan geometry with a fluid standoff that is advantageous in maximizing sensitivity and minimizing potential distortions due to refraction. Scanning speed, however, is relatively slow, and sequential meridians must be scanned one by one.

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Dr Silverman has a commercial interest in Arcscan, Inc. The remaining authors have no financial interest in the materials presented herein.

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In contrast to ultrasound, optical systems are advantageous in providing high speed, noncontact examinations, but require ray-trace models to compensate for refraction to reconstruct corneal geometry. Only a limited number of studies have compared PCT among instruments. No study has yet compared noncontact (immersion) ultrasound PCT with optical techniques. This study compares the Artemis 2 arc-scanned immersion ultrasound to Visante OCT measurements of CCT and PCT to determine the correlation and interchangeability of these two systems and their comparative measurement uncertainties.

PATIENTS AND METHODS

After receiving local institutional review board approval and individual consent, 14 noncontact lens–using healthy participants without diagnosed corneal disease or prior corneal surgery were imaged using Visante OCT and the Artemis 2 ultrasound system. Both eyes were imaged, first by Visante in half of the participants and by Artemis in the other half, with random selection order. All Artemis and Visante imaging was performed by a single physician (M.F.).

Visante

Three corneal scans were acquired in the horizontal meridian for each eye using the high-resolution scan protocol (scan length 10 mm; transverse x axial resolution: 512×1024 pixels). Scans were centered on the corneal vertex as determined by the presence of a strong hyperreflective signal. Corneal thickness was measured using the standard flap tool (set to ‘no flap’) that performed automatic detection of anterior and posterior corneal surfaces and reported corneal thickness in microns and the distance in millimeters from the corneal vertex.

Artemis 2

The Artemis 2 uses a broadband polymer transducer with center frequency of 38 MHz. Three standard cornea protocol scans (256 vectors over a 70° arc with 2048 8-bit axial samples at 500 MSamples/second) were acquired for each eye in the horizontal meridian. This provided an approximate scan depth of 3.2 mm and width in the focal plane of 11 mm. Scans were centered on the corneal vertex based on simultaneous camera views of the pupil and adjustment for maximum echo amplitude, occurring in the focal plane at normal incidence between the ultrasound beam axis and the corneal surface. Corneal scans were analyzed with ArtPro software, which analyzes the stored phase-resolved radiofrequency echo data from each scan. ArtPro automatically selects the width over which the corneal echo data exceed a threshold level sufficient for reliable analysis and then determines the spatial positions of the anterior and posterior corneal surfaces and Bowman layer along each vector within the selected area. A corneal speed-of-sound constant of 1636 m/second was used to convert time-delay measurements to thickness values. The data from ArtPro were postprocessed in MATLAB version 7.11 (MathWorks Inc, Natick, Massachusetts) to correct for decentration.

One of the 28 eyes was excluded from the analysis due to improper calibration. In 11 eyes, only 2 scans (rather than 3) were processed due to eye motion.

Statistical Analysis

The data were analyzed separately for right and left eyes and with both eyes pooled.

The lateral range over which corneal thickness values were determinable with each instrument was determined and compared. Visante and Artemis 2 corneal thickness values were measured at intervals ranging up to 4 mm temporally and nasally about the center, and the position of the thinnest point relative to the center was determined. Artemis and Visante data from both eyes were then arranged from temporal to nasal relative to the thinnest point prior to subsequent analyses.

Mean thickness and repeatability (square root of the mean variance) values for each eye within triplicate scans were determined for both instruments at 0, 0.5, 1.0, 1.75, 2.5, and 3.5 mm temporal and nasal to the thinnest position. We compared CCT values in participants scanned first versus last by Artemis. Bland-Altman plots were generated centrally and at 2.5 mm temporally and nasally. The correlation coefficients were computed between the thicknesses measured by Visante and Artemis 2 at each position and were compared by paired *t* and Wilcoxon test. In addition, an analysis of variance was performed with main effects of position, eye, and instrument. Lastly, left and right eye symmetry was examined by measuring the differences in corneal thickness at equivalent positions in each eye for each instrument.

RESULTS

The scan widths over which valid data were acquired averaged 7.73±0.37 mm for Artemis and 7.42±0.48 mm for Visante (paired, two-tailed t=2.42, P=.022).

The mean position of the thinnest point was 0.78±0.53 mm temporal to the corneal vertex in the Visante and 0.62±0.49 mm temporal in the Artemis 2. This displacement is attributable to deviation between the visual and optic axes with the patient gazing at the fixation target.

The effect of scanning order (ie, Artemis first vs Visante first) was examined in consideration of the

TABLE 1

Corneal Thickness Measurements From Temporal (−) to Nasal (+) Positions for All Eyes

Position (mm)	Mean±SE (μm) Visante	Mean±SE (μm) Artemis	N Pairs	R	Visante−Artemis (μm)	*P* Value
−3.5	607±12	662±12	12	0.934	−15	.006
−2.5	567±6	577±7	24	0.969	−10	<.001
−1.75	550±6	559±7	27	0.977	−9	<.000
−1.0	538±6	546±7	27	0.984	−8	<.001
−0.5	533±6	541±7	27	0.989	−8	<.001
0.0	531±6	539±7	27	0.984	−8	<.001
0.5	534±6	540±7	27	0.981	−6	<.001
1.0	538±6	545±7	27	0.981	−7	<.001
1.75	546±6	557±7	27	0.981	−11	<.001
2.5	559±7	557±7	27	0.978	−12	<.001
3.5	587±8	614±9	25	0.958	−27	<.001

R = correlation coefficient, SE = standard error
P *values are for paired* t *tests (two-tailed).*

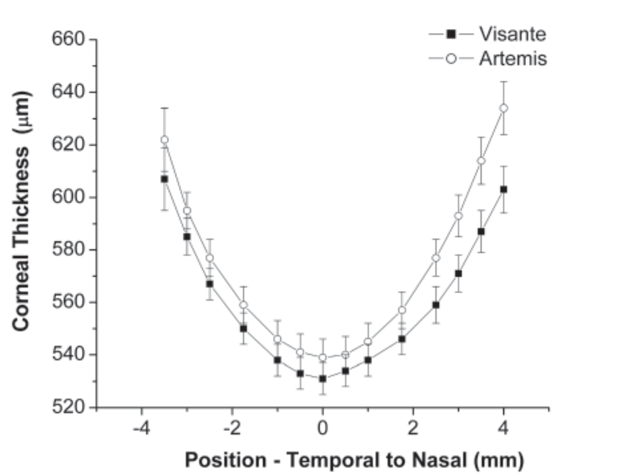

Figure 1. Comparative plots of mean corneal thickness±standard error as a function of horizontal position in Artemis and Visante for all eyes.

potential effects of topical anesthetic drops and the Artemis immersion technique. Thirteen eyes were first scanned by Artemis, and 15 eyes were first scanned by Visante. Central corneal thickness grouped by scan order was not found to be statistically significant by Student *t* or Mann-Whitney U tests.

Tables A and B (available as supplemental material in the PDF version of this article) and Table 1 show the mean values, differences in corneal thickness, and correlation coefficients ±3.5 mm relative to the thinnest point as determined by Artemis and Visante for right, left, and all eyes. The data are presented graphically in Figures A and B (available as supplemental material in the PDF version of this article) and Figure 1.

Correlation coefficients between instruments were approximately >0.98 centrally, decreasing to 0.95 at the periphery. Over all positions and eyes, Visante corneal thickness values were significantly thinner than Artemis values. Centrally, the mean difference was 8 μm, but increased to 15 μm at 3.5 mm temporally and 27 μm at 3.5 mm nasally.

Bland-Altman plots comparing the two devices centrally and 2.5 mm nasally and temporally are presented in Figure 2. The results demonstrate systematic differences between methods, but no error associated with magnitude or proportionality.

The results of *t* and Wilcoxon tests provide overwhelming evidence that the measurements of the two instruments are different ($P<10^{-15}$). The analysis of variance also confirmed the significant effects of instrument (ie, Visante vs Artemis) (F=11.42, $P<.001$) and measurement position (F=202.0, $P<.001$). In addition, a linear effect was associated with measurement position. Eye (left vs right) was not found to be a significant factor.

Figure 3 plots repeatability as a function of position for each device. Within the central ±1 mm, repeatability averaged 3.5 μm for Visante and 3.7 μm for Artemis 2, equivalent to coefficients of variation of 0.65% (Visante) and 0.68% (Artemis). As illustrated in Figure 3, measurement uncertainty increased with distance from the center, with Visante uncertainty increasing somewhat more than Artemis at the periphery.

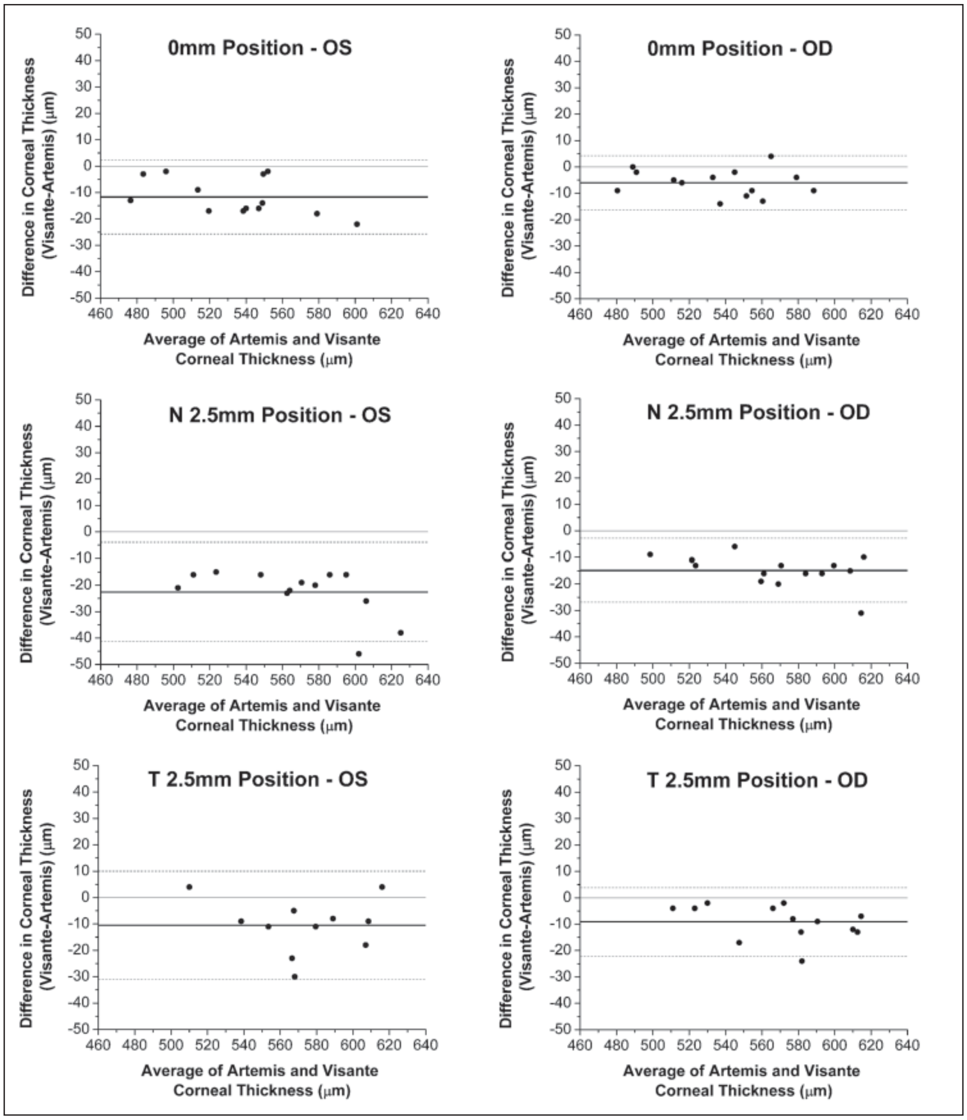

Figure 2. Bland-Altman plots comparing Artemis and Visante determinations of corneal thickness centrally (top), 2.5-mm nasally (middle), and 2.5-mm temporally (bottom) for left (OS) and right (OD) eyes. The solid line represents the mean difference (Visante–Artemis) and dashed lines represent the 95% confidence bounds.

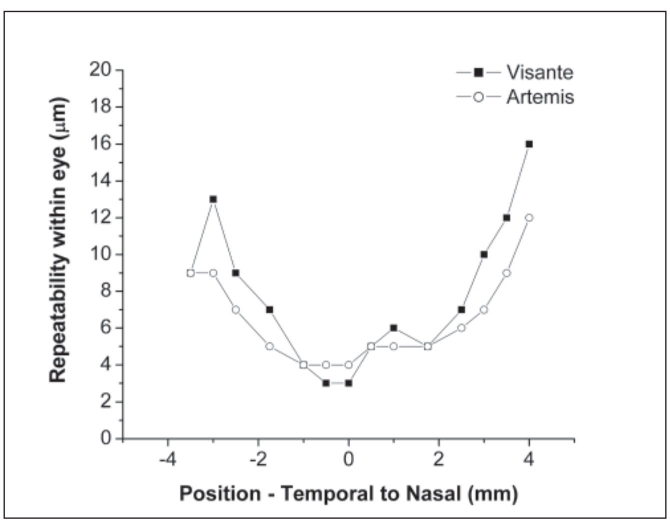

Figure 3. Comparative plots of reproducibility for repeated measurements of corneal thickness as a function of position for Artemis 2 and Visante.

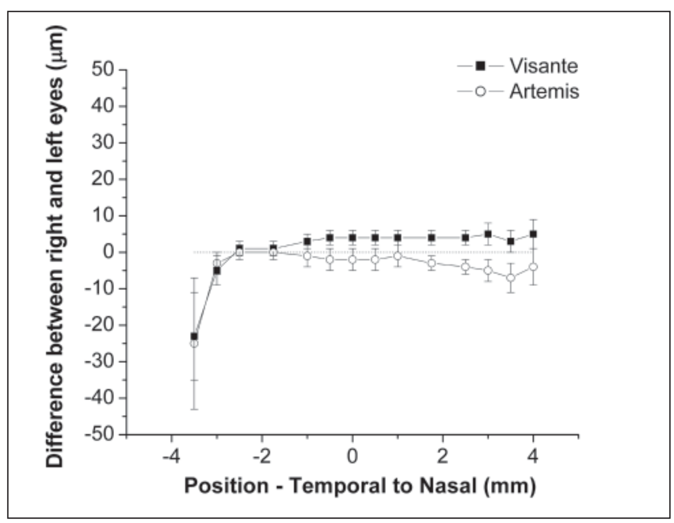

Figure 4. Plot of mean difference±standard deviation between comparable positions on the left and right eyes for Artemis 2 and Visante.

Left/right eye symmetry was examined by comparing thickness values at comparable positions of each eye obtained by each technique. The data, plotted in Figure 4, demonstrate right to left eye symmetry with both methods, with a mean difference between comparable positions of <3 μm within 3 mm of the center.

DISCUSSION

In the present study, we compared central and peripheral corneal thickness values obtained with Artemis 2 arc-scanned high-frequency ultrasound and Visante OCT. Although highly correlated, and with comparable reproducibility, Visante values were systematically thinner than Artemis values, and increasingly so with distance from the center.

Central corneal thickness is appreciated to be an important factor affecting the accuracy of applanation tonometry, and hence, glaucoma screening and management.[4] Central corneal thickness measurement also plays an important function in screening for keratoconus[5] and for preoperative assessment in corneal refractive surgery.[6] Peripheral corneal thickness has been shown to relate to CCT in a regular fashion. Fares et al[7] compared Pentacam CCT and PCT and found PCT values to correlate with CCT (R=0.845 at 3 mm, R=0.635 at 7 mm), concluding that this supports use of CCT as a proxy for PCT. Similarly, Reinstein et al[8] demonstrated that peripheral stromal thickness (and PCT) closely follows a quadratic function of range from the thinnest point along any hemi-meridian (R^2=0.999) using Artemis 1 in normal corneas. Although these findings justify CCT as a reasonable and easily obtained parameter characterizing overall corneal thickness, the corneal cross-sectional profile provides a more complete means for assessing the biometry and biomechanical properties of the cornea than would be the case for measurement of CCT alone, especially where the cornea deviates from the normal pattern. In fact, aberrations from the expected pattern may be useful for detection of such abnormalities such as keratoconus.[9,10] Furthermore, accurate measurement of PCT is of importance in peripheral corneal and limbal procedures (eg, femtosecond laser arcuate keratotomy and intrastromal ring implantation).

Few studies have compared PCT among instruments. González-Méijome et al[11] reported Orbscan (Bausch & Lomb, Rochester, New York, New York) CCT to be significantly thinner (30 μm) than USP, but relatively thicker than USP with increasing distance from the center. Li et al[2] reported Orbscan PCT values to be significantly thicker (mean 10.35 μm) than those obtained with the Visante (Carl Zeiss Meditec, Dublin, California) anterior segment OCT system. Milla et al[12] showed Visante to give consistently thinner results than the Sirius Scheimpflug system (Schwind, Kleinostheim, Germany) centrally and peripherally. Prospero Ponce et al[13] also found Visante PCT to be thinner (by 33.4 μm on average) than Scheimpflug (Pentacam; Oculus, Wetzlar, Germany), although the difference centrally was <1 μm. Buehl et al[14] compared Pentacam, Orbscan, and the AC-Master (Carl Zeiss Meditec) partial coherence interferometer to measure PCT at four points 1.5 mm from the center, noting higher variability and larger differences between all methods at peripheral versus central cornea. Similarly, both González-Pérez et al[15] and Bourges et al[16] found greater measurement variability and differences between Orbscan and Pentacam at peripheral versus central cornea.

It is also appreciated that different techniques provide nonequivalent CCT values. We found Visante OCT CCT to average 8 μm thinner than Artemis 2 immersion high-frequency ultrasound. Paul et al[17] found Artemis 2 CCT values to average 11 μm thinner than USP, which, together with the 8-μm difference observed in our present study, suggests an expected difference between Visante and USP of ~19 μm. This is comparable to differences, averaging ~15 μm, reported in several studies comparing USP with Visante.[2,13,18-20] Although corneal compression by a USP probe may be expected to lead to thinner values than immersion ultrasound, contact probes have a 1- to 2-mm aperture and hence functionally average thickness over the central cornea rather than detecting the thinnest point. In addition, the probe may not be placed on the thinnest point in the central cornea. In contrast, the focal point of the Artemis probe is ~80 μm in diameter and scanning permits identification of the thinnest point.

In terms of reproducibility, both Artemis and Visante were roughly equivalent centrally, having within-examination variability of approximately 3 to 4 μm. This is slightly higher than the 2 μm variability reported both by Li et al[21] using a prototype anterior segment OCT and by Reinstein using the Artemis 1.[8] Piñero et al[22] reported perfect intrasession reproducibility for the Visante and a coefficient of variation of 0.42% (equivalent to approximately 2 μm) for the Artemis 2. Piñero et al also reported no significant difference in CCT measurements between Artemis 2 and Visante; however, their Artemis biometric methods relied on manual caliper placement on images, which is less precise or objective than the automated ArtPro analysis of ultrasound echo data used in our study.

Peripherally, we found that Visante PCT measurements became increasingly thin relative to Artemis values as range from the center increased. Although the 8-μm difference centrally was statistically significant, it is of arguable clinical significance. However, the larger differences with peripheral position call for caution where absolute values of PCT may be required. We attach no particular significance to the almost identical >20 μm difference between left and right eyes measured with both devices at the temporal extreme position. There are fewer data points at this position (because positions are measured relative to the thinnest point, which is temporal to the center) and, as the plot indicates, the uncertainty ranges here are significantly larger than at the other positions.

Although the present study is limited to a small cohort and to the horizontal meridian, the statistical findings are definitive and the general conclusions are likely to be applicable to all meridians. Certainly a larger study comparing Artemis to other techniques, especially Pentacam, is warranted.

The present study showed Visante and Artemis 2 to give reproducible and highly cross-correlated corneal thickness profiles, but that Visante values were systemically thinner. The high axial and lateral resolution of the Artemis, optical monitoring of eye position, provision of fixation light, and avoidance of direct contact between the probe and the cornea confer obvious advantages for Artemis over USP, while retaining its advantage as a "gold standard" ultrasound technique.

AUTHOR CONTRIBUTIONS

Study concept and design (Ro.U., R.H.S.); data collection (Ro.U., M.F.); analysis and interpretation of data (M.F., Ra.U., A.R., R.H.S.); drafting of the manuscript (A.R., R.H.S.); critical revision of the manuscript (Ro.U., M.F., Ra.U., A.R.); statistical expertise (A.R., R.H.S.)

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TABLE A

Right Eye Corneal Thickness Measurements From Temporal (−) to Nasal (+) Position

	Mean±SE (μm)					
Position (mm)	Visante	Artemis	N Pairs	R	Visante−Artemis (μm)	*P* Value
−3.5	610±14	630±9	5	0.852	−20	.067
−2.5	556±9	575±10	13	0.984	−9	<.001
−1.75	551±9	560±10	14	0.987	−9	<.001
−1.0	540±9	546±10	14	0.992	−6	<.001
−0.5	535±9	540±9	14	0.994	−5	<.001
0.0	533±9	539±9	14	0.989	−6	<.001
0.5	536±9	540±9	14	0.990	−4	.012
1.0	540±9	545±10	14	0.982	−5	.038
1.75	548±9	556±10	14	0.983	−8	<.001
2.5	561±10	576±10	14	0.990	−15	<.001
3.5	590±10	612±11	14	0.983	−22	<.001

R = correlation coefficient, SE = standard error
P *values are for paired* t *tests (two-tailed).*

TABLE B

Left Eye Corneal Thickness Measurements From Nasal (−) to Temporal (+) Position

	Mean±SE (μm)					
Position (mm)	Visante	Artemis	N Pairs	R	Visante−Artemis (μm)	*P* Value
−3.5	583±12	616±15	11	0.964	−33	<.001
−2.5	556±10	578±11	13	0.979	−23	<.001
−1.75	543±9	558±11	13	0.990	−15	<.001
−1.0	535±9	545±11	13	0.986	−10	<.001
−0.5	531±10	541±10	13	0.980	−10	.001
0.0	528±10	540±10	13	0.986	−12	<.001
0.5	531±9	541±11	13	0.991	−10	<.001
1.0	536±9	546±10	13	0.978	−10	<.001
1.75	550±9	559±11	13	0.968	−9	.008
2.5	568±10	578±11	11	0.949	−10	.007
3.5	604±20	616±19	7	0.962	−12	.074

R = correlation coefficient, SE = standard error
P *values are for paired* t *tests (two-tailed).*

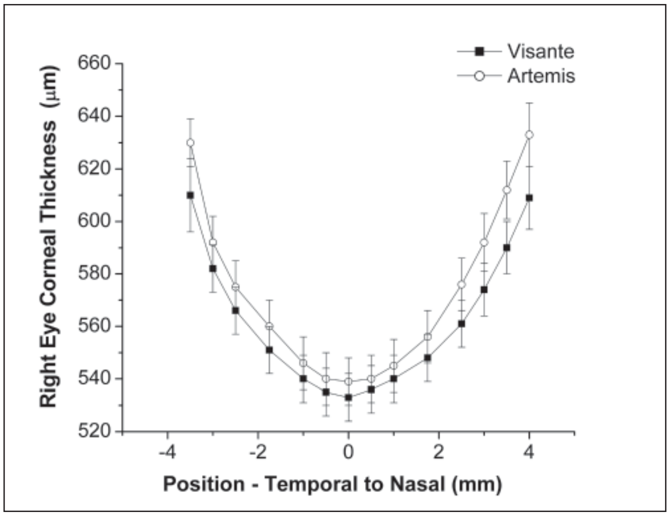

Figure A. Comparative plots of mean corneal thickness±standard error as a function of horizontal position in Artemis and Visante for right eyes.

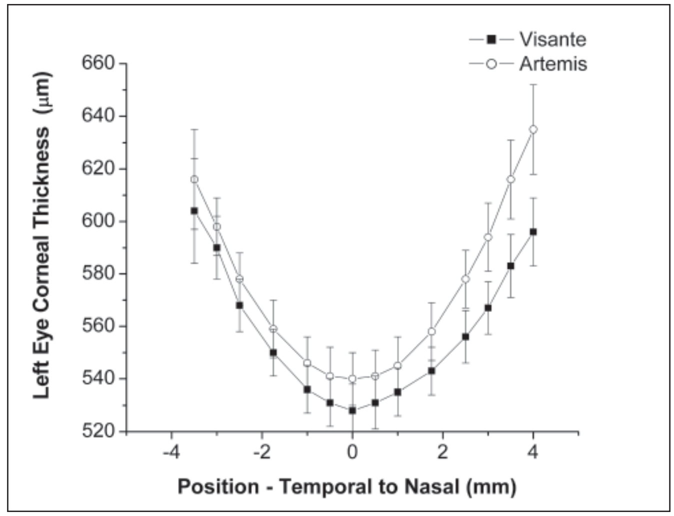

Figure B. Comparative plots of mean corneal thickness±standard error as a function of horizontal position in Artemis and Visante for left eyes.