Heidelberg Anterion Swept-Source OCT Corneal Epithelial Thickness Mapping: Repeatability and Agreement With Optovue Avanti

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ABSTRACT

PURPOSE: To assess the repeatability of corneal epithelial thickness mapping in virgin, post-laser refractive surgery (PLRS), and keratoconic eyes using a novel swept-source optical coherence tomographer (SS-OCT), and to determine the agreement of the measurements with a validated spectral-domain (SD) OCT.

METHODS: Analysis of 90 virgin, 46 PLRS, and 122 keratoconic eyes was performed. Three consecutive measurements of each eye were acquired with the Anterion SS-OCT and Avanti SD-OCT devices, and averages of the epithelial thickness mapping were calculated in the central 2-mm zone and in the 2- to 5-mm and 5- to 7-mm diameter rings. The repeatability was analyzed using pooled within-subject standard deviation (S_w). The agreement was assessed by Bland-Altman analysis and paired *t* tests.

RESULTS: The repeatability ranges of the Anterion and Avanti epithelial thickness mapping measurements were S_w: 0.60 to 1.36 µm and S_w: 0.75 to 1.96 µm, respectively. The 95% limits of agreement of the Anterion and Avanti were 0.826 to 8.297. All values of the thickness measurements with the Anterion were lower than those of the Avanti, with the mean differences being 4.06 ± 1.81, 3.26 ± 2.52, and 3.68 ± 2.51 µm in virgin, PLRS, and keratoconic eyes, respectively ($P < .001$ for all).

CONCLUSIONS: The repeatability of the Anterion's epithelial thickness mapping was higher than that of the Avanti. In terms of the agreement between the Anterion and Avanti, the epithelium measured by the Anterion was always thinner than that of the Avanti, making their interchangeable use unsuitable without corrections.

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As its first cellular layer and refractive medium, the corneal epithelium has an important role in the refractive system of the eye. Being highly reactive to irregularities in the underlying stroma, it is always attempting to smooth the ocular surface by growing thicker over depressions and becoming thinner over bumps, a phenomenon described as epithelial remodeling.[1] This way, the epithelium regularizes the corneal optics and, in most cases, leads to less corneal astigmatism, less change of asphericity, and fewer higher order

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aberrations in both virgin and irregular corneas and as in eyes after refractive surgery,[2,3] compared to the same parameters measured on the stromal surface. The epithelium also decreases the refractive power of the eye by simply increasing the corneal radius of curvature by its thickness.[4] On the other hand, due to the effect of eyelid blinking mechanics, a slightly non-uniform epithelial thickness profile is induced.[5]

Epithelial thickness mapping (ETM) has recently become an indispensable tool in corneal and refractive surgery. It has contributed to the early diagnosis of keratoconus[1,6,7] and subsequently increased the safety of refractive surgery.[8,9] It is also valuable for therapeutic refractive surgery to help further understand irregular astigmatism.[10] ETM was pioneered by Reinstein et al, who were the first to measure[5] and map[11] the corneal epithelium across the whole cornea.[12] They also described the epithelial behavior[1,13-16] after corneal laser refractive surgery[17] and in keratoconus,[1,18] and were the first to use the term "epithelial remodeling."

Reinstein et al also introduced clinically applicable ETM using very high-frequency (VHF) digital ultrasound scanning (Artemis Insight 100; ArcScan, Inc) as early as 1994.[11] ETM based on optical coherence tomography (OCT) appeared in 2011. It did not surpass the former in terms of precision, but due to its ease of use, it became the most prevalent technology in current clinical practice. The first commercially available OCT-based instrument that provided 6-mm diameter epithelial mapping was the Optovue RT-100 (Optovue, Inc), featuring spectral-domain (SD) OCT technology, otherwise mainly used for the posterior segment diagnostics. SD-OCT technology has since been used for ETM on several devices, of which the Avanti (Optovue, Inc) is currently the most prevalent one.[19]

Swept-source (SS) OCT technology with a longer wavelength light source was introduced to allow a greater image depth and high-contrast imaging of the entire anterior segment.[20] The Anterion (Heidelberg Engineering) is a recently introduced, high-resolution anterior segment OCT device featuring SS-OCT technology.[21] However, the manufacturers of both the Anterion and the Casia2 (Tomey Corporation), another anterior segment OCT featuring SS-OCT technology, have yet to release their instruments' ETM capabilities commercially. The current study is the first to measure and analyze the ETM using SS-OCT technology, employing the Anterion's investigational software.

The purpose of this study was to assess the repeatability of ETM measurements with the Anterion across the central 7-mm diameter of the cornea and its agreement with the Avanti SD-OCT for healthy virgin, post-laser refractive surgery (PLRS), and keratoconic eyes. In addition, we analyzed the spatial variations in ETM with the two devices. By using the Avanti as the reference device in this study, we also assessed its repeatability, which previously has been reported only scarcely.[22]

PATIENTS AND METHODS

Ninety virgin eyes of 90 consecutive patients who were candidates for elective laser vision correction or cataract surgery (virgin eyes) and 46 eyes of 45 patients with a history of previous laser refractive surgery (PLRS eyes) were examined at Øyelegesenteret Eye Clinic (Tromsø, Norway), whereas 122 eyes of 118 patients with diagnosed keratoconus (keratoconic eyes) were examined at the Department of Ophthalmology of the University Hospital North Norway. In the virgin eyes, only one eye of each patient was used to avoid statistical bias. In the PLRS and keratoconic groups, we used both eyes from 1 and 4 patients, respectively, because there was a large difference between these patients' 2 eyes. All examinations were performed between March 2020 and February 2021. This was a prospective study approved by the Norwegian Regional Committee for Medical & Health Research Ethics (REK Nord 72084) and it complied with the tenets of the Declaration of Helsinki. All patients provided informed consent for the anonymous use of their data in scientific analyses and publications, following a detailed explanation of the study.

Inclusion criteria were age 18 years or older and healthy virgin corneas for the virgin eyes; age 18 years and older and previous corneal laser vision surgery (both myopic and hyperopic treated eyes) at least 3 months before the examination[23] for the PLRS eyes; and age 16 years or older and a diagnosis of keratoconus and spherical equivalent of myopia of 8.00 diopters (D) or less for the keratoconic eyes. Exclusion criteria were a history of other previous ocular surgery (except for PLRS eyes); patients with pterygium or other conjunctival, limbal, or corneal disease (except for keratoconus); poor fixation or inability to complete the examination; and use of hard contact lenses.

Age, sex, and personal and family history of eye diseases were recorded. Refraction, visual acuity, standard ophthalmological examination with the slit-lamp examination and funduscopy were performed before ETM measurements.

ETM Measurements

The sequence of the ETM measurements with the two devices was randomized. Three consecutive measurements were taken with each device. For both devices, each single measurement lasted approximately 20 seconds, including computer processing, and hanging from one device to the other took less than 10 min-

utes. All examinations were taken by the same experienced examiner (YF) between 10 AM and 2 PM.

The patients were asked to fixate on the device's fixation target to achieve a coaxial position with the infrared camera and the corneal vertex. For each measurement, the examiner centered the scan on the corneal vertex by adjusting the joystick until a bright vertical flare line was seen at the center of the real-time OCT image. Patients were instructed to blink immediately before each measurement to ensure that the tear film would be spread out evenly, and to keep their eyes wide open during the measurement. Patients were then asked to sit back and look away from the fixation light between the measurements. No eye drops were applied during testing.

Anterion

The Anterion SS-OCT generates images using a laser light source with a 1,300-nm wavelength to obtain B-scans with an axial resolution of less than 10 µm and a transversal resolution of 45 µm. An active eye-tracker is used. The software version 1.2.2 with activated investigational epithelium feature provides corneal ETM and various derived statistics. The ETMs are acquired quickest using the "Cornea APP" mode on the device, but the same data are also acquired with the "Cataract APP" mode; both perform 65 radial scans with 256 A-scan lines centered on the corneal vertex over a 7-mm diameter. Acquisition time with the Cornea APP is less than 1 second.

After the acquisition, the instrument presents ETM, displaying mean thicknesses at 41 points, evenly distributed across the map, but the user may measure the epithelium thickness at any given point on the map by pointing the mouse. For comparison with the Avanti, we calculated averages of the same 17 zones/rings/sections that are used by Avanti, shown in **Figure A** (available in the online version of this article). Measurements from the 7- to 9-mm diameter ring on the Avanti were not used in this study. The technical specifications of the device are summarized in **Table A** (available in the online version of this article).

Avanti

The Avanti SD-OCT operates using a super luminescent diode light source at a wavelength of 840 nm. It obtains B-scans with an axial resolution of 5 µm and a transversal resolution of 15 µm. It does not use an eye-tracker. Corneal thickness mapping and ETM are produced using the "pachymetry wide scan pattern" mode and attaching the "long adaptor lens" to the instrument (software v. 6.11.0.12). The ETM measurement consists of eight radial scans at 22.5-degree intervals repeated five times for each meridian, with 1,024 A-scan lines over a 9-mm diameter. Acquisition time is 0.58 second.

ETM and corneal pachymetry maps are generated by an automatic algorithm and divided into a total of 25 sections over a 9-mm diameter: a central 2-mm diameter zone and eight sections equally distributed (superior, superior temporal, temporal, inferior temporal, inferior, inferior nasal, nasal, and superior nasal) within three annular rings (2- to 5-, 5- to 7-, and 7- to 9-mm) (**Figure A**). Only the mean epithelial thickness of each section is presented. Only high-quality images centered at the corneal vertex, with complete coverage and free of motion artifacts, were accepted for analysis. The technical specifications of the device are summarized in **Table A**.

Statistical Analysis

We used vertically mirrored symmetry superimposition: thickness values for left eyes were reflected in the vertical axis and superimposed onto the right eye values so that the nasal/temporal characteristics could be combined.[16]

To assess the repeatability, we calculated pooled within-subject standard deviation (S_w) (lower values of S_w indicate higher repeatability).[24,25] The repeatability limit (r) defined as $1.96 \sqrt{2} \times S_w$ ($= 2.77 \times S_w$) gives the value below which the absolute difference between two measurements would lie with 0.95 probability.[26]

To assess the agreement, we calculated the following parameters: difference in thickness readings (a positive difference indicates a thinner epithelium in the Anterion), 95% limits of agreement (LoA = mean ± 1.96 × standard deviation, and paired two-tailed *t* tests.

The Bland-Altman plot was added to visualize the agreement between the devices.

Data were entered into Microsoft Excel 2016 (Microsoft Corporation) and then imported into a statistical software (SPSS v25; IBM Corporation). A *P* value of less than .05 was considered to be statistically significant.

RESULTS

This study evaluated 258 eyes of 253 patients for both repeatability and agreement analyses. The demographic data are displayed in **Table 1**.

Repeatability

The repeatability of the measurements (expressed as S_w) were calculated in the central 2-mm zone and in the 2- to 5-mm and 5- to 7-mm diameter rings with results displayed in **Table 2** for the three groups of eyes. The repeatability of all 17 sections is shown in **Table B** (available in the online version of this article). S_w ranges for the Anterion were 0.64 to 1.01 µm in virgin eyes, 0.60 to 1.36 µm in PLRS eyes, and 1.15 to 1.36

TABLE 1
Demographic Data

Parameter	Total (n = 258)	Virgin (n = 90)	PLRS (n = 46)	KC (n = 122)
Age (year)				
Mean ± SD	42.00 ± 15.51	48.77 ± 16.83	48.25 ± 13.41	34.53 ± 11.36
Range	16 to 76	18 to 76	21 to 72	16 to 75
Sex				
Male	173	46	29	98
Female	80	44	16	20
Eye				
Right	173	67	31	75
Left	85	23	15	47
Postop time (year)				
Mean ± SD	–	–	6.27 ± 6.51	–
Range	–	–	0.25 to 19.83	–

KC = keratoconus; PLRS = post-laser refraction surgery; postop = postoperative; SD = standard deviation

TABLE 2
Repeatability of ETM Measurements

Group	Repeatability, Sw (Repeatability Limit, r)	
	Anterion	Avanti
Virgin		
Zone 0 to 2 mm	0.64 (1.77)	0.98 (2.72)
Ring 2 to 5 mm	0.79 (2.18)	1.14 (3.15)
Ring 5 to 7 mm	1.01 (2.80)	1.11 (3.08)
Area 0 to 7 mm	0.88 (2.44)	1.12 (3.10)
PLRS		
Zone 0 to 2 mm	0.60 (1.67)	0.75 (2.06)
Ring 2 to 5 mm	0.84 (2.33)	1.40 (3.88)
Ring 5 to 7 mm	1.36 (3.77)	1.96 (5.42)
Area 0 to 7 mm	1.08 (2.99)	1.62 (4.49)
KC		
Zone 0 to 2 mm	1.15 (3.19)	1.37 (3.78)
Ring 2 to 5 mm	1.18 (3.26)	1.45 (4.02)
Ring 5 to 7 mm	1.36 (3.76)	1.60 (4.44)
Area 0 to 7 mm	1.26 (3.49)	1.52 (4.21)
All		
Zone 0 to 2 mm	0.91 (2.52)	1.15 (3.19)
Ring 2 to 5 mm	1.00 (2.77)	1.34 (3.71)
Ring 5 to 7 mm	1.26 (3.49)	1.53 (4.24)
Area 0 to 7 mm	1.12 (3.10)	1.42 (3.39)

ETM = epithelial thickness mapping; KC= keratoconus; PLRS = post-laser refractive surgery
The Anterion is manufactured by Heidelberg Engineering and the Avanti is manufactured by Optovue.

µm in keratoconic eyes. For the Avanti, S_w ranges were 0.98 to 1.11 µm in virgin eyes, 1.37 to 1.96 µm in PLRS eyes, and 1.37 to 1.60 µm in keratoconic eyes.

Agreement Between Anterion and Avanti Measurements

The mean difference in thickness (Avanti minus Anterion), 95% LoA, and paired, two-tailed *t* tests *P* values in the central 2-mm zone and the 2- to 5-mm and 5- to 7-mm diameter rings are displayed in **Table 3** for the three groups. The Anterion showed significantly thinner mean epithelium than the Avanti in all measured areas in all groups of eyes, with a mean difference ranging from 2.66 to 4.35 µm. The difference between the devices was most pronounced in the 2- to 5-mm ring in all three groups of eyes. If we look at the individual eyes, the Anterion measured the central 2-mm zone epithelium thickness thinner than the Avanti in 100% of virgin eyes, 93.48% (43 of 46 eyes) of PLRS eyes, and 87.70% (107 of 122 eyes) of keratoconic eyes.

In all of the 17 sections, the mean difference (Avanti minus Anterion), 95% LoA, and paired, two-tailed *t* tests *P* values are shown in **Table C** (available in the online version of this article). The mean ETM for each of the 17 sections for both Anterion and Avanti, and a map for the difference between the two devices in virgin, PLRS, and keratoconic eyes, are shown in **Figures B-D**, respectively.

Bland-Altman plots for the agreement between the epithelial thickness measured by the Anterion and Avanti for virgin, PLRS, and keratoconic eyes are shown in **Figures E-F**, respectively. The mean difference in epithelial thickness was larger in the virgin eyes than in the other two groups of eyes, whereas the range of 95% LoA was wider in the PLRS and keratoconic eyes than in the virgin eyes. Both the mean difference and the 95% LoA increased from the center to the periphery in all three groups. The epithelial thickness differences in the rings, as well as in the opposite corneal sections in the three groups of eyes, are shown in **Table 4**.

DISCUSSION

The current study investigated for the first time the epithelial thickness mapping obtained by any SS-OCT–based instrument, notwithstanding a recent article[27] reporting ETM measured by the MS-39 (CSO), which is an SD-OCT device, erroneously described as SS-OCT.

The repeatability of the Heidelberg Anterion SS-OCT in the three groups of eyes (virgin, PLRS, and keratoconic) was good, and higher compared to the traditional SD-OCT (the Avanti), whereas the Anterion's

TABLE 3

Agreement of ETM Measurements Between the Two Devices

	Mean ± SD (μm)		Difference		95% LoA (μm)	
Group	**Anterion**	**Avanti**	**Mean ± SD (μm)**	***P***	**Lower**	**Upper**
Virgin						
Zone 0 to 2 mm	51.59 ± 3.27	55.60 ± 3.26	4.02 ± 1.38	< .001	1.307	6.73
Ring 2 to 5 mm	50.93 ± 3.31	55.28 ± 3.25	4.35 ± 1.73	< .001	0.95	7.75
Ring 5 to 7 mm	50.56 ± 3.70	54.34 ± 3.44	3.78 ± 1.93	< .001	-0.001	7.554
Area 0 to 7 mm	50.80 ± 3.49	54.86 ± 3.34	4.06 ± 1.81	< .001	0.523	7.598
PLRS						
Zone 0 to 2 mm	53.79 ± 6.07	56.96 ± 5.87	3.17 ± 1.99	< .001	-0.736	7.069
Ring 2 to 5 mm	54.05 ± 5.68	57.85 ± 5.45	3.80 ± 2.18	< .001	-0.475	8.071
Ring 5 to 7 mm	54.77 ± 6.53	57.50 ± 5.71	2.73 ± 2.93	< .001	-3.002	8.468
Area 0 to 7 mm	54.37 ± 6.10	57.63 ± 5.60	3.26 ± 2.52	< .001	-1.679	8.199
KC						
Zone 0 to 2 mm	50.49 ± 5.69	53.15 ± 5.61	2.66 ± 2.12	< .001	-1.501	6.829
Ring 2 to 5 mm	51.16 ± 4.90	55.12 ± 4.79	3.96 ± 2.14	< .001	-0.237	8.157
Ring 5 to 7 mm	52.55 ± 5.00	56.07 ± 4.36	3.52 ± 2.94	< .001	-2.238	9.273
Area 0 to 7 mm	51.78 ± 5.00	55.45 ± 4.64	3.68 ± 2.51	< .001	-1.253	8.604
All						
Zone 0 to 2 mm	51.46 ± 5.18	54.69 ± 5.19	3.23 ± 1.96	< .001	-0.62	7.07
Ring 2 to 5 mm	51.60 ± 4.86	55.66 ± 4.68	4.07 ± 2.04	< .001	0.075	8.059
Ring 5 to 7 mm	52.25 ± 5.15	55.72 ± 4.52	3.47 ± 2.66	< .001	-1.751	8.689
Area 0 to 7 mm	51.90 ± 5.02	55.63 ± 4.63	3.74 ± 2.33	< .001	-0.826	8.297

ETM = epithelial thickness mapping; KC = keratoconus; LoA = limits of agreement; PLRS = post-laser refractive surgery; SD = standard deviation
The Anterion is manufactured by Heidelberg Engineering and the Avanti is manufactured by Optovue.

TABLE 4

ETM Measurement Differences in the Rings and in the Opposite Sections for Both Devices

	Virgin				PLRS				KC			
	Anterion		Avanti		Anterion		Avanti		Anterion		Avanti	
Parameter	**Mean ± SD (μm)**	***P***	**Mean ± SD (μm)**	***P***	**Mean ± SD (μm)**	***P***	**Mean ± SD (μm)**	**P**	**Mean ± SD (μm)**	***P***	**Mean ± SD (μm)**	***P***
S-I	-4.08 ± 3.24	< .001	-3.16 ± 2.65	< .001	-3.76 ± 5.81	< .001	-3.40 ± 5.69	< .001	-0.43 ± 5.57	.230	-0.76 ± 5.04	.019
T-N	-0.36 ± 2.13	.024	-0.71 ± 1.86	< .001	0.35 ± 4.84	.492	0.10 ± 4.03	0.816	-1.76 ± 5.58	< .001	-1.93 ± 4.53	< .001
ST-IN	-3.1.0 ± 2.67	< .001	-2.93 ± 2.28	< .001	-1.93 ± 4.68	< .001	-1.67 ± 4.55	0.001	-0.57 ± 4.90	.069	-1.05 ± 4.06	< .001
SN-IT	-2.42 ± 3.15	< .001	-1.99 ± 2.53	< .001	-1.96 ± 5.39	.001	-1.93 ± 5.02	< .001	2.02 ± 6.42	< .001	1.55 ± 5.16	< .001
Center-Outer	1.02 ± 2.36	0.007	1.27 ± 2.19	.001	-0.98 ± 4.65	.342	-0.55 ± 4.11	.549	-2.06 ± 5.30	< .001	-2.92 ± 2.55	< .001
Inner-Outer	0.37 ± 2.06	< .001	0.96 ± 1.94	< .001	-0.73 ± 6.75	.041	0.34 ± 5.49	.231	-1.39 ± 4.73	< .001	-0.95 ± 4.13	< .001

Center = central 2 mm; ETM = epithelial thickness mapping; I = inferior; IN = inferior nasal; Inner = 2- to 5-mm diameter ring; IT = inferior temporal; KC = keratoconus; N = nasal; Outer = 5- to 7-mm diameter ring; PLRS = post-laser refractive surgery; S = superior; SN = superior nasal; ST = superior temporal; T = temporal
The Anterion is manufactured by Heidelberg Engineering and the Avanti is manufactured by Optovue.

measurements of the mean epithelial thickness in all 17 sections of all three groups of eyes were lower than the Avanti's.

The first ETM measurements by Reinstein et al[28] with the Artemis VHF digital ultrasound in 1994 showed an S_w of 0.58 μm at the corneal vertex, and 0.43 to 1.36 μm

in 90% of locations within the central 6-mm diameter after five consecutive measurements of 10 eyes of 10 patients 1 year after laser in situ keratomileusis.[28] Their S_w is similar to what we measured with the Anterion (0.60 to 1.36 µm) but lower (ie, higher repeatability) than what we measured with the Avanti (0.75 to 1.96 µm) in the PLRS eyes within the 7-mm diameter. However, repeatability should also be considered in the context of the measurement resolution of the device; VHF digital ultrasound can measure the epithelial thickness with less than 1 µm resolution, whereas OCT devices have a resolution of closer to approximately 5 µm for the Avanti and 8 µm for the Anterion. Therefore, although repeatability may be comparable, it could be expected that the accuracy of OCT devices might be lower than VHF digital ultrasound.

Although introduced 17 years later than the Artemis, ETM in virgin eyes measured by SD-OCT Optovue RT-100 showed an S_w as high as 0.70 µm within the central 2-mm zone and 0.7 to 0.9 µm in the paracentral ring (4 to 6 mm).[29] This is similar to what we obtained in virgin eyes with the Anterion (S_w: 0.64 to 1.01 µm), but lower than what we obtained with Avanti (S_w: 0.98 to 1.14 µm) for the central 2-mm zone and the outer 5- to 7-mm ring.

Sedaghat et al[22] calculated the repeatability of ETM with the Avanti within the 7-mm zone of 52 eyes before and after photorefractive keratectomy, and found an S_w of 1.73 µm preoperatively and 4.50 µm 6 months postoperatively. Within the 7 mm zone, our data showed a lower S_w (ie, higher repeatability) than theirs in our PLRS eyes obtained with both the Anterion (S_w: 0.60 to 1.36 µm) and Avanti (S_w: 0.75 to 1.96 µm). Even if we included all eyes, our data showed that the S_w of the Avanti (1.34 µm) was lower than that reported by Sedaghat et al (1.73 µm).

Using the MS-39 SD-OCT, Vega-Estrada et al[30] found in the central 3-mm zone an S_w of 1.24 µm in virgin eyes and an S_w of 2.03 µm in keratoconic eyes, whereas we, in the central 2-mm zone, found an S_w of 0.64 µm in virgin eyes and an S_w of 0.98 µm in keratoconic eyes with the Anterion and an S_w of 1.18 µm in virgin eyes and an S_w of 1.37 µm in keratoconic eyes with the Avanti. **Table D** (available in the online version of this article) summarizes the literature findings of the repeatability of ETM measurements in other studies.

We assume that 65 radial scans used by the Anterion versus eight radial scans used by Avanti, as well as the Anterion's eye-tracking ability, are the likely factors explaining the Anterion's better repeatability compared to the Avanti's.

Using VHF ultrasound, Reinstein et al[14,31,32] reported central epithelial thickness of 53.4 ± 4.6 µm in virgin eyes[32] and 45.7 ± 5.9 µm in eyes with keratoconus.[31] These measurements excluded the pre-corneal tear film thickness, whereas our measurements of the central epithelial thickness in virgin eyes with the Avanti that include the tear film[22] showed 55.60 ± 3.26 µm and the Anterion showed only 51.59 ± 3.27 µm. The manufacturer of the Anterior is neither claiming nor denying the inclusion of the tear film (Sandro Gunkel, Heidelberg Engineering, personal communication, November 19, 2021).

In both virgin and PLRS eyes, both devices measured a thicker epithelium inferiorly than superiorly (**Table 4** and **Figures B-C**), similar to other investigators.[22,31,33,34] In keratoconic eyes, both devices measured a thinner epithelium inferiorly than superiorly, and the differences in thickness between the superior and inferior sections were greater than for the other two groups of eyes (**Table 4**). In keratoconic eyes, the thinnest part of the epithelium, measured by both devices, was located in the inferior temporal section within the 2- to 5-mm ring (**Figure D**), which is also consistent with other researchers.[31,35]

Concerning the agreement between the Anterion and the Avanti, the mean epithelial thickness for all sections in all three groups of eyes was significantly different: 3.74 ± 2.33 µm ($P < .001$). We also calculated the agreement for each of the 17 sections (**Table C**) and showed maps of the difference between the measured thicknesses of the two devices in all three groups of eyes (**Figures B-D**), and we found a close correlation with respect to the thickness distribution. This close correlation results in registering similar recognizable ETM patterns that are important in the diagnosis of pathologic conditions in clinical practice. However, because one of the main applications for epithelial thickness measurement is keratoconus screening, where the thicknesses need to be measured on a scale of a few microns, the precise difference between the two devices must be known if their interchangeability is considered.

The Anterion and Avanti use their own proprietary methods for their respective segmentation algorithms. According to Heidelberg Engineering, their segmentation is looking for the highest intensity of the anterior surface, which can provide the ability to reliably find the underlying structure in a repeatable way (Sandro Gunkel, Heidelberg Engineering, personal communication, November 19, 2021). Because the axial resolution of the Anterion is limited to approximately 8 µm, the tear film cannot really be imaged/resolved, and that is why it is uncertain whether the tear film is included in the Anterion's OCT measurements. The Avanti has an axial resolution of approximately 5 µm and its ETM measurements include the tear film.[22]

Both the Anterion and Avanti use Fourier domain detection, but they feature different imaging wavelengths and bandwidths, whereas the Anterion uses a tunable

swept laser light source (center wavelength of 1,300 nm),[36,37] The Avanti uses broadband near-infrared super luminescent diode as its light source (center wavelength of 840 nm). This results in different lateral resolution (10 × 45 µm for the Anterion and 5 × 15 µm for the Avanti), which presumably leads to different performance. Both technologies record an interference spectrum that carries the information of the sample, but SS-OCT features a light source that sweeps the wavelength in time and SD-OCT uses a spectrometer for wavelength separation. SS-OCT imaging features a denser scan pattern, due to its higher acquisition speed, and a larger scan depth and area, due to the use of a longer wavelength and reduced sensitivity roll-off. Hence, SS-OCT may quickly acquire the images of the whole anterior segment,[36] whereas SD-OCT provides higher contrast and resolution within a shorter depth range. In addition, the Anterion features real-time eye-tracking during the acquisition of multiple B-scans, which allows precise alignment and enhanced detail imaging.[21] It appears that multiple factors may influence the repeatability of a device, such as axial resolution, image contrast and penetration rate, tracking, scanning speed, and scanning density (lateral resolution/data points). So, just by looking at the technical specifications, one cannot decide which device is superior, which emphasizes the importance of real-world clinical evaluation studies.

Although our study included a total of 258 eyes, we still did not have a sufficient sample size for our PLRS eyes to divide them according to the type of treated refractive error. Furthermore, we did not separately consider patients with other conditions such as dry eye disease and epithelial basement membrane dystrophy. Such considerations should be a subject for future studies.

We found that the repeatability of the ETM measurements with the Anterion SS-OCT was higher than with the Avanti SD-OCT in virgin, PLRS, and keratoconic corneas. However, the mean epithelial thickness measurements of the Anterion were always thinner than the Avanti's, something that must be considered if the devices are to be used interchangeably.

AUTHOR CONTRIBUTIONS

Study concept and design (XC, TPU, AS); data collection (YF); analysis and interpretation of data (YF, DZR, TN, TJA, CM, GB, AS); writing the manuscript (YF); critical revision of the manuscript (DZR, TN, TJA, CM, XC, GB, TPU, AS); statistical expertise (DZR, TN, TJA, CM, GB); supervision (XC, GB, TPU, AS)

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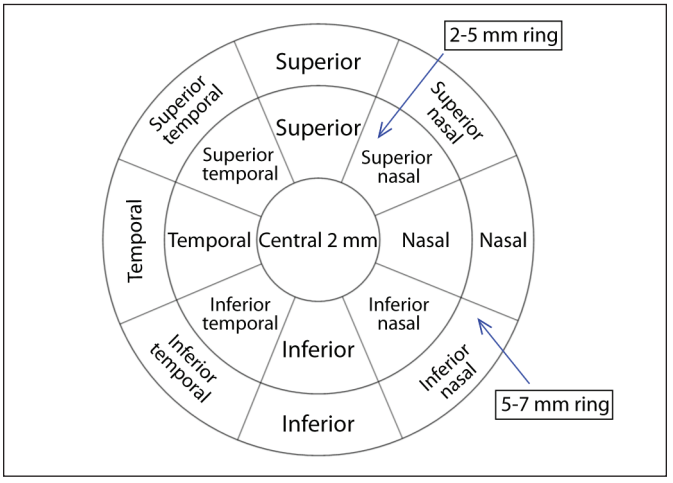

Figure A. 17 sections and two rings used in the analysis of the measurements.

TABLE A

Specifications of the OCT Devices for ETM

Device	Anterion	Avanti
Light source wavelength (nm)	1,300	840
A-scan speed (Hz)	50,000	70,000
Axial resolution (μm)	< 10	5
Transverse resolution (μm)	< 45	15
A-scan depth (mm)	14 ± 0.5	3
Maximum scan width (mm)	16.5	12
B-scan	65 × 1	8 × 5
No. of A-scans per B-scan	256	1,024

ETM = epithelial thickness mapping; OCT = optical coherence tomography
The Anterion is manufactured by Heidelberg Engineering and the Avanti is manufactured by Optovue.

TABLE B

Repeatability of ETM Measurements of All 17 Sections

	Repeatability, S_w (Repeatability Limit, r)							
	Virgin		PLRS		KC		All	
Parameter	Anterion	Avanti	Anterion	Avanti	Anterion	Avanti	Anterion	Avanti
Zone 0 to 2 mm								
Central	0.64 (1.77)	0.98 (2.72)	0.60 (1.67)	0.75 (2.06)	1.15 (3.19)	1.37 (3.78)	0.91 (2.52)	1.15 (3.19)
Ring 2 to 5 mm								
Nasal	0.73 (2.03)	1.08 (2.99)	0.85 (2.35)	1.48 (4.10)	1.23 (3.42)	1.32 (3.64)	1.02 (2.83)	1.27 (3.52)
Superior nasal	0.81 (2.24)	1.18 (3.26)	0.96 (2.65)	1.49 (4.12)	1.14 (3.16)	1.28 (3.56)	1.00 (2.77)	1.28 (3.55)
Superior	0.89 (2.46)	1.18 (3.26)	0.81 (2.25)	1.36 (3.76)	1.29 (3.56)	1.32 (3.65)	1.09 (3.02)	1.27 (3.52)
Superior temporal	0.86 (2.37)	1.19 (3.30)	0.79 (2.19)	1.43 (3.97)	1.00 (2.76)	1.72 (4.77)	0.91 (2.52)	1.51 (4.18)
Temporal	0.73 (2.03)	1.14 (3.16)	0.87 (2.41)	1.41 (3.91)	1.06 (2.95)	1.78 (4.94)	0.93 (2.58)	1.52 (4.21)
Inferior temporal	0.81 (2.25)	1.13 (3.12)	0.85 (2.35)	1.49 (4.11)	1.16 (3.21)	1.71 (4.74)	1.00 (2.77)	1.49 (4.13)
Inferior	0.76 (2.11)	1.13 (3.14)	0.82 (2.28)	1.07 (2.97)	1.24 (3.44)	1.37 (3.80)	1.03 (2.85)	1.24 (3.43)
Inferior nasal	0.69 (1.91)	1.08 (2.98)	0.77 (2.14)	1.49 (4.13)	1.28 (3.56)	1.10 (3.06)	1.03 (2.85)	1.17 (3.24)
Ring 2 to 5 mm total	0.79 (2.18)	1.14 (3.15)	0.84 (2.33)	1.40 (3.88)	1.18 (3.26)	1.45 (4.02)	1.00 (2.77)	1.34 (3.71)
Ring 5 to 7 mm								
Nasal	0.96 (2.65)	1.03 (2.84)	1.57 (4.36)	2.40 (6.66)	1.30 (3.61)	1.72 (4.75)	1.25 (3.46)	1.67 (4.63)
Superior nasal	1.11 (3.08)	1.25 (3.46)	1.43 (3.97)	1.97 (5.44)	1.37 (3.80)	1.90 (5.27)	1.31 (3.63)	1.72 (4.76)
Superior	1.01 (2.80)	1.27 (3.53)	2.05 (5.68)	1.70 (4.70)	1.50 (4.15)	1.99 (5.50)	1.47 (4.07)	1.71 (4.74)
Superior temporal	1.11 (3.07)	1.13 (3.14)	1.22 (3.39)	1.77 (4.89)	1.11 (3.07)	1.60 (4.42)	1.13 (3.13)	1.49 (4.13)
Temporal	1.03 (2.85)	1.10 (3.05)	1.27 (3.52)	1.95 (5.40)	1.20 (3.33)	1.50 (4.16)	1.16 (3.21)	1.47 (4.07)
Inferior temporal	0.99 (2.74)	0.96 (2.66)	1.07 (2.96)	1.93 (5.34)	1.37 (3.79)	1.56 (4.33)	1.20 (3.32)	1.46 (4.04)
Inferior	1.02 (2.83)	1.20 (3.32)	1.15 (3.18)	1.74 (4.83)	1.76 (4.89)	1.50 (4.16)	1.44 (3.99)	1.45 (4.02)
Inferior nasal	0.86 (2.39)	0.94 (2.60)	1.13 (3.13)	2.20 (6.08)	1.24 (3.44)	1.04 (2.88)	1.10 (3.05)	1.29 (3.57)
Ring 5 to 7 mm total	1.01 (2.80)	1.11 (3.08)	1.36 (3.77)	1.96 (5.42)	1.36 (3.76)	1.60 (4.44)	1.26 (3.49)	1.53 (4.24)

ETM = epithelial thickness mapping; KC = keratoconus; PLRS = post-laser refractive surgery; Repeatability limit = 2.77 × S_w; S_w = pooled within-subject standard deviation

TABLE C

Agreement of ETM Measurements Between the Two Devices in All 17 Sections

	Virgin				PLRS				KC				All			
	Difference		95% LoA (µm)		Difference		95% LoA (µm)		Difference		95% LoA (µm)		Difference		95% LoA (µm)	
Parameter	Mean ± SD (µm)	*P*	Lower	Upper	Mean ± SD (µm)	*P*	Lower	Upper	Mean ± SD (µm)	*P*	Lower	Upper	Mean ± SD (µm)	*P*	Lower	Upper
Zone 0 to 2 mm																
Central	4.02 ± 1.38	< .001	1.307	6.73	3.17 ± 1.99	< .001	-0.736	7.069	2.66 ± 2.12	< .001	-1.501	6.829	3.23 ± 1.96	< .001	-0.62	7.07
Ring 2 to 5 mm																
Nasal	4.43 ± 1.58	< .001	1.331	7.536	4.01 ± 2.23	< .001	-0.358	8.387	3.68 ± 2.07	< .001	-0.367	7.733	4.00 ± 1.97	< .001	0.15	7.86
Superior nasal	4.43 ± 1.63	< .001	1.239	7.62	3.75 ± 2.27	< .001	-0.698	8.191	3.87 ± 2.00	< .001	-0.047	7.79	4.04 ± 1.94	< .001	0.23	7.86
Superior	4.77 ± 1.75	< .001	1.335	8.213	3.95 ± 2.01	< .001	0.012	7.886	4.08 ± 2.15	< .001	-0.124	8.293	4.30 ± 2.02	< .001	0.35	8.25
Superior temporal	4.43 ± 1.58	< .001	1.337	7.53	3.85 ± 1.99	< .001	-0.062	7.757	3.61 ± 2.13	< .001	-0.563	7.793	3.94 ± 1.96	< .001	0.10	7.78
Temporal	4.22 ± 1.45	< .001	1.37	7.067	3.95 ± 2.04	< .001	-0.04	7.939	3.57 ± 2.04	< .001	-0.44	7.576	3.86 ± 1.87	< .001	0.19	7.54
Inferior temporal	4.04 ± 1.86	< .001	0.393	7.688	3.60 ± 2.32	< .001	-0.956	8.158	4.46 ± 2.66	< .001	-0.747	9.676	4.16 ± 2.36	< .001	-0.47	8.79
Inferior	4.29 ± 2.03	< .001	0.304	8.267	3.54 ± 2.25	< .001	-0.877	7.949	4.41 ± 2.13	< .001	0.245	8.575	4.21 ± 2.13	< .001	0.03	8.39
Inferior nasal	4.18 ± 1.99	< .001	0.287	8.076	3.74 ± 2.33	< .001	-0.818	8.297	3.98 ± 1.96	< .001	0.15	7.817	4.01 ± 2.03	< .001	0.02	8
Ring 2 to 5 mm total	4.35 ± 1.73	< .001	0.95	7.75	3.80 ± 2.18	< .001	-0.475	8.071	3.96 ± 2.14	< .001	-0.237	8.157	4.07 ± 2.04	< .001	0.075	8.059
Ring 5-7 mm																
Nasal	3.76 ± 1.79	< .001	0.255	7.263	2.80 ± 2.05	< .001	-1.222	6.831	3.34 ± 3.43	< .001	-3.38	10.05	3.39 ± 2.74	< .001	-1.97	8.75
Superior nasal	3.78 ± 2.05	< .001	-0.239	7.794	2.32 ± 3.10	< .001	-3.759	8.396	3.17 ± 3.43	< .001	-3.547	9.88	3.23 ± 2.99	< .001	-2.62	9.08
Superior	4.46 ± 2.31	< .001	-0.067	8.993	3.04 ± 3.28	< .001	-3.388	9.46	3.62 ± 2.88	< .001	-2.027	9.27	3.81 ± 2.81	< .001	-1.70	9.32
Superior temporal	3.94 ± 1.87	< .001	0.273	7.609	3.30 ± 3.28	< .001	-3.131	9.725	3.43 ± 2.59	< .001	-1.658	8.51	3.58 ± 2.52	< .001	-1.35	8.52
Temporal	3.28 ± 1.62	< .001	0.102	6.461	2.37 ± 3.35	< .001	-4.203	8.942	3.12 ± 2.31	< .001	-1.404	7.64	3.04 ± 2.34	< .001	-1.55	7.63
Inferior temporal	3.30 ± 1.75	< .001	-0.131	6.738	2.43 ± 2.91	< .001	-3.269	8.124	3.51 ± 2.99	< .001	-2.361	9.37	3.24 ± 2.63	< .001	-1.91	8.4
Inferior	3.83 ± 1.87	< .001	0.165	7.502	2.72 ± 2.01	< .001	-1.229	6.664	3.95 ± 2.86	< .001	-1.643	9.55	3.69 ± 2.44	< .001	-1.10	8.48
Inferior nasal	3.86 ± 2.15	< .001	-0.364	8.075	2.89 ± 3.42	< .001	-3.815	9.598	4.01 ± 3.01	< .001	-1.883	9.91	3.76 ± 2.84	< .001	-1.81	9.33
Ring 5-7 mm total	3.78 ± 1.93	< .001	-0.001	7.554	2.73 ± 2.93	< .001	-3.002	8.468	3.52 ± 2.94	< .001	-2.238	9.273	3.47 ± 2.66	.001	-1.75	8.689

ETM = epithelial thickness mapping; KC = keratoconus; LoA = limits of agreement; PLRS = post-laser refractive surgery; SD = standard deviation

TABLE D

Repeatability of ETM Measurements Reported by Previous Investigators

	Repeatability, Sw (Repeatability Limit, r) (μm)				
Authors	**Virgin**	**PLRS**	**KC**	**Diameter**	**Instrument Used**
Reinstein et al[29]	–	0.58 (1.61)	–	Corneal vertex	VHF-ultrasound Artemis
	–	0.43 to 1.36 (1.19 to 3.77)	Central 6 mm	–	–
Ma et al[22]	0.70 (1.94)	–	–	Central 2 mm	Optovue RT-100 SD-OCT
	0.7 to 0.9 (1.94 to 2.49)	–	–	4 to 6 mm	–
Sedaghat et al[23]	1.73 (4.79)	4.50 (12.47)	–	Central 7 mm	Avanti SD-OCT
Vega-Estrada et al[30]	1.24 (3.43)	–	2.03 (5.62)	Central 3 mm	MS 39 SD-OCT

ETM = epithelial thickness mapping; KC = keratoconus; OCT = optical coherence tomography; PLRS = post-laser refractive surgery; Repeatability limit = 2.77 × S_w; S_w = pooled within-subject standard deviation

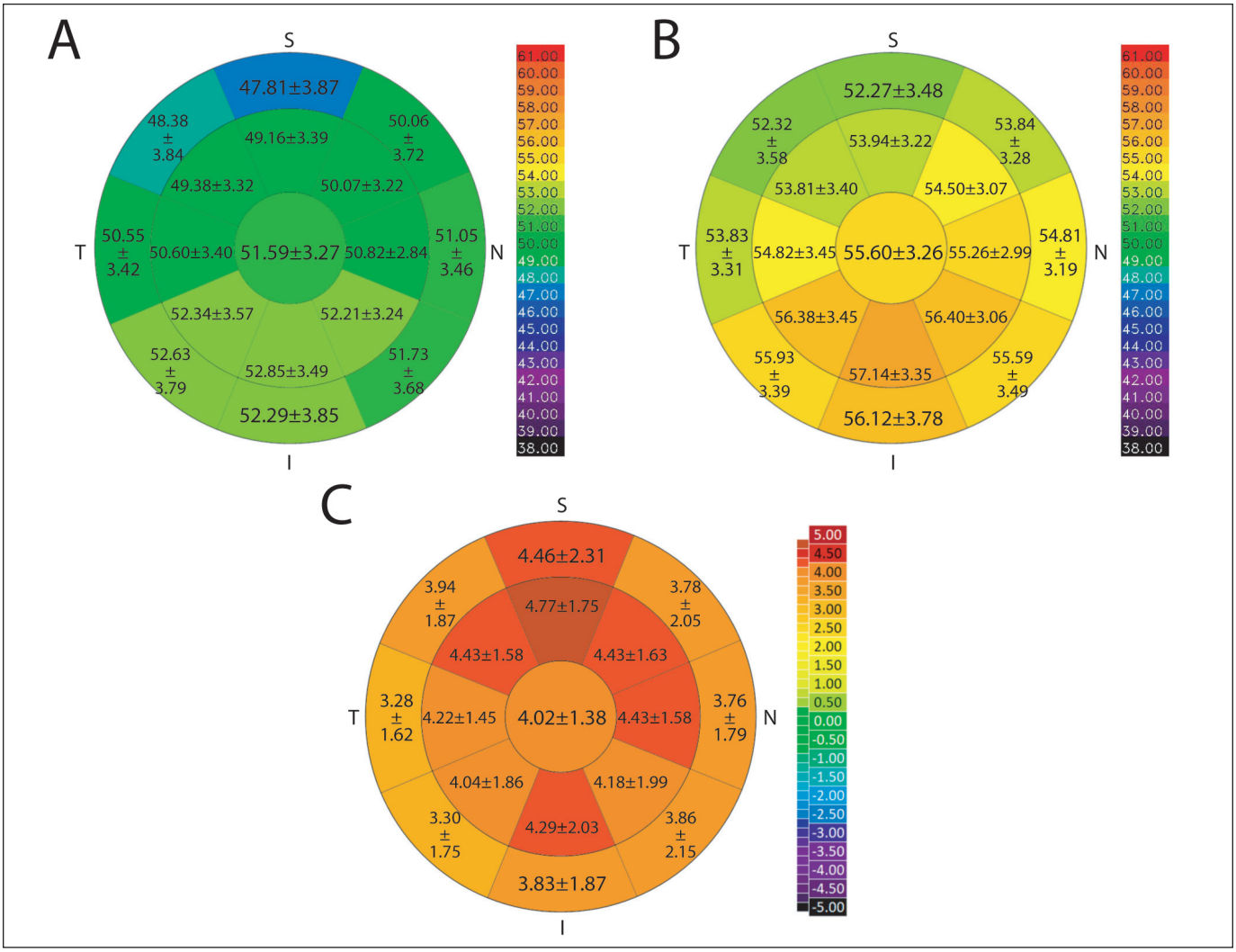

Figure B. Mean epithelial thickness mapping for the (A) Anterion (Heidelberg Engineering) and (B) Avanti (Optovue, Inc) between the two devices in virgin eyes over the central 7-mm diameter. N = nasal; S = superior; T = temporal; I = inferior; Unit: μm

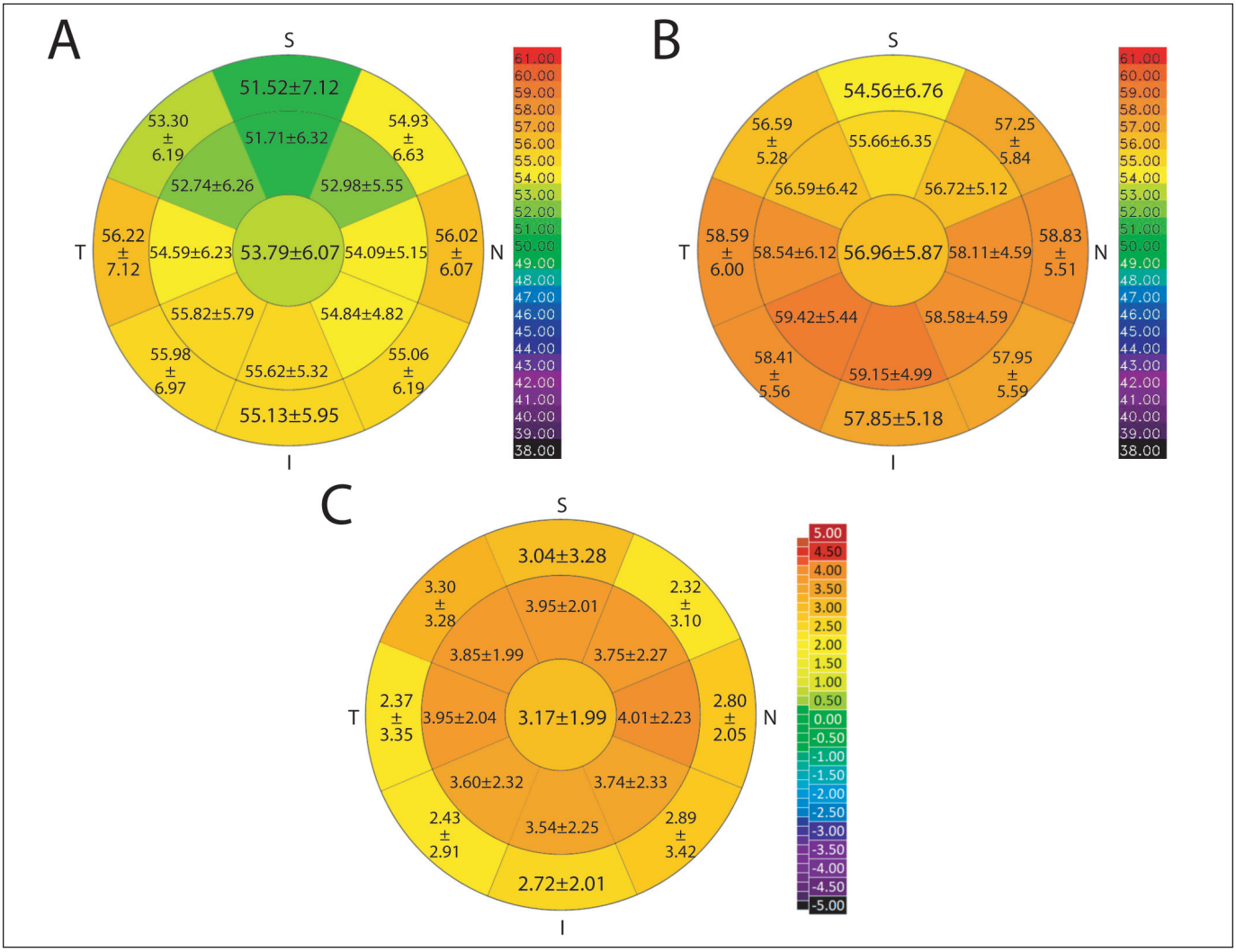

Figure C. Average epithelial thickness mapping for the (A) Anterion (Heidelberg Engineering) and (B) Avanti (Optovue, Inc) between the two devices in post-laser refractive surgery eyes over the central 7-mm diameter. N = nasal; S = superior; T = temporal; I = inferior; Unit: μm

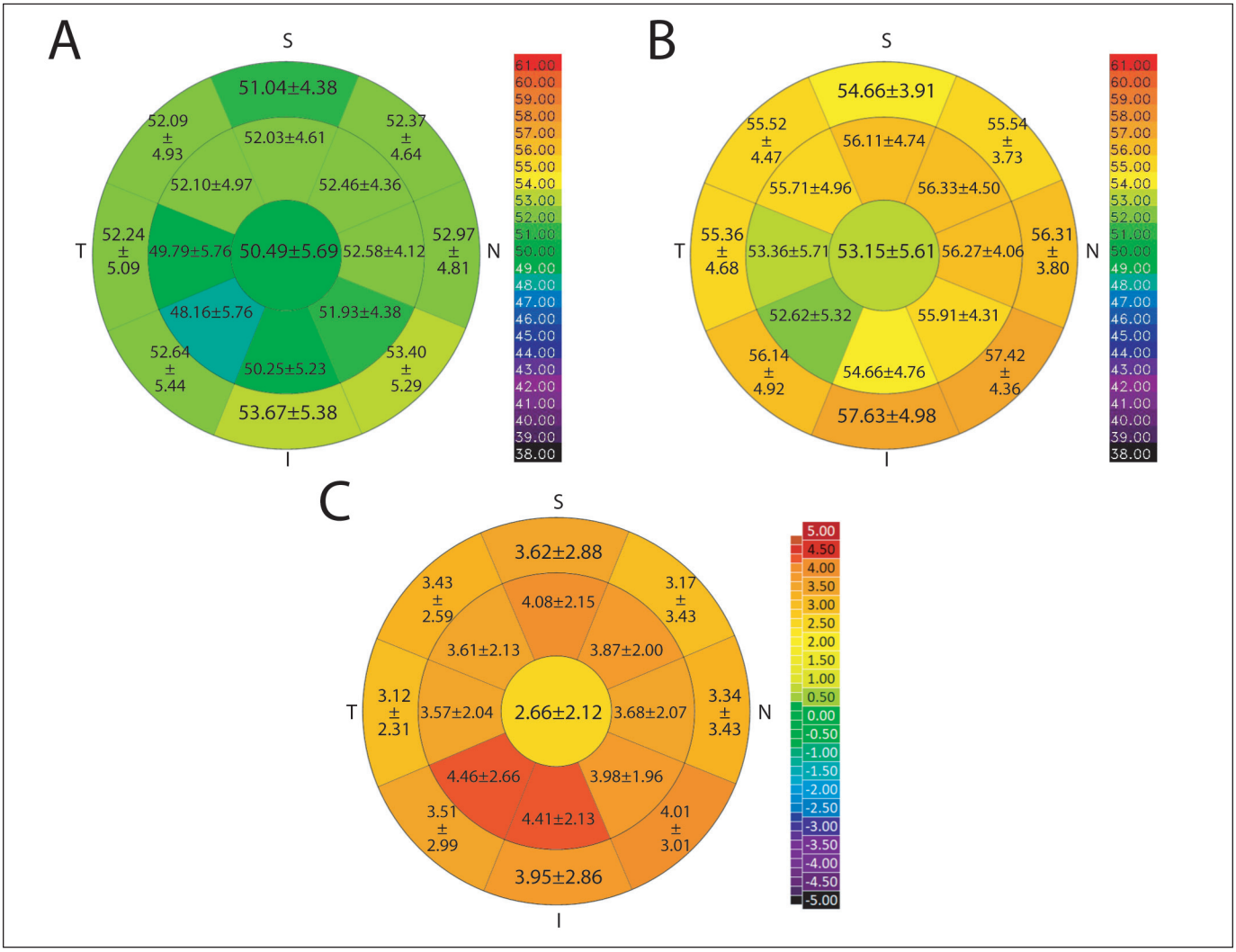

Figure D. Average epithelial thickness mapping for the (A) Anterion (Heidelberg Engineering) and (B) Avanti (Optovue, Inc), and differential mapping (C) between the two devices in keratoconic eyes over the central 7-mm diameter. N = nasal; S = superior; T = temporal; I = inferior; Unit: μm

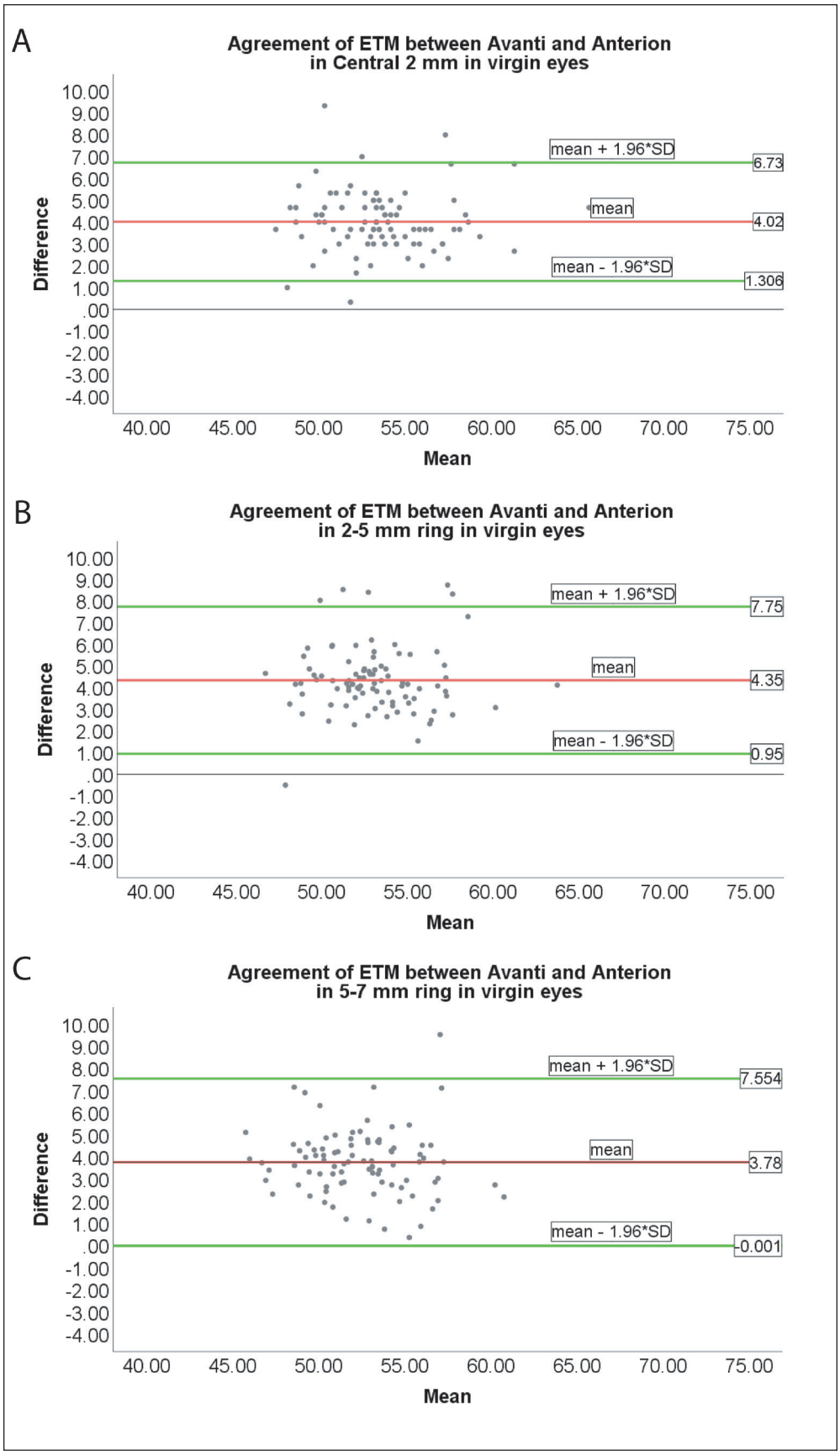

Figure E. Bland-Altman plots of virgin eyes, showing the difference in epithelial thickness measurements (ETM) (Avanti [Optovue, Inc] − Anterion [Heidelberg Engineering]), as a function of the mean epithelial thickness of both devices in the (A) central 2-mm zone, (B) 2- to 5-mm, and (C) 5- to 7-mm diameter rings, respectively. The red lines represent the mean difference; green lines represent the limits of agreement. SD = standard deviation; unit = μm

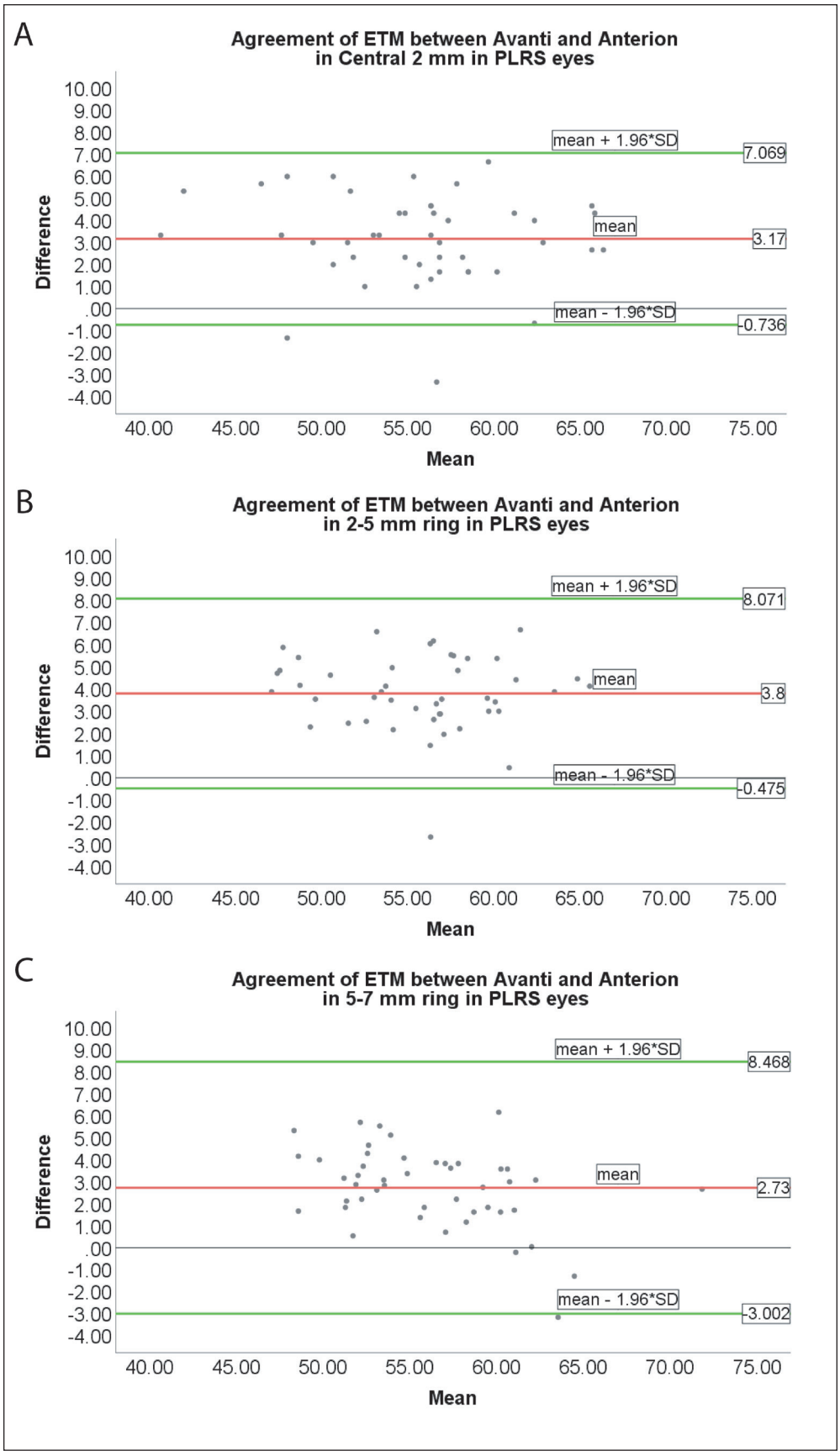

Figure F. Bland-Altman plots of post-laser refractive surgery (PLRS) eyes, showing the difference in epithelial thickness measurements (ETM) (Avanti [Optovue, Inc] − Anterion [Heidelberg Engineering]), as a function of the mean epithelial thickness of both devices in the (A) central 2-mm zone, (B) 2- to 5-mm, and (C) 5- to 7-mm diameter rings, respectively. The red lines represent the mean difference; green lines represent the limits of agreement. SD = standard deviation; unit = μm

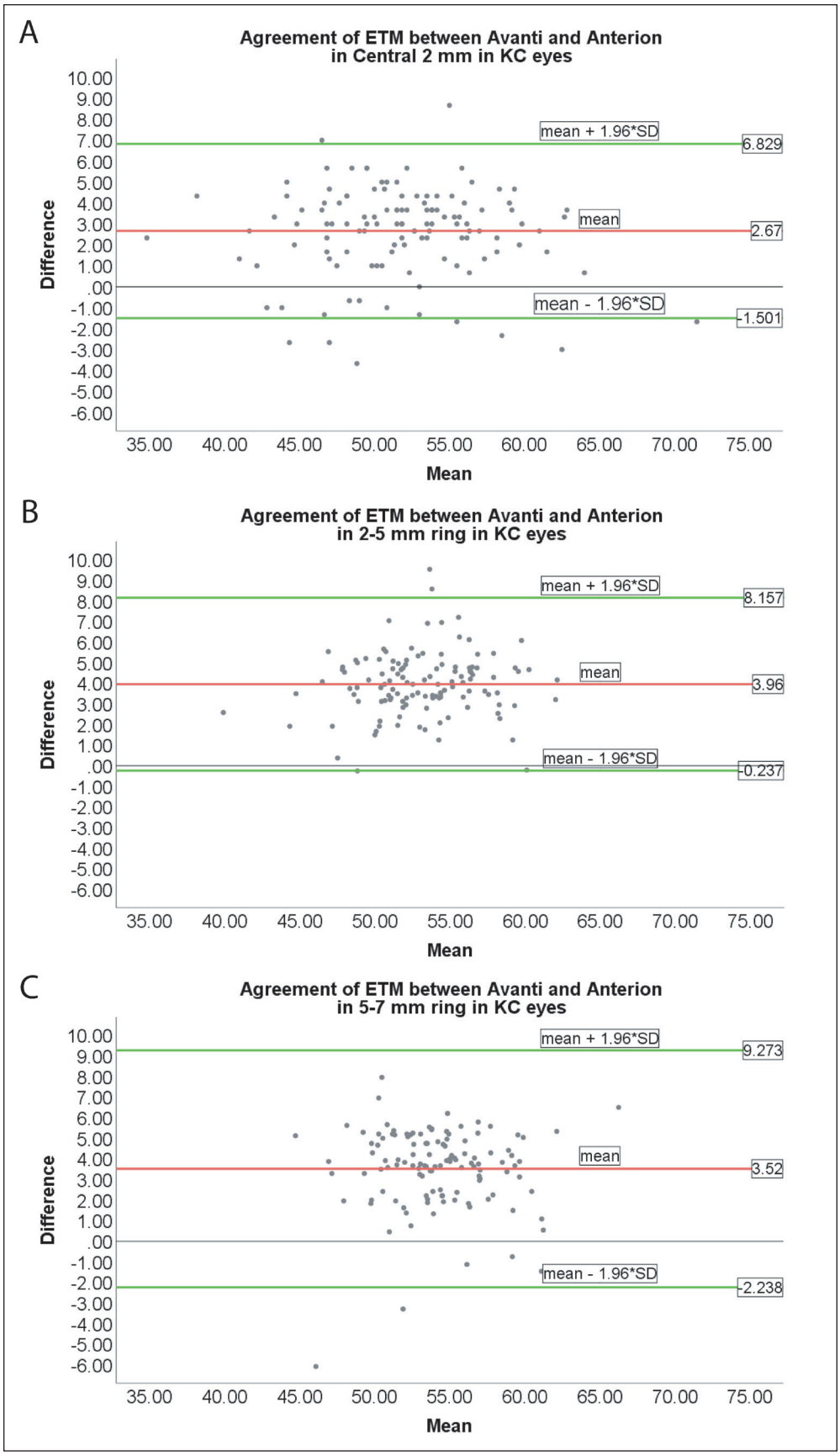

Figure G. Bland-Altman plots of keratoconic (KC) eyes, showing the difference in epithelial thickness measurements (ETM) (Avanti [Optovue, Inc] – Anterion [Heidelberg Engineering]), as a function of the mean epithelial thickness of both devices in the (A) central 2-mm zone, (B) 2- to 5-mm, and (C) 5- to 7-mm diameter rings, respectively. The red lines represent the mean difference; green lines represent the limits of agreement. SD = standard deviation; unit = μm