

Repeatability and comparative study of corneal thickness using the Visante™ OCT, OCT II and Orbscan II™

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Abstract

The first purpose of this study was to measure the repeatability the Visante™ Optical coherence tomographer (OCT) in a normal sample. The second was to compare corneal thickness measured with the Visante™ OCT to the Zeiss-Humphrey OCT II (model II, Carl Zeiss Meditec) adapted for anterior segment imaging and to the Orbscan II™ (Bausch and Lomb). Fifteen healthy participants were recruited. At the Day 1 visit, the epithelial and total corneal thickness across the central 10 mm of the horizontal meridian was measured using the OCT II and the Visante™ OCT. Only total corneal thickness across the central 10 mm of the horizontal meridian was measured using the Orbscan II. These measurements were repeated on Day 2. Mean central corneal and epithelial thickness using the Visante™ OCT at the apex of the cornea was $536 \pm 27 \mu\text{m}$ and $55 \pm 2.3 \mu\text{m}$. Mean corneal and epithelial thickness using OCT II at the apex was $520 \pm 25 \mu\text{m}$ and $56 \pm 4.9 \mu\text{m}$. Mean total corneal thickness measured with the Orbscan II was $609 \pm 29 \mu\text{m}$. The coefficient of repeatability (COR) ranged from ± 7.71 to $\pm 8.98 \mu\text{m}$ for total corneal thickness and from ± 8.72 to $\pm 9.92 \mu\text{m}$ for epithelial thickness. Correlation coefficients of concordance (CCC's) were high for total corneal thickness for test-retest differences ranging from 0.97 to 0.99, CCCs for epithelial thickness showed moderate concordance for both the instruments. There is good repeatability of corneal and epithelial thickness using each OCT for test-retest differences compared to the between instrument repeatability. Measurements of epithelial thickness were less robust.

Introduction

Imaging of the ocular adnexa has evolved significantly since its conception. The early forms of capturing images began with the use of film based slit lamp cameras. Ultrasound A and B scans gave axial length, position and

thickness of the crystalline lens, anterior chamber depth and information about the posterior pole.¹ Although these forms of imaging are still of value, computer technology has allowed for advancements in the imaging field. Various imaging techniques have been used over the past few years to improve identification, characterization and quantification of ophthalmic disorders. In recent studies, optical coherence tomography (OCT) has been used as a microscopic imaging technique for *in vivo* examination of the posterior and the anterior segments.²⁻⁷

Techniques for measuring central corneal thickness (CCT) include ultrasound pachymetry,⁸ confocal microscopy,⁹ ultrasound biomicroscopy,¹⁰ scanning slit imaging (Orbscan II™),¹¹ specular microscopy,⁸ scheimpflug imaging (Pentacam™)¹² and OCT.¹³⁻¹⁵ OCT is a non-invasive, non-contact imaging technique that typically uses infrared light to obtain high resolution cross-sectional images *in vivo*.¹⁵ Although the technique has been used primarily in the diagnosis of optic nerve and retinal pathology, more recently it has been shown to be of value for the study of the cornea.¹⁴⁻¹⁷

The Visante™ OCT (Zeiss Meditec, CA, USA) is time domain OCT (TD-OCT) utilizing optical coherence tomography to image the anterior segment. The Visante™ OCT Model 1000 can provide detailed *in vivo* examination of the anterior segment of the eye without eye contact. It provides high resolution cross-sectional images. The axial resolution of the Visante™ OCT image is $18 \mu\text{m}$ and the transverse resolution is $60 \mu\text{m}$.^{18,19} Visante™ and Stratus™ OCT devices allow the scanning probe to move transversely, thus allowing for the reconstruction of a 2-dimensional image from a series of transversely displaced axial scans. The difference between the Stratus OCT and Visante OCT is in the wavelength of light that is used in the device.^{16,20} The Stratus™ OCT uses a near-infrared light with a wavelength of 820 nm , whereas the Visante™ OCT uses a wavelength of 1310 nm . By increasing the wavelength of light, the amount of signal scattering is reduced, and this allows for better penetration past the limbal and sclera. The structures in the anatomical angle which were previously blocked by the limbus in the Stratus OCT are now clear images with the Visante™ OCT.^{16,20}

The first purpose of this study was to measure the repeatability the Visante™ OCT in a normal sample. The second was to compare this instrument with other measurement methods of topographic total corneal thickness as measured with the Zeiss-Humphrey OCT II (OCT II) (model 2000, Carl Zeiss Meditec, Jena, Germany) adapted for anterior segment imaging²¹ and the Orbscan II™ (Bausch and Lomb, Rochester, NY, USA).

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Key words: corneal thickness, epithelial thickness, optical coherence tomography.

Conflict of interests: the authors declare no potential conflict of interests.

Received for publication: 4 October 2011.

Revision received: 3 May 2012.

Accepted for publication: 3 May 2012.

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Optometry Reports 2012; 2:e4

doi:10.4081/optometry.2012.e4

Materials and Methods

Study design

Ethics approval was obtained from the Office of Research Ethics at the University of Waterloo prior to study commencement and the study was conducted according to the Declaration of Helsinki. Fifteen healthy participants (9 women, 6 men) were recruited and their eligibility was determined at a screening appointment; age range 20-32 years. Participants did not present any ocular disorder and had no history of eye surgery, ocular trauma, or current systemic disease. Informed consent was obtained from all participants prior to enrolment in the study. The measurements were taken for both the eyes (randomized) at approximately the same time on each day with the same instructions and procedure by the same investigator (JM).

Study subjects were positioned on the chin and fore headrest and were encouraged to keep their eyes open as wide as possible but were allowed to blink as needed. At the screening visit (Day 0), visual acuity was measured and biomicroscopy was performed. At the Day 1 visit the epithelial and total corneal thickness across the central 10 mm of the horizontal meridian was measured using the OCT II and the Visante™ OCT. Total corneal thickness across the central 10 mm of the horizontal meridian was measured using the Orbscan II™. Three measurements were taken across the cornea at the apex, nasal and temporal cornea with the Visante™ OCT, OCT II and the Orbscan II™. Nasal and temporal corneal

measurements were 3 mm away from the apex. A custom designed external fixation target was used to control eye position to enable measurement of nasal and the temporal corneas of the study participants. Measurements were taken 3 mm nasally and temporally from the central corneal scan with the OCT II using the external fixation target and were compared to the total corneal and epithelial thickness in the same area for the Visante™ OCT and the Orbscan II™. The order of these measurements was randomized. These measurements were repeated on Day 2. Each individual measurement was repeated three times on both Day 1 and Day 2, and the measurements were averaged to give a single result.

Instruments

Visante™ optical coherence tomographer

The Visante™ OCT (Zeiss Meditec) uses a wavelength of 1310 nm and has a nominal axial resolution of 18 μm and transverse resolution of 60 μm. The study subject was comfortably positioned at the chin rest and aligned for the scan. The study subject was asked to fixate at the start burst fixation pattern inside the instrument. A high resolution corneal single map was acquired for the study. The scanned image was considered to be optimally aligned when the specular reflex, which is a high intensity reflection from the front surface of the cornea, was visible on the screen. Data were analyzed using the inbuilt calliper tool that automatically places itself on the boundaries delineating anterior/posterior surfaces of the cornea. Measurements of corneal and epithelial thickness at Day 1 and Day 2 for central, nasal and temporal locations on the cornea were taken using the Visante™ OCT.

Optical coherence tomographer II

The OCT II (Carl Zeiss Meditec) adapted for anterior segment imaging^{22,24} was used to obtain the images of the cornea and the epithelium. A scan width of 1.13 mm was used to acquire images.

Study subjects were seated comfortably at the OCT instrument with their chin and forehead on the headrest and were asked to fixate the peripheral fixation lights of the fixation target. The incident beam was aligned with the fixation light of the target on the corneal surface, and the specular reflection confirmed that the scan was perpendicular to the cornea.

Once the specular reflection was obtained at the 3 mm nasal and temporal locations from the center of the cornea, an optimal image and the raw data were captured. Central corneal and epithelial thickness was obtained using

customized analysis software. Customized software read the raw files consisting of position *versus* reflected intensity for each of the 100 sagittal scans. The software imported the raw data from the instrument and then located the peak reflectance that corresponded to front and back surfaces of the cornea. From the curves fitted to these surfaces, thicknesses were calculated for each pixel point along the front surface *i.e.* the shortest distance between the anterior and posterior surfaces. The averages of these thicknesses were then used.

Orbscan II™

The Orbscan II™ (Bausch & Lomb) provides topographical images of both the front and back surfaces of the cornea, and also provides pachymetric thickness measurements of the cornea. The Orbscan II™ is based on Placido disk technology. The instrument is used to acquire and analyze the elevation and curvature measurements on both the anterior and posterior surfaces of the cornea.^{11,25,26} The study subject is positioned with a chin and forehead rest and asked to look at a fixation target. The device projects 40 slits, 20 from the right and 20 from the left, at an angle of 45° to the instrument axis. As the light from these slits passes through the cornea, it is scattered in all directions and is backscattered toward the digital video camera of the device which records the appearance in 2-dimensional images.

Data management and analysis

Data analysis was carried out using Statistica (Version 7, StatSoft, Tulsa, OK, USA). The coefficient of repeatability (COR), Bland-Altman limits of agreement²⁷ and the correlation coefficient of concordance (CCC) were used.²⁸ The coefficient of repeatability was 1.96 x test-retest differences taking into account the degree of freedom or method 1 and method 2 differences. CCC describes concordance between repeated measurements by analyzing the deviation of test and re-test measures from a perfect 45° line through the origin (*i.e.* CCC=1). CCCs less than 1 represent deviations from this perfect line and correspond to a weaker repeatability. $P < 0.05$ was considered statistically significant. Analysis of measurements taken from the apex and ± 3 mm on either side are reported.

Results

There were 9 females and 6 males enrolled in the study; age 20-32 years. The measurements were taken on two separate days but at

the same time of day ± 60 min. Mean central corneal thickness imaged by the Visante™ OCT at the apex of the cornea was 536 ± 27 μm (range 563-509 μm) and the mean epithelial thickness using the Visante™ OCT was 55 ± 2.3 μm (range 57.3-52.7 μm). Table 1 represents the mean corneal and epithelial thickness at the apex imaged by the Visante™ OCT and OCT II and the mean corneal thickness using the Orbscan II. A t-test showed that there was a significant difference in apical corneal thickness imaged by the Visante™ OCT and OCT II ($P < 0.05$). A significant difference was also found in corneal thickness ($P < 0.05$) between measurements using the Visante™ OCT and the Orbscan II™ at the apex. There was no statically significant between the epithelial thickness measured with Visante™ OCT and the OCT II ($P > 0.05$).

The mean corneal and epithelial thickness at the temporal location imaged by the Visante™ OCT was 554 ± 26 μm and 53 ± 0.7 μm, respectively, the 5th and 95th percentiles for corneal and epithelial thickness were between 580 to 528 μm and 53.7 to 52.3 μm, respectively. Table 1 shows the mean corneal and epithelial thickness at the nasal position imaged using the OCT II the Visante™ OCT, and the Orbscan II™. Nasally, there was no significant difference in the corneal and epithelial thicknesses between measurements from the Visante™ OCT and OCT II ($P > 0.05$), but there was a difference between measures from the Visante™ OCT and Orbscan II™ ($P < 0.05$) (Table 2).

Table 3 shows the mean corneal and epithelial thickness at the temporal location acquired using the Visante™ OCT, OCT II and Orbscan II™. There was no significant difference in the corneal thickness at the apex between data from Visante™ OCT and OCT II ($P > 0.05$). Epithelial thickness at the nasal location measured using the Visante™ OCT and OCT II was statistically significantly different ($P < 0.05$).

Tables 4 and 5 present the COR of the corneal thickness and the epithelial thickness for the three instruments (Visante™ OCT, OCT II and Orbscan II™). There is better repeatability of corneal and epithelial thickness measured with Visante™ OCT between the sessions when compared to the OCT II and Orbscan II™ imaging systems.

CCC was also estimated between sessions for the Visante™ OCT, OCT II and Orbscan II™ imaging systems. There was good concordance of total corneal thickness with the Visante™ OCT (0.90-0.99 at either apex, temporal or nasal locations), the OCT II (0.97-0.99 at either apex, temporal or nasal locations) and the Orbscan II™ (0.97-0.98 at either apex, temporal or nasal locations) between sessions (Table 6).

There is moderate concordance with epithelial thickness for both Visante™ OCT and the

OCT II with CCC. CCC was 0.52 and 0.81, respectively (Table 7).

The CCC was estimated between instruments comparing the measurements of corneal and epithelial thickness from the Visante™ OCT with the OCT II and for corneal thickness and epithelial thickness measurements (Tables 8 and 9). There was good concordance of corneal thickness measurements on Day 2 (range 0.86-0.97 apex, temporal and nasal cornea) comparing Visante™ OCT and the OCT II measurements and moderate concordance on Day 1 (range 0.66-0.68 at the

apex, nasal and temporal cornea).

CCCs were also estimated from corneal thickness measurements obtained using the Visante™ OCT and the Orbscan II™ (Table 10). Measurements were moderately concordant on either Day 1 or Day 2 (range 0.55-0.78 apex, nasal and temporal cornea). Visante™ OCT and the OCT II epithelium thickness measurements also demonstrated moderate concordance on either Day 1 or Day 2 (range 0.53-0.75 apex, nasal and temporal cornea). In summary, the CCCs revealed good agreement between measurements of

corneal and epithelial thickness within all the three instruments compared to between the instruments where the CCC was moderately concordant.

Agreement between the measurements of the three instruments was examined with the Bland-Altman plot and limits of agreement were calculated.²⁹ Plots of the difference between measurements on the y axis *versus* the averages of the corneal or epithelial thickness measurements from the Visante™ OCT, OCT II and Orbscan II™ on the x axis on different days are shown in Figures 1-6.

Table 1. Mean corneal and epithelial thickness at apex (Visante™ OCT, OCT II and Orbscan).

Central thickness	Visante™ OCT	OCT II	Orbscan II
Total thickness	536±27 µm	520±25 µm	609±29 µm
Epithelial thickness	55±2.3 µm	56±4.9 µm	NA

OCT, optical coherence tomographer; NA, not applicable.

Table 2. Mean corneal and epithelial thickness at the temporal position using the OCT II and mean corneal thickness using the Orbscan II™.

Nasal thickness	Visante™ OCT	OCT II	Orbscan II
Total thickness	554±26 µm	599±36 µm	609±27 µm
Epithelial thickness	53±0.7 µm	56±3.4 µm	NA

OCT, optical coherence tomographer; NA, not applicable.

Table 3. Mean corneal and epithelial thickness at the nasal location from the Visante™ OCT, OCT II and Orbscan II™.

Temporal thickness	Visante™ OCT	OCT II	Orbscan
Total thickness	565±26 µm	555±39 µm	600±29 µm
Epithelial thickness	53±0.8 µm	54±2.2 µm	NA

OCT, optical coherence tomographer; NA, not applicable.

Table 4. Coefficient of repeatability of total corneal thickness with Visante™ OCT, OCT II and Orbscan II™.

COR Instruments	Total corneal thickness (test-retest)		
	Apex	Temporal (3 mm)	Nasal (3 mm)
OCT II	±13.31 µm	±13.98 µm	±19.94 µm
Visante OCT	±8.98 µm	±8.62 µm	±7.71 µm
Orbscan II	±10.71 µm	±13.66 µm	±11.53 µm

COR, coefficient of repeatability; OCT, optical coherence tomographer.

Table 5. Coefficient of repeatability of epithelial thickness with Visante™ OCT, OCT II and Orbscan II™.

COR Instruments	Epithelial thickness (test-retest)		
	Apex	Temporal (3 mm)	Nasal (3 mm)
OCT II	±8.81 µm	±9.68 µm	±9.49 µm
Visante™ OCT	±8.72 µm	±9.92 µm	±9.72 µm
Orbscan II	NA	NA	NA

COR, coefficient of repeatability; OCT, optical coherence tomographer; NA, not applicable.

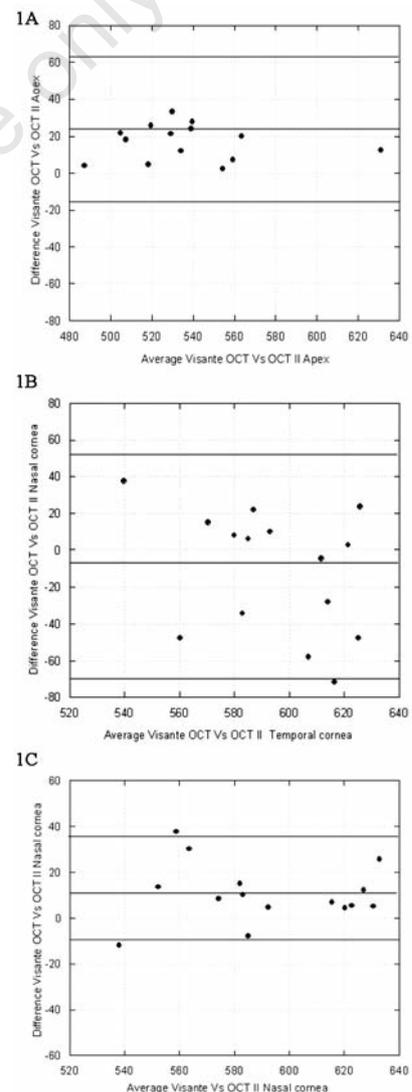


Figure 1. A) Apex, B) Nasal cornea, C) Temporal. Represent Bland and Altman graph of Visante™ OCT versus OCT II (total corneal thickness Day 1).

Discussion

Ultrasound pachymetry has been the gold standard for central corneal thickness measurement because of its established reliability, but no corneal contact and high speed anterior segment OCT provides a promising alternative. Izatt *et al.*³⁰ were the first to show the potential for corneal imaging, and they demonstrated that epithelium and endothelium layers could be distinguished in an OCT image. Bechmann *et al.* and Wong *et al.* have reported that ultrasound pachymetry overestimates corneal thickness by approximately 49 microns and 31.9 microns, respectively.^{15,31} Commercially used anterior segment OCTs have been most commonly used for looking at

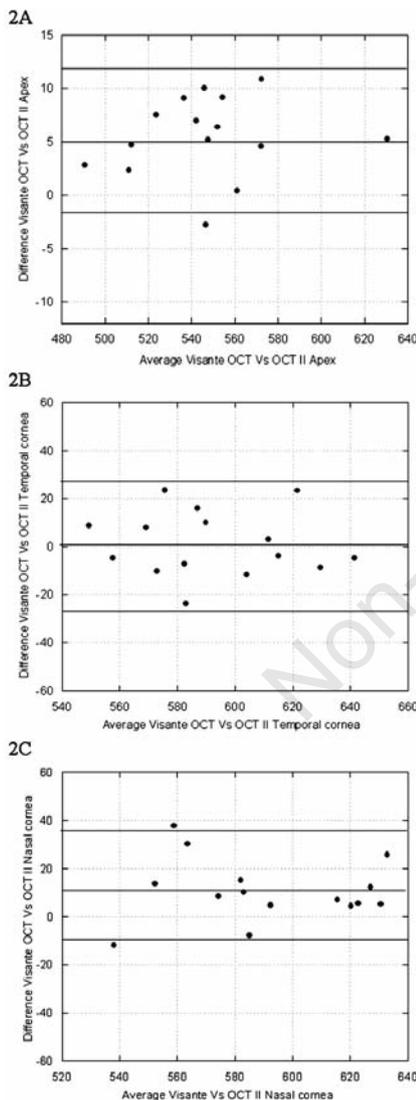


Figure 2. A) Apex, B) Nasal cornea, C) Temporal cornea. Represent Bland and Altman graph of Visante OCT versus OCT II (total corneal thickness Day 2).

Table 6. Correlation coefficient of concordance of total corneal thickness with Visante™ OCT, OCT II and Orbscan II™.

CCC Instruments	Apex	Total corneal thickness	
		Temporal (3 mm)	Nasal (3 mm)
OCT II	0.97	0.98	0.99
Visante™ OCT	0.99	0.90	0.97
Orbscan II	0.98	0.97	0.98

CCC, coefficient of concordance; OCT, optical coherence tomographer.

Table 7. Correlation coefficient of concordance of total corneal thickness with Visante™ OCT and OCT II.

CCC Instruments	Apex	Epithelial thickness	
		Temporal (3mm)	Nasal (3mm)
OCT II	0.70	0.58	0.52
Visante™ OCT	0.81	0.53	0.54
Orbscan II	NA	NA	NA

CCC, coefficient of concordance; OCT, optical coherence tomographer; NA, not applicable.

Table 8. Correlation coefficient of concordance of total corneal thickness between instruments comparing the Visante™ OCT and OCT II.

CCC Visante™ OCT vs OCT II	Apex	Total corneal thickness	
		Temporal (3 mm)	Nasal (3 mm)
Day 1	0.68	0.68	0.66
Day 2	0.97	0.88	0.86

CCC, coefficient of concordance; OCT, optical coherence tomographer.

Table 9. Correlation coefficient of concordance of epithelial thickness between instruments comparing the Visante™ OCT and OCT II.

CCC Visante™ OCT vs OCT II	Apex	Epithelial thickness	
		Temporal (3 mm)	Nasal (3 mm)
Day 1	0.54	0.75	0.53
Day 2	0.34	0.54	0.57

CCC, coefficient of concordance; OCT, optical coherence tomographer.

Table 10. Correlation coefficient of concordance of total corneal thickness between instruments comparing the Visante™ OCT and Orbscan.

CCC Visante™ OCT vs Orbscan	Apex	Total corneal thickness	
		Temporal (3 mm)	Nasal (3 mm)
Day 1	0.59	0.59	0.73
Day 2	0.67	0.55	0.78

CCC, coefficient of concordance; OCT, optical coherence tomographer.

corneal and epithelial thickness,³² diurnal variation in corneal thickness,²¹ measurement of tear film thickness,³³ measurement of corneal thickness pre- and post-refractive surgery³⁴ and also to assess corneal morphological effects of corneal edema.²⁴

In this study, we compared repeatability of two commercially available TD-OCT (Visante™ OCT and the adapted Zeiss-Humphrey retinal OCT II) and looked at the measurements of total corneal and epithelial thickness across central, temporal and nasal locations on the cornea. Repeatability of Orbscan II™ was also examined for the total corneal thickness at the same three locations on the cornea. The average corneal thickness for Day 1 and Day 2 at the apex of the cornea

was $536 \pm 27 \mu\text{m}$, the nasal and temporal corneas were $554 \pm 26 \mu\text{m}$ and $565 \pm 26 \mu\text{m}$ respectively using the Visante™ OCT. When these results were compared to the Orbscan II™, there was a significant difference, with Orbscan producing higher average corneal thickness measurements of $609 \pm 29 \mu\text{m}$, $609 \pm 27 \mu\text{m}$ and $600 \pm 29 \mu\text{m}$ for the central, nasal and temporal corneas, respectively. The nasal measurement of corneal thickness with the OCT II was by $45 \mu\text{m}$ higher than the Visante™ OCT. The average CCT with the OCT II at the apex was $520 \pm 25 \mu\text{m}$, which is very similar to the results obtained by Muscat *et al.* and Bechmann *et al.* of $526 \pm 28 \mu\text{m}$ and $530 \pm 32 \mu\text{m}$, respectively.^{14,31}

Muscat *et al.* evaluated the repeatability of

CCT using Humphrey-Zeiss OCT found an CCC of 0.998 which is comparable to the results of Muscat *et al.*¹⁴ The repeatability of the central corneal thickness was similar for all the three instruments although the Visante™ OCT produced the highest CCC of 0.99, similar to the results in other recent studies with reported CCCs of 0.962³⁵ and 0.998.³⁶ The range of corneal thickness CCCs for all the three instruments was 0.97 to 0.99. The nasal and temporal locations measured with both the instruments showed less repeatability compared to the apex with CCC values ranging from 0.52 to 0.58. The epithelial thickness measurements showed poor repeatability with Visante™ OCT and OCT II values ranging from 0.34 to 0.75.

Peripheral corneal pachymetry measure-

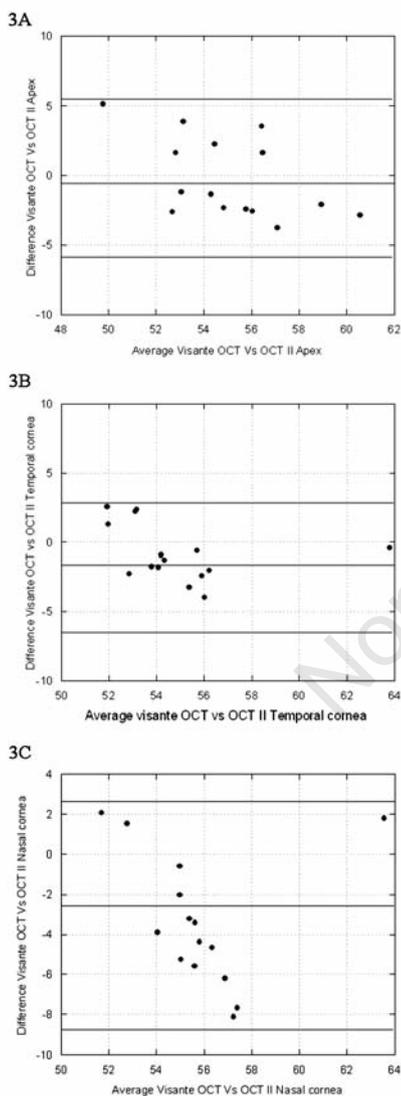


Figure 3. A) Apex, B) Nasal cornea, C) Temporal cornea). Represent Bland and Altman graph of Visante™ OCT versus OCT II (epithelial thickness Day 1).

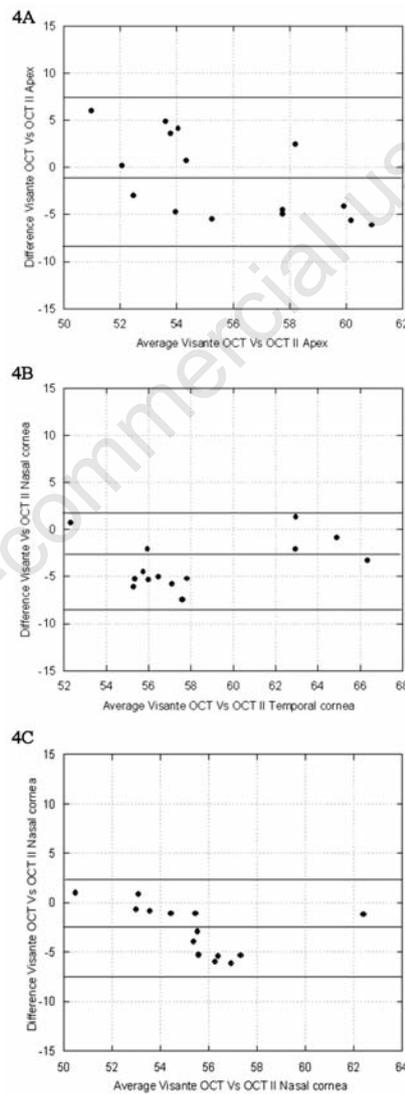


Figure 4. A) Apex, B) Nasal cornea, C) Temporal cornea. Represent Bland and Altman graph of Visante™ OCT versus OCT II (epithelial thickness Day 2).

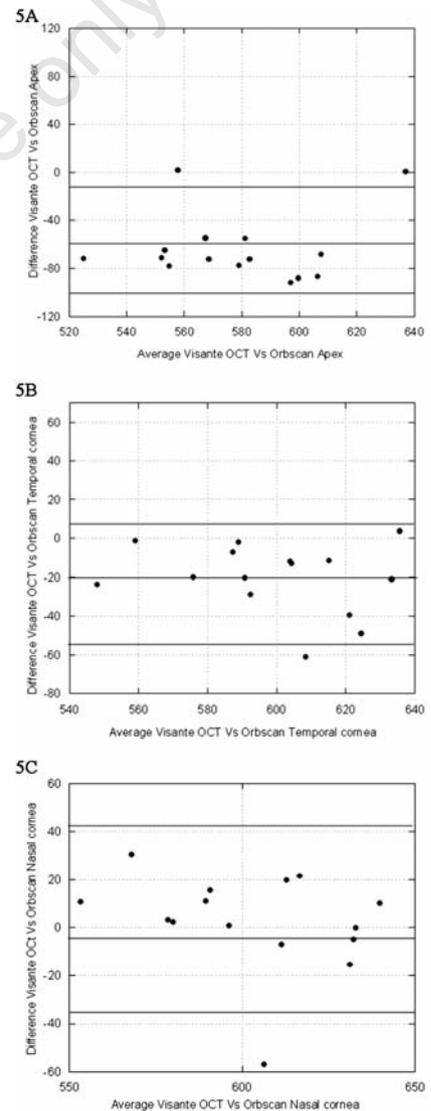


Figure 5. A) Apex, B) Nasal cornea, C) Temporal cornea. Represent Bland and Altman graph of Visante™ OCT versus Orbscan (total corneal thickness Day 1).

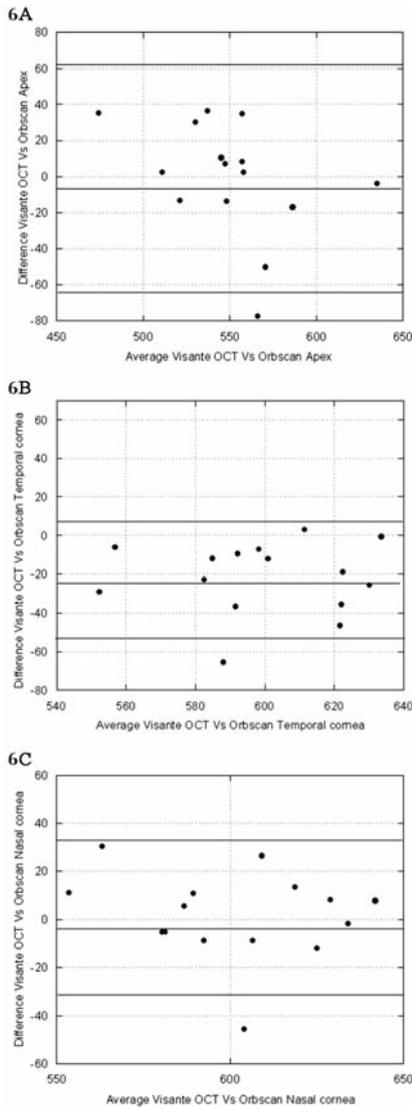


Figure 6. A) Apex, B) Nasal, C) Temporal cornea. Represent Bland and Altman graph of Visante™ OCT versus Orbscan (total corneal thickness Day 2).

ments were difficult to repeat. Some of the previous studies have also shown similar results; Li *et al.* reported thinner and less reliable measurements in the peripheral zone of 7 mm diameter or greater.³⁷ Sin *et al.* have also reported central corneal epithelial thickness repeatability to be much lower compared to the corneal thickness measurement repeatability and have emphasized the importance of averaging images and the requirement of increasing sample size to potentially overcome this.³²

As discussed above, the *within* device repeatability was generally good. There was poorer concordance *between* the instruments compared to within instrument test-retest. The highest CCC of 0.97 was between the Visante™ OCT and the OCT II for measurements of apical central corneal thickness on

Day 2. The range of between-device apical corneal thickness CCCs was 0.66 to 0.97. The epithelium measurements were less repeatable, ranging from 0.53 to 0.57, similar to the report by Muscat *et al.*¹⁴

Our study showed the Visante™ OCT is the most repeatable for total corneal thickness and epithelial thickness compared to the OCT II and the Orbscan II™ in the central, nasal and temporal cornea with CORs ranging from 7.71 μm to 9.92 μm . Similarly Muscat *et al.*¹⁴ have shown a COR of 11 μm averaged for 6 radial scans and a COR of 10 μm for central corneal thickness of three horizontal scans;³² our study also showed similar results of 13.31 μm for CCT and 8.81 μm CCT at the apex.

The Orbscan II™ corneal thickness measurements were significantly higher ($P < 0.05$) than the Visante™ OCT and OCT II but the repeatability was similar for all the three instruments. The CORs estimated using the measurements from the Orbscan II™ were $\pm 11 \mu\text{m}$, similar to those of apical measurements reported by Marsich and Bullimore.³⁸

An important reason for performing the repeatability studies is to obtain information about the measurements themselves. Our results were that the test-retest and between-device measurements were generally consistent, and that the within-device Visante™ OCT repeatability was the best. On the other hand, the repeatability of the epithelial thickness measurements was poorer; this variability can be minimized by averaging multiple images. This was also suggested by Sander *et al.* who showed that OCT averaging enables recovery of detailed structural information about the retina, and averaging helps in improved imaging of the retina. Sander *et al.* also showed that averaged images correlate well with known pathology.³⁹ Our results are similar to these and also to those reported by Sin and Simpson.³² Because clinicians typically do not collect multiple images and average them, greater care should be taken in the interpretation of these measurements.

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