Original Article

Agreement of Two Different Spectral Domain Optical Coherence Tomography Instruments for Retinal Nerve Fiber Layer Measurements

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Purpose: To determine the agreement between Spectralis and Cirrus spectral domain optical coherence tomography (SD-OCT) measurements of peripapillary retinal nerve fiber layer (RNFL) thickness.
Methods: Suspected or confirmed cases of glaucoma who met the inclusion criteria underwent peripapillary RNFL thickness measurement using both the Spectralis and Cirrus on the same day within a few minutes.
Results: Measurements were performed on 103 eyes of 103 patients with mean age of 50.4±17.7 years. Mean RNFL thickness was 89.22±15.87 versus 84.54±13.68 μm using Spectralis and Cirrus, respectively. The difference between measurements and the average of paired measurements with the two devices showed a significant linear relationship. Bland-Altman plots demonstrated that Spectralis thickness values were systematically larger than that of Cirrus.
Conclusion: Spectralis OCT generates higher peripapillary RNFL thickness readings as compared to Cirrus OCT; this should be kept in mind when values obtained with different instruments are compared during follow-up.

Keywords: Glaucoma; Optical Coherence Tomography; Peripapillary Retinal Nerve Fiber Layer

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INTRODUCTION

Ancillary tests have become an integral part in the evaluation and follow-up of patients with established glaucoma or glaucoma suspects. The diagnosis of glaucoma suspects and management of glaucoma patients has been a challenging issue for ophthalmologists and a number of paraclinical tests have been utilized.[1-11]

With the advent of optical coherence tomography (OCT), it became possible to measure retinal nerve fiber layer (RNFL) thickness. The importance and specificity of OCT for detection and management of glaucoma has been suggested by many authors.[12-17]

Several companies now manufacture OCT systems, such as the Spectralis (Heidelberg Engineering, Heidelberg Germany), Cirrus (SD-OCT, Carl Zeiss Meditec Inc., Dublin, CA, USA), and RTVue-100 (Optovue Inc., Fremont, CA, USA). The methods of RNFL measurement are different among OCT modalities. Ophthalmologists often have to make a decision for a patient based on two or more follow-up examinations with two or more different OCT modalities. Herein we compare peripapillary

RNFL thickness measurements using Spectralis OCT versus Cirrus OCT.

METHODS

This study includes 103 eyes of 103 patients with glaucoma or glaucoma suspects who were visited at our glaucoma clinic. The study protocol was reviewed by the Institutional Review Board of our research center. Each participant was informed of the purpose of the study and provided written consent to participate. All patients underwent a thorough ophthalmologic examination including refraction, determination of best corrected visual acuity, slit lamp biomicroscopy, IOP measurement using Goldmann applanation tonometry, gonioscopy using Zeiss four-mirror indirect goniolens (Carl Zeiss Meditec, Dublin, CA, USA), stereoscopic fundus examination using a 90D lens, and automated perimetry with the Humphrey visual field analyzer (Carl Zeiss Meditec, Dublin, CA, USA). After pupillary dilation, RNFL thickness was measured using both Spectralis OCT (Spectralis HRA+OCT, Heidelberg Engineering, Heidelberg, Germany) and Cirrus SD-OCT (Carl Zeiss Meditec, Dublin, CA, USA [software version 4.0]) consecutively on the same day, within a few minutes. Patients with other conditions such as diabetes mellitus, hazy media, poor cooperation precluding high quality image acquisition or other causes of optic nerve damage were excluded from the study.

Glaucoma was defined as presence of cup/disc ratio (CDR) more than 0.6 or CDR asymmetry more than 0.2, or a neuroretinal rim width reduced to ≤ 0.1 CDR that showed a definite visual field (VF) defect consistent with glaucoma. In the lack of perimetry or unconfirmed visual field defects, patients with solely advanced structural damage were diagnosed as having glaucoma. Glaucoma suspect was defined as: 1. Presence of cup/disk ratio (CDR) more than 0.6 or CDR asymmetry exceeding 0.2, or a neuroretinal rim width reduced to ≤ 0.1 without proven field defects. 2. Those with definite field defects without disc signs. 3. Those with optic disc margin hemorrahages. 4. Those with IOP > 21 mmHg.

For the Cirrus SD-OCT, the optic disc cube (200×200 A-scans) protocol was used for image acquisition and analysis. This protocol generates a cube of data through a 6 mm square grid by acquiring a series of 200 horizontal scan lines, each composed of 200 A-scans. For analysis, the Cirrus algorithm identifies the center of the optic disc and automatically places a calculation circle 3.46 mm in diameter around it.

RNFL thickness was measured in the temporal, nasal, superior, and inferior quadrants. Layer-seeking algorithms detected RNFL boundaries for the entire cube, except at the optic disk. On the basis of the RNFL layer boundaries in the extracted circle scan image, the system calculates RNFL thickness at each point along the measurement circle. Scans with signal strength <6 were repeated for better quality or excluded if not improved.

For the Spectralis OCT, a scan circle with a diameter of approximately 3.45 mm was manually positioned at the center of the optic disc. Nine images at the same location were captured and averaged automatically by the built-in software to increase image signal to noise ratio (SNR) and improve the quality of subsequent images. All captured images had a signal quality of equal or greater than 20 dB.

In each image, artifacts and segmentation were checked and corrected manually in both devices. All measurements were performed on the same day within 1 hour of pupil dilation. All measurements were obtained by the same operator (FH) who is experienced with acquisition of OCT images.

Two parameters were included for comparison of RNFL thickness measurements, quadrant thicknesses and global RNFL thickness. Mean and standard deviation (SD) values were calculated for each series of RNFL measurements and were compared using paired t-test between the two methods. Pearson correlation coefficients were used to test the correlation between RNFL measurements using Cirrus and Spectralis OCT. Mean difference and 95% LoA (limit of agreement) were used to assess Interdevice agreement. The 95% LoA was calculated as mean ± SD×1.96 of differences between paired measurements, and illustrated in Bland-Altman plots.

Table 1. Mean RNFL thickness in different sectors measured by Spectralis and Cirrus OCT devices

	Spectralis (µm)	Cirrus (µm)	Correlation coefficient	P-value
	Mean ± SD (CV)	Mean ± SD (CV)		
Superior	107.9 ± 22.5 (0.21)	99.89 ± 19.04 (0.19)	0.854	<0.001
Inferior	111.29 ± 24.88 (0.22)	105.24 ± 22.62 (0.21)	0.924	<0.001
Temporal	68.57 ± 12.5 (0.18)	62.27 ± 11.02 (0.18)	0.696	<0.001
Nasal	68.75 ± 14.63 (0.21)	71.01 ± 11.55 (0.16)	0.804	<0.001
Average	89.22 ± 15.87 (0.18)	84.54 ± 13.68 (0.16)	0.912	<0.001

RNFL, retinal nerve fiber layer; OCT, optical coherence tomography; SD, standard deviation; CV, coefficient of variation

RESULTS

A total of 103 eyes of 103 patients with mean age of 50.4±17.7 years including 50 (48%) male subjects were studied. Glaucoma patients were significantly older than glaucoma suspects; 54.9±16.9 versus 45.4±17.4 years, respectively (P=0.013).

Table 1 summarizes RNFL thickness values using the two OCT systems. Mean image quality was 26.9±4.4 (range, 20-38) dB with Spectralis and 7.8±1.3 (range, 6-10) with Cirrus.

A significant linear relationship was found between inter-measurement differences and their average. Bland-Altman plots showed that Spectralis measurements were systematically larger than those of Cirrus.

Table 2 shows mean differences between RNFL measurements using the two devices in different anatomical locations. We also compared RNFL thickness between glaucoma and glaucoma suspect groups. No significant difference was found in terms of RNFL thicknesses measured using either of the two devices in any of the four quadrants (superior, inferior, temporal and nasal). The results are shown in Table 3.

Figure 1 shows the agreement between the two methods of measurement, as analyzed by Bland-Altman plots (95% LoA for the two devices in all quadrants). Figure 2 shows the correlation between the two methods (r=0.912, P<0.001). The 95% LoA for the two devices was between -17.50 and 8.16 µm (Figure 3).

Table 2. Mean difference (Spectralis minus Cirrus) between the two instruments at different locations

Anatomical location	Mean ± SD (95%CI)	P-value
Superior	8.01 ± 11.71 (5.7 -10.32)	<0.001
Inferior	6.05 ± 9.5 (4.17 -7.93)	<0.001
Temporal	6.31 ± 9.27 (4.48 -8.14)	<0.001
Nasal	-2.26 ± 8.69 (-3.97 --0.54)	0.01
Average	4.67 ± 6.55 (3.38 -5.97)	<0.001

SD, standard deviation; CI, confidence interval

DISCUSSION

OCT-based RNFL thickness measurement is a useful method for detecting early glaucomatous damage.[16,17] Following the availability of a variety of OCT machines, various studies have reported RNFL thickness in glaucoma. Many studies compared old and new generations of OCT[13,18-20] but differences among newer generation OCTs are now challenging in the diagnosis, management, and follow-up of glaucoma patients.

In a recent study by Savini et al,[21] RNFL thicknesses were compared between two Fourier domain OCTs (Cirrus and RTVue). The RTVue yielded higher mean RNFL thickness values in all quadrants; average values were 105.88±114.59

Table 3. RNFL thickness measurements in glaucoma patients and glaucoma suspects using Spectralis and Cirrus OCT

	Number	Mean (µm)	SD	SE
Spectralis				
Glaucoma	62.00	86.83	17.83	2.30
Glaucoma suspect	41.00	92.71	11.80	1.84
Cirrus				
Glaucoma	62.00	82.33	14.99	1.94
Glaucoma suspect	41.00	87.78	10.87	1.70

RNFL, retinal nerve fiber layer; OCT, optical coherence tomography; SD, standard deviation; SE, standard error

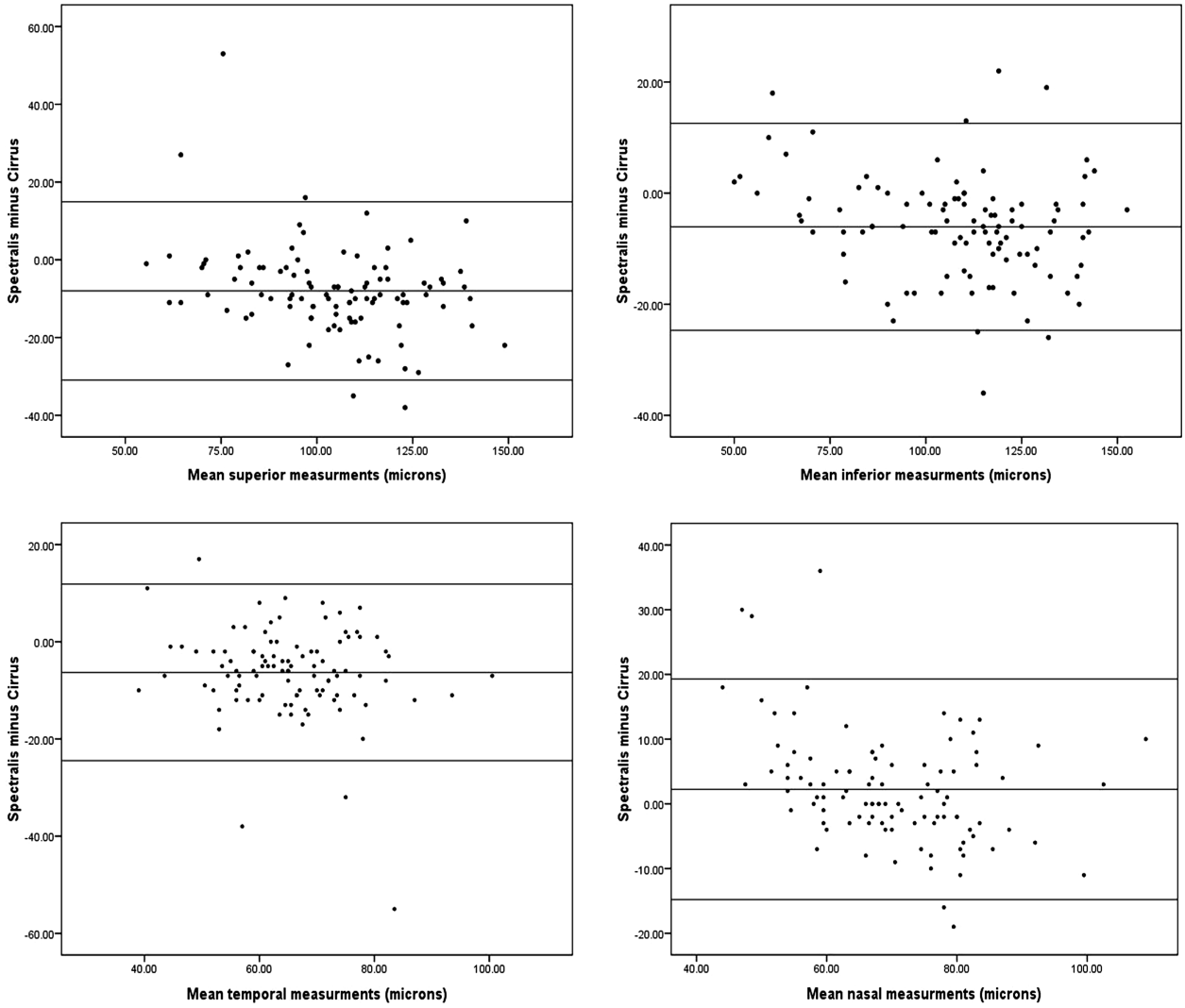

Figure 1. Top Left: Agreement between Spectralis and Cirrus optical coherence tomography (OCT) measurements of superior retinal nerve fiber layer (RNFL) thickness. The middle line indicates the mean difference and the two side lines show the 95% limits of agreement (range, -30.95 to 14.93 µm). Top Right: Agreement of inferior RNFL thickness values. 95% limits of agreement range from -24.67 to 12.57 µm. Bottom Left: Agreement between temporal RNFL thickness. 95% limits of agreement range from -24.47 to 11.86 µm. Bottom Right: Agreement between nasal RNFL thickness. 95% limits of agreement range from -14.78 to 19.29 µm.

vs. 95.21±12.45 µm using RTVue vs. Cirrus modes, respectively. These values are higher than our measurements which is most probably due to the fact that Savini et al measured RNFL thickness in normal subjects.

In another study by Kanamori et al,[16] OCT scans were performed using the OCT-2000 system. They reported average RNFL thicknesses higher than Cirrus measurements in the current study (mean thickness of 107.4±13.9 µm in a group of glaucoma suspects and 84.5±21.1 µm in patients with definite glaucoma).

Sung et al[22] measured RNFL thickness in normal and abnormal eyes using Cirrus and Stratus systems and found that measurements using the Stratus system were significantly higher than those obtained with the Cirrus system. Average RNFL thickness using the Cirrus system in their study was very similar to those obtained in the current study (85.6±14.6 vs. 84.54±13.68 µm, respectively). Compared with the time-domain stratus OCT, Cirrus tended to produce higher retinal thickness measurements but lower RNFL thickness measurements which

may be due to an higher resolution and a greater volume of data acquired with each scan.[23]

Image resolution is 5 µm with the Cirrus and 3.9 µm in the Spectralis, but the number of A-scans per second is 27,000 for the former versus 40,000 in the latter.[24]

In the current study, RNFL thickness using Spectralis was greater as compared to those obtained with Cirrus. This difference may be due to dissimilarity in RNFL boundary segmentation algorithms, signal strength, scan acquisition and registration, data processing, and/or software properties between the two devices. Pakravan et al[25] also found out that the measurement of RNFL thickness by Topcon apparatus is higher than Cirrus. According to Balasubramanian et al,[26] an image quality of ≥7 SNR with Cirrus and ≥19 dB with Spectralis is assumed to provide optimal quality in glaucoma suspects. In our study, image quality with both devices seemed to be at the same level, although it was somehow in the lower range (mean 7.8 SNR) with Cirrus and in the higher range with Spectralis (mean 26.9 dB). Perhaps images with Spectralis are of higher quality. The reason for this finding is not clear, since image acquisition conditions were the same with both devices (same day, within minutes).

Figure 4 shows differences in layer segmentation and image sharpness between the devices employed in the current study. Spectralis enables real-time eye tracking and can acquire 1 to 100 B-scans at the same location.[27] This provides very high repeatability and reproducibility with a small coefficient of variation (0.53%).[28] Additionally, software processing is able to reduce noise and speckle, which can provide higher precision aside from

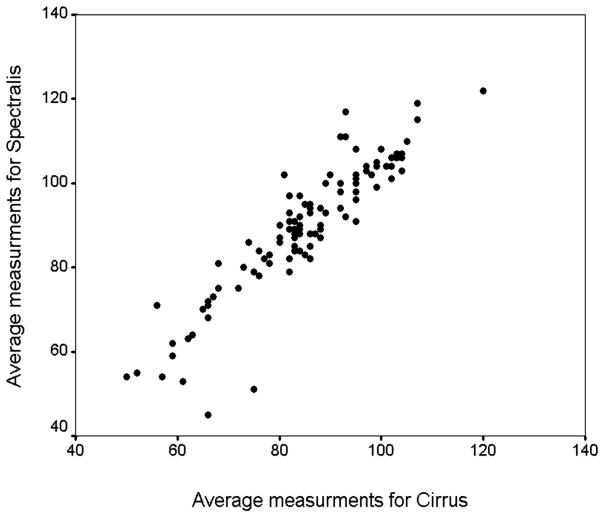

Figure 2. Correlation between average retinal nerve fiber layer thickness measurements using Spectralis and Cirrus optical coherence tomography.

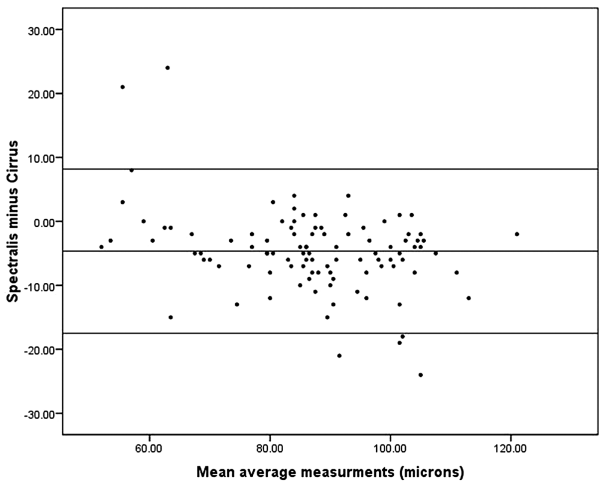

Figure 3. Agreement between Spectralis and Cirrus optical coherence tomography for average retinal nerve fiber layer measurements. The middle line indicates the mean difference, and the two side lines show the 95% limits of agreement (range, -17.51 to 8.16 µm).

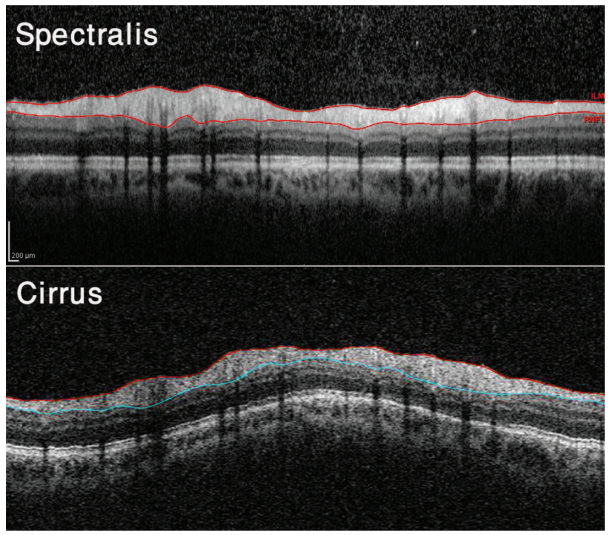

Figure 4. Top: Spectralis RNFL circular cut of an OCT with image quality of 26 dB. Bottom: RNFL cut of the same patient with Cirrus and image quality of 8 SNR. Image segmentation algorithms and layering are different in the devices and RNFL is clearly thinner in the Cirrus image.
RNFL, retinal nerve fiber layer; OCT, optical coherence tomography

a higher resolution or A-scan speed alone. Therefore, the system can make follow-up images exactly in the same location.[23] Hence, higher precision and resolution of images might be explained by better image acquisition (eye tracking) and post processing (averaging) with Spectralis.

In a study by Samarawickrama et al[29] higher signal strength led to larger measurements in the OCT examination. In a study by Velthoven et al[30] increased retinal thickness measurements following cataract surgery resulted from increased image quality. This issue may explain the larger measurements we observed with the Spectralis device with higher image quality in our study. However, we did not grade cataracts and did not include normal eyes, which could be limitations to our study.

The current study showed that Spectralis measurements are higher than those obtained with the Cirrus device. Although measurements are not interchangeable from device to device, it may become necessary to estimate the differences between them and account for these differences during follow-up OCT examinations.

Conflicts of Interest

None.

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