Original Article

Comparison of the Diagnostic Ability of Retinal Nerve Fiber Layer Thickness Measured using Time Domain and Spectral Domain Optical Coherence Tomography in Primary Open Angle Glaucoma

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Abstract

Purpose: To evaluate and compare the diagnostic ability of retinal nerve fiber layer (RNFL) thickness measurements using time domain (Stratus) and spectral domain (Cirrus HD) optical coherence tomography (OCT) in preperimetric and early primary open angle glaucoma (POAG).

Methods: A total of 62 eyes from 62 normal subjects, 47 eyes from 47 early perimetric damage POAG patients and 30 eyes from 30 preperimetric glaucoma patients were chosen in the study. All the subjects underwent peripapillary RNFL thickness measurements using Stratus OCT and Cirrus HD-OCT on the same day by a single trained operator. The RNFL thickness measured by Stratus OCT and Cirrus HD-OCT was statistically compared using paired t-tests. The relationship between RNFL thickness measured by two OCT instruments was evaluated using Pearson's correlation coefficient. Areas under the receiver operating characteristic curves (AROC) were calculated and compared.

Results: RNFL thickness measured using Stratus OCT was generally thicker than that using Cirrus HD-OCT ($P<0.05$). A highly significant correlation between the two OCT instruments measurements was found in four quadrants and average RNFL thickness measurements ($P<0.001$). The average RNFL thickness of Cirrus HD-OCT had significantly ($P=0.006$) higher diagnostic ability (AROC=0.951) than that of Stratus OCT (AROC=0.881) in preperimetric glaucoma. There were no significant differences between the AROCs for other RNFL thickness parameters from Cirrus HD-OCT and Stratus OCT in preperimetric and early glaucoma ($P>0.05$).

Conclusion: Significant differences and an excellent correlation were noted in terms of RNFL thickness measurements using Stratus OCT and Cirrus HD-OCT. Cirrus HD-OCT presented higher diagnostic ability for preperimetric glaucoma. (***Eye Science 2011;26:132-137***)

Keywords: optical coherence tomography; retinal nerve fiber layer; glaucoma

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Optical coherence tomography (OCT) is widely used for in vivo measurements of retinal nerve fiber layer (RNFL) thickness. The measurements have been shown to have good reproducibility[1-2], and to correlate well with histological parameters[3-4]. Assessment of the RNFL thickness is of diagnostic significance in glaucoma. Numerous studies have shown that the time domain OCT (Stratus OCT, Carl Zeiss Meditec, Inc., Dublin, CA) can effectively detect and monitor the changes in RNFL thickness of glaucoma[5-6]. The recent introduction of spectral domain OCT offers a faster scan speed and a higher imaging resolution for RNFL measurement[7], such as the Cirrus HD-OCT (Carl Zeiss Meditec, Inc.). Glaucoma is a progressive disease, so longitudinal follow-up for tracking glaucomatous change is crucial. It is important to know whether the RNFL thickness measurements using time domain and spectral domain OCT instruments are comparable, and which instrument is better for early diagnosis of primary open angle glaucoma (POAG). The study was designed to compare and evaluate the diagnostic ability of the peripapillary retinal nerve fiber layer (RNFL) thickness measurements using the two OCT instruments (Stratus OCT and Cirrus HD-OCT) in preperimetric and early perimetric damage POAG.

Methods

This study included 139 subjects who were imaged with both instruments on the same day during the period from May to December 2010 at Shenzhen Eye Hospital. There were 62 normal subjects, 47 early perimetric damage POAG and 30 preperimetric glaucoma (PPG) patients. All subjects underwent a comprehensive ocular examination including review of the medical history, visual acuity, refraction, slit lamp biomicroscopy, gonioscopy, intraocular pressure (IOP) measurement with Goldmann tonometry, fundus examination, and visual field (VF, Humphrey 750i) examination. The inclusion criteria for all subjects aged 20~60 years, best corrected visual acuity no worse than 0.9 (Snellen decimal scale) and spherical refractive error within the range of −6.00 to +3.00 D. One eye fitting the study criteria was selected randomly from each subject in the analysis. All subjects gave informed consent before enrollment.

Normal subjects had no ocular or intraocular dis eases, with Goldmann applanation tonometer (GAT) ≤ 21 mmHg and a normal Humphrey SITA 24−2 standard VF for both eyes. A central corneal thickness was 520~580 μm, a normal appearing optic disc head and no RNFL defects.

The early POAG inclusion criteria: 1) GAT >22 mmHg; 2) Typical glaucomatous optic disc appearance, such as rim thinning, notching, excavation, hemorrhage, or RNFL defects; 3) Early glaucomatous VF loss on at least two separate occasions with mean deviation ≥−6 dB, exhibited a typical arcuate or paracentral scotoma and/or nasal step on their VF test, with clusters of three or more adjacent points depressed more than 5 dB or two or more adjacent points depressed more than 10 dB; 4) Open and wide anterior chamber angle; 5) No other diseases except glaucoma that may affect the IOP measurement results and optic nerve atrophy.

The PPG patients had all the same inclusion criteria for the POAG patients except the VF loss.

After undergoing mydriasis and with 6~8 mm pupil size, each subject was imaged with the two OCT instruments on the same day by a single trained operator. RNFL was scanned with the protocol of Stratus OCT (Fast RNFL scan mode) and Cirrus HD-OCT (200×200 Optic Disc cube mode) in a random order.

The protocol of Stratus OCT (software version 3.0; Carl Zeiss Meditec) consists of 3 consecutive scan circles with 3.4 mm diameter, and 256 A−scans of each circle taken over 1.92 seconds. The scan circle was positioned manually at the center of the optic disc. The average and quadrant RNFL thicknesses were recorded. We excluded the images with signal strength <7 and the scan circle not centered on the optic nerve head.

The protocol of Cirrus HD-OCT (software version 3.0; Carl Zeiss Meditec) captures a 6×6×2 mm^3 "cube" of data consisting of 200 A-scans from 200 linear B-scans (40000 points) in 1.5 seconds. The RNFL thickness at each scan point was analyzed and a RNFL map (6×6 mm) was constructed. Cirrus algorithms identified the center of the optic disc and automatically placed a calculation circle of 3.4 mm diameter around it. The system software calculates the RNFL thickness on the circle and generates the average and quadrant RNFL measurements. Scans with movement artifact or signal strength of less than 7 were excluded from the analysis.

Statistical analysis was performed on computer (SPSS ver.15.0; SPSS Inc, Chicago, IL). The average and quadrant RNFL thickness measurements between two OCT instruments were compared by using paired-sample t-tests. A Bland-Altman plot was graphed to assess the agreement between the two OCT instruments. The relationship between RNFL thickness measurements of the two OCT instruments were evaluated using Pearson's correlation coefficient. Areas under the receiver operating characteristic curves (AROC) were calculated and compared. $P<0.05$ was considered statistically significant.

Results

A total of 139 eyes of 139 subjects were enrolled, which were placed into the following groups: normal (n=62), early POAG (n=47), PPG (n=30). Table 1 summarizes the demographic and clinical characteristics of subjects. The age and average spherical e quivalent were matched among the normal, early

POAG and PPG groups.The mean deviation and pattern standard deviation of VF loss were significantly different among the three groups. There was no significant difference in terms of the image quality (signal strength) between the two OCT instruments ($P>0.05$, paired t-test).

The average and each quadrant RNFL thicknesses obtained from Stratus OCT were significantly thicker than those obtained with Cirrus HD-OCT ($P<0.05$, paired t-test, Table 2).

Table 1 Clinical characteristics of the normal, early POAG and PPG groups ($\bar{x}\pm s$)

Group	*n*	Age (yrs)	Spherical error (D)	MD (dB)	PSD (dB)
Normal	62	46.9±13.7	−2.12±1.70	−0.51±1.04	1.45±0.55
PPG	30	48.6±13.8	−2.24±2.68	−1.32±1.51	1.73±0.80
Early POAG	47	48.6±13.7	−1.91±2.65	−3.96±1.98	4.52±2.16
F^*		0.220	2.517	70.815	74.819
P^*		0.803	0.084	0.000	0.000

* ANOVA analysis

Table 2 Comparison of retinal nerve fiber layer (RNFL) thickness measurement by Stratus OCT and Cirrus HD−OCT ($\bar{x}\pm s$, μm)

groups (*n*)	RNFL thickness	Cirrus HD−OCT	Stratus OCT	Difference (Stratus-Cirrus)	t^*	P^*
Normal (*n*=62)	Average	101.7±9.7	115.3±14.8	13.6±8.8	12.110	0.001
	Superior	128.8±14.9	141.2±15.6	12.4±11.3	8.606	0.001
	Temporal	72.3±9.1	83.4±12.9	11.0±8.1	10.739	0.001
	Inferior	133.5±19.4	148.6±21.3	15.1±12.2	9.799	0.001
	Nasal	72.3±11.1	84.0±15.5	11.6±10.6	8.681	0.001
PPG (*n*=30)	Average	83.6±7.8	95.1±11.5	11.4±7.6	8.253	0.001
	Superior	100.5±12.8	118.4±17.0	15.9±7.9	11.052	0.001
	Temporal	69.1±13.7	78.7±16.2	9.53±14.2	3.656	0.001
	Inferior	102.5±12.8	118.4±17.0	15.9±7.8	11.052	0.001
	Nasal	62.4±11.1	68.1±18.6	6.9±17.5	2.961	0.047
Early POAG (*n*=47)	Average	72.0±10.9	81.6±13.5	9.5±8.9	7.337	0.001
	Superior	87.5±18.1	98.9±19.3	11.3±9.5	8.168	0.001
	Temporal	59.7±13.6	66.2±14.4	6.6±13.9	3.245	0.002
	Inferior	81.0±18.6	95.6±22.6	14.5±11.6	8.562	0.001
	Nasal	59.7±11.1	65.7±15.4	6.0±13.1	2.633	0.042

* Paired-samples t-test

Table 3 shows significant correlations between the RNFL thickness measurements using the two OCT instruments. Figure 1 shows the scatter plot and regression line of the average RNFL thickness measurements with Stratus OCT and Cirrus HD-OCT ($Y=14.615+0.735X$, $R^2=0.907$; X: Stratus OCT, Y: Cirrus HD-OCT). Figure 2 shows the agreement of the average RNFL thickness between Stratus OCT and Cirrus HD-OCT.

Table 3 Correlation of retinal nerve fiber layer (RNFL) thickness measurement on average and each quadrant using Stratus OCT and Cirrus HD−OCT

	r (95%CI)	*P*	Equation
Average	0.907 (0.872~0.932)	0.000	Y=14.615+0.735X
Superior	0.913 (0.881~0.937)	0.000	Y=3.372+0.871X
Temporal	0.684 (0.584~0.763)	0.000	Y=24.714+0.557X
Inferior	0.935 (0.910~0.953)	0.000	Y=0.574+0.873X
Nasal	0.676 (0.574~0.757)	0.000	Y=33.364+0.436X

The AROC provides a summary measure of the accuracy of diagnosing early POAG (Table 4, Figure 3) and PPG (Table 5, Figure 4) against the normal reference group. The average RNFL thickness of Cirrus HD-OCT had significantly ($P=0.006$) higher AROC (0.951) than that of Stratus OCT (AROC=0.881) in PPG group. There were no significant differences between the AROCs for the other RNFL thickness parameters from Cirrus HD-OCT and Stratus OCT in PPG and early POAG groups ($P>0.05$).

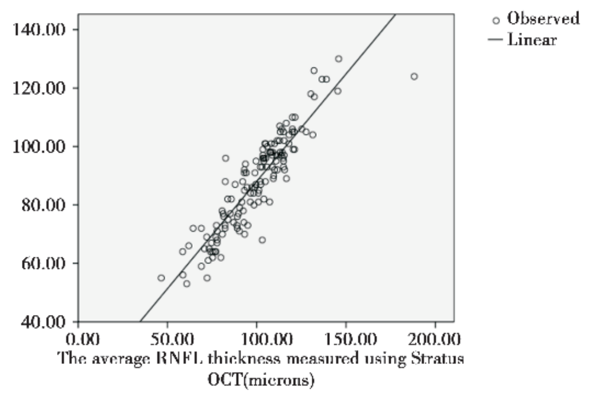

Figure 1 Scatter plot and regression line shows the correlation of average retinal nerve fiber layer (RNFL) thickness measurements between Stratus OCT and Cirrus HD-OCT.

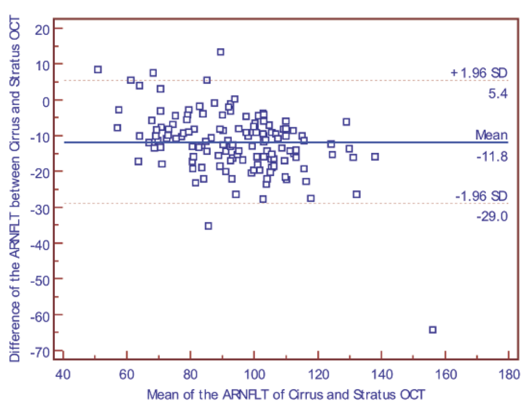

Figure 2 Bland-Altman plot of the agreement of average RNFL thickness (ARNFLT) measurements between Stratus OCT and Cirrus HD-OCT, with the mean difference -11.8 μm (solid line) and 95% limits of agreement (dashed line).

Table 4 Diagnostic accuracy of Cirrus HD-OCT and Stratus OCT Parameters in PPG and normal groups

RNFLT parameter	OCT instrument	AROC(95%CI)	*P*
Average	Cirrus HD-OCT	0.951 (0.884~0.985)	0.006
	Stratus OCT	0.881 (0.797~0.939)	
Superior	Cirrus HD-OCT	0.931 (0.859~0.973)	0.149
	Stratus OCT	0.897 (0.816~0.951)	
Inferior	Cirrus HD-OCT	0.915 (0.838~0.963)	0.052
	Stratus OCT	0.871 (0.785~0.932)	
Nasal	Cirrus HD-OCT	0.758 (0.657~0.841)	0.242
	Stratus OCT	0.698 (0.594~0.790)	
Temporal	Cirrus HD-OCT	0.597 (0.489~0.698)	0.967
	Stratus OCT	0.599 (0.492~0.700)	

To investigate whether the RNFL thickness measured using Cirrus HD-OCT can help to detect glaucomatous abnormalities not picked up by that using Stratus OCT, we constructed Venn diagrams of RNFL thickness abnormalities in both the early POAG and PPG groups (Figure 5). We defined the abnormal RNFL parameter as any of the RNFL thickness parameters below the percentile of the 95% normal reference.

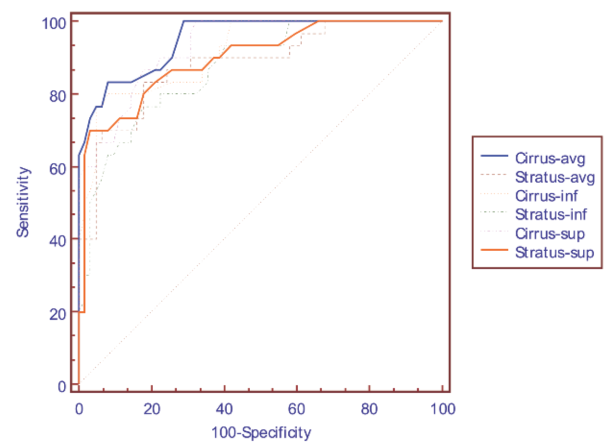

Figure 3 ROC curves of the average, superior and inferior quadrants RNFL thickness parameters from the Cirrus HD-OCT and Stratus OCT in PPG and normal groups.

Table 5 Diagnostic accuracy of Cirrus HD-OCT and Stratus OCT parameters in early POAG and normal groups

RNFLT parameter	OCT instrument	AROC(95%CI)	*P*
Average	Cirrus HD-OCT	0.976(0.927~0.995)	0.450
	Stratus OCT	0.984(0.939~0.998)	
Superior	Cirrus HD-OCT	0.951(0.892~0.983)	0.820
	Stratus OCT	0.954(0.896~0.985)	
Inferior	Cirrus HD-OCT	0.979(0.931~0.996)	0.097
	Stratus OCT	0.955(0.898~0.985)	
Nasal	Cirrus HD-OCT	0.806(0.719~0.875)	0.583
	Stratus OCT	0.785(0.696~0.858)	
Temporal	Cirrus HD-OCT	0.799(0.711~0.869)	0.905
	Stratus OCT	0.803(0.716~0.873)	

Discussion

This study found in normal, PPG and early POAG groups, the Cirrus HD-OCT produced thinner RNFL thickness measurements than the Stratus OCT. In some cases of PPG and early POAG groups, the RNFL of subjects was thinner and the difference between OCT measurements became smaller, even in several cases the Cirrus HD-OCT yielded thicker RNFL thickness measurements than the Stratus OCT.

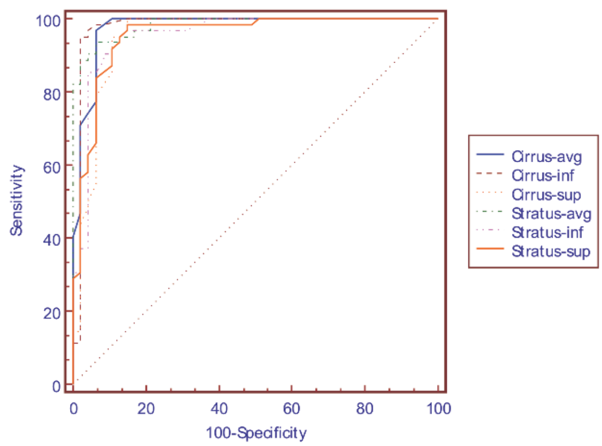

Figure 4 ROC curves of the average, superior and inferior quadrants RNFL thickness parameters from the Cirrus HD-OCT and Stratus OCT in early POAG and normal groups.

This finding was also confirmed by Knight et al[8], and we also think there is a systemic difference in the RNFL thickness measurements with the two OCT instruments, which is not in a single direction.

Several reasons can be offered to explain the discrepancy between the two OCT measurements. Firstly, Cirrus HD-OCT and Stratus OCT use different scan technologies, although the basic principle of the two OCT instruments is the same. Stratus OCT relies on time domain technology with a scan speed of 400 A-scans per second and an axial resolution of 10 μm, and the scan circle with 256 data points is positioned manually around the optic disc[9-10]. Cirrus HD-OCT uses a wider band light source, with spectrometer and Fourier transformation technology, and so vastly improves the scan speed to 27000 A-scans per second and axial resolution to 5 μm[11]. Furthermore the calculation circle with the same data points was determined automatically by the Cirrus HD-OCT. It is expected that the fast scan speed, high axial resolution and precise location of scan circle should improve the accuracy of RNFL measurement and reduce the measurement variability secondary to movement artifact and scan displacement[9-12]. Secondly, there are differences in the image-segmentation algorithms and data analysis system between the two OCT instruments[8-9,12]. However due to the lack of histological evidence or manual segmentation, it is impossible to know which instrument is more accurate. Thirdly, when the RNFL thickness became thinner in some cases of the PPG and early POAG groups, RNFL thickness measurement with Cirrus HD-OCT were thicker than those with Stratus OCT. It was possibly due to a less accurate segmentation algorithm in measuring the thinner RNFL and the exposed blood vessels disturbance[8-9,13], which could only be confirmed histologically.

Figure 5 Venn diagrams show the overlap between abnormal RNFL thicknesses measured using Cirrus HD-OCT and Stratus OCT in both early POAG and PPG groups.

We also found there was high correlation between the RNFL thickness measurements using the two OCT instruments, no matter whether the differences were significant. In a study by Sung et al, 163 participants were recruited and the results also demonstrated the Cirrus RNFL measurements correlated well with those from Stratus OCT[12]. The correlation between the two OCT measurements was higher on average, the inferior and superior quadrant. This finding is of clinical importance because glaucomatous damage frequently is detected at the locations[14–16]. It is important for clinical repeated evaluation and tracking of glaucomatous changes with either or both of the two OCT instruments. The correlation of RNFL thickness measures by the two OCT instruments for the nasal quadrant was weaker than for the other quadrants, possibly due to the poorer reproducibility of the nasal quadrant RNFL measurement with Cirrus and Stratus OCT[2,10,17].

Our study showed the average RNFL thickness measured using Cirrus HD-OCT was significantly better at diagnosing glaucoma in the PPG group, compared with that using Stratus OCT. The Venn diagrams also showed the Cirrus HD-OCT had higher sensitivity than the Stratus OCT in PPG group. This was very important for early diagnosis of POAG especially when the VF was not damaged in the early stage (PPG) of the disease. It could be explained by the fact that the spectral domain OCT has improved imaging resolution, scan speed and sensitivity[18]. The Cirrus HD-OCT shows almost 65 times faster than the Stratus OCT, better axial resolution and faster imaging acquisition, which ensures both higher definition and less motion errors.

We also found the AROC of the RNFL thickness parameters in early POAG group was higher than that in PPG groups with both OCT instruments. Its diagnostic ability of the two OCT instruments might be able to satisfy clinical purpose at the early perimetric damage of the disease. It should be confirmed by further longitudinal studies, recruiting more subjects, and also to investigate the Cirrus HD-OCT in the detection and monitoring of glaucoma progression, compared with the conventional Stratus OCT.

In summary, RNFL thickness measurements generally were thinner using Cirrus HD-OCT than using Stratus OCT with an excellent correlation because of the systematic differences between the two OCT instruments.Both the Cirrus HD-OCT and Stratus OCT show high diagnostic ability for early perimetric damage POAG, and the Cirrus HD-OCT has higher diagnostic ability for preperimetric glaucoma.

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