Original article

Comparative evaluation of time domain and spectral domain optical coherence tomography in retinal nerve fiber layer thickness measurements

Dewang Angmo,[1] Shibal Bhartiya,[1] Sanjay K Mishra,[2] Reetika Sharma,[1] Amar Poojari,[1] Tanuj Dada[1]
[1]Dr Rajendra Prasad Centre for Ophthalmic Sciences, All India Institute of Medical Sciences
[2] R & R, Army Hospital, New Delhi 110029

Abstract

Introduction: Before any new device can replace another for use in clinical practice, it is imperative that its reproducibility, diagnostic accuracy, and ability to detect changes over time are tested. **Objective:** To evaluate retinal nerve fiber layer (RNFL) measurements between two optical coherence tomography (OCT) systems: the Stratus OCT, a time domain system, and the Cirrus HD-OCT, a spectral domain system (both by Carl Zeiss Meditec, Inc., Dublin, CA). **Materials and methods:** An observational cross-sectional study was carried out involving 20 eyes with primary open angle glaucoma and 32 eyes of healthy controls. One eye of each patient was imaged on the same day with each instrument.The RNFL thicknesses measured by the two instruments were compared. **Main outcome measures:** Each clock hour, quadrant, and average RNFL thickness was determined on each of the two instruments. **Statistics**: The reliability was assessed by the intra-class correlation coefficient (ICC) and the Bland Altman plot for the limits of agreement for the overall mean RNFL thickness and for each quadrant. **Results:** A randomly selected eye of each of the 52 participants was analyzed. The mean temporal, superior, nasal and inferior RNFL thickness (in microns) were found to be 65.42 ±18.98, 114.85±26.67, 75.83±28.61 and 116.35±29.43 when measured by the Stratus OCT. In glaucoma patients these values were 55.06±18.22, 97.86±29.37, 63.44±24.89, and 102.94±38.20; and in controls these values were 70.59±17.40, 123.61±20.65, 82.03±28.67 and 123.06±21.63 respectively. The mean temporal, superior, nasal and inferior RNFL thickness (in microns) were 62.00±13.08, 112.00±25.13, 68.56±16.66 and 114.23±25.82 respectively, when measured with the Cirrus OCT. In glaucoma patients these values were 57.88±12.99, 98.56±26.88, 64.63±12.52 and 105.50±29.49; while in the control group these were 64.06±12.82, 118.72±21.63, 70.53±18.33, and 118.59±23.05 respectively. Intraclass correlation coefficient alpha (ICC alpha) for the temporal, superior, nasal and inferior quadrant RNFL thickness measurements were 0.81, 0.85, 0.66 and 0.93 respectively. Bland-Altman plots showed the limits of agreement (95%CI) for average RNFL to be 4.59 ±20.10 in the control group. In patients of glaucoma, Bland-Altman plots showed the limits of agreement (95%CI)

Received on: 11.03.2014 Accepted on: 15.06.2014

Address for Correspondence
Dr Tanuj Dada, Professor of Ophthalmology
Dr Rajendra Prasad Centre for Ophthalmic Sciences, All India Institute of Medical Sciences,
New Delhi 110029, Fax 91-1126588919,
E-mail: tanujdada@gmail.com

for average RNFL to be 1.56±21.50. **Conclusions:** There is considerable variability in the RNFL thickness measurements made by the Cirrus and Stratus OCT that exceeds the limits of resolution afforded by the instruments. RNFL measurements obtained from the two OCT systems may not be used interchangeably.

Key-words: RNFL thickness, spectral domain OCT, time domain OCT, glaucoma

Introduction

Optical coherence tomography is used to scan through the layers of a structured tissue sample, such as the retina, with very high axial resolution (3 to 15 ìm), using low-coherence interferometry to determine the echo time delay and magnitude of backscattered light reflected off an object of interest (De Boer, 2003; Fujimoto, 2003).

The Stratus (Time Domain, TD) OCT encodes the location of each reflection in the time information relating the position of a moving reference mirror. The Cirrus (Spectral Domain, SD) OCT, on the other hand, acquires data by evaluating the frequency spectrum (using Fourier transformation) of the interference between the reflected light and a stationary reference mirror. This method is much faster, resulting in a large increase in the amount of data that can be obtained during a given scan duration using SD-OCT, with greater resolution than the time domain OCT (De Boer, 2003; Fujimoto, 2003).

However, before any new device can replace another for use in clinical practice, it is imperative that its reproducibility, diagnostic accuracy, and ability to detect changes over time are tested. It is with this objective that we initiated the present study to evaluate retinal nerve fiber layer (RNFL) measurements using two optical coherence tomography (OCT) systems: the Stratus OCT, a time domain system, and the Cirrus HD-OCT, a spectral domain system (both by Carl Zeiss Meditec Inc. Dublin, CA) and to compare their precision in the diagnosis of glaucoma

Material and methods

A total of 52 eyes of 52 subjects (20 eyes with primary open angle glaucoma and 32 eyes of healthy controls) were enrolled for this cross-sectional observational study. Informed consent was obtained from all participants.

All subjects underwent a thorough ophthalmologic examination, including assessment of medical and family history, visual acuity testing with refraction, slit-lamp biomicroscopy including gonioscopy, Goldmann applanation tonometry, and dilated stereoscopic fundus examination with a +90 D lens. Visual fields were evaluated using the Standard Automated Perimetry (SAP) Humphrey Field Analyzer (Humphrey-Zeiss Systems, Dublin, California, USA) 30-2 Swedish interactive threshold algorithm (SITA).

The inclusion criteria for all participants were a best-corrected visual acuity of 6/12 or better, a spherical refraction within ±5.0 diopters(D), open angles on gonioscopy and reliable (false positives, fixation losses, and false negatives of less than 33%) visual fields – Humphrey 30-2 SITA Standard. Glaucoma patients had evidence of glaucomatous optic neuropathy with reproducible visual field defects on SAP.

Exclusion criteria were media haze precluding disc evaluation, any other diseases affecting the visual fields (VF) (e.g., pituitary lesions, demyelinating diseases, traumatic optic neuropathy), and any history of intraocular surgery.

One eye of each of the subjects was evaluated on the Stratus and Cirrus OCT machines at an interval of 30 minutes, by the same observer on each machine. The order of the testing was decided by the toss of a coin and only scans with signal strengths equal to or greater than seven were used for analysis.

For this study, the Stratus OCT software version 4.0.7 (OCT Model 3000) fast RNFL (retinal nerve fibre layer) thickness was used. Details about the Stratus OCT are described elsewhere (Medeiros et al, 2005). In brief, a total of 3 scans, each composed of 256 A scans, are acquired consecutively using a circle with a diameter of 3.4 mm. An automated computerized algorithm delineates the anterior and posterior margins of the RNFL. The RNFL thickness parameters are measured by assessing 768 data points between the anterior and posterior RNFL borders, and the TSNIT (Temporal – Superior – Nasal – Inferior-Temporal) graph is compared to the normative database. The optic disc scan of the Cirrus OCT is a cube scan with a 6x6mm^2 area with 200x200 scans (200 A-scans per B-scan; 200 B-scans). The center of the optic disc is automatically identified for precise registration and repeatability. The RNFL thickness display is of a 1.73mm radius circle around the disc and the computed TSNIT graph is compared to the normative database as in the stratus OCT (Schuman, 2008).

The average RNFL thickness, as well as the thickness in each quadrant was evaluated. The data analysis was done using SPSS 11.00 (Chicago, II.)

Results

The mean age of the patients enrolled in the study was 54.6$\pm$5.1 years for the glaucoma patients and 52.2$\pm$4.6 years for the control group. The mean average RNFL thickness as measured in the overall subject population was 92.52 ±19.95 microns and 89.97 ±15.46 microns by the Stratus and Cirrus OCT, respectively. In the control group this value was 98.88±14.20 and 94.2±13.05, and in the glaucoma patients it was 79.81±23.94 and 81.38±16.71 microns as measured by the Stratus and Cirrus machines, respectively. The difference between the means, however, as measured by the two machines was not statistically significant (p values >0.01 on the paired t-test). The overall mean thickness of the quadrants measured by the Stratus OCT was consistently higher than that by the Cirrus, though this difference was not found to be statistically significant. This was true of the control group also. The TSNIT mean, however, as estimated by the stratus was less than that by the Cirrus in the case of glaucoma patients, the difference being insignificant statistically (Tables 1 and 2). The intra-class correlation coefficient alpha (ICC alpha) showed a good correlation between the average RNFL thicknesses measured by the two operating systems (0.90, 0.93 and 0.84μm for overall, glaucoma patients and control groups respectively). The correlation between the readings of the inferior quadrant was found to be the strongest (0.94), while that of the nasal quadrant was found to be the weakest (0.66); (Table 3).

Table 1: The average RNFL thickness as measured by the Stratus and Cirrus OCT machines

	Stratus OCT (μm)	Cirrus OCT (μm)
Average	92.52±19.95	89.97 ±15.46
Temporal	65.42 ±18.98	62.00±13.08
Superior	114.85±26.67	112.00±25.13
Nasal	75.83±28.61	68.56±16.66
Inferior	116.35±29.43	114.23±25.82

Table 2: The average RNFL thickness as measured by the Stratus and Cirrus OCT machines, broken up into the control and glaucoma patients

	Stratus OCT (µm)	Cirrus OCT (µm)
Control		
Temporal	70.59±17.40	64.06±12.82
Superior	123.61±20.65	118.72±21.63
Nasal	82.03±28.67	70.53±18.33
Inferior	123.06±21.63	118.59±23.05
Average	98.88±14.20	94.28±13.05
Glaucoma		
Temporal	55.06±18.22	57.88±12.99
Superior	97.86±29.37	98.56±26.88
Nasal	63.44±24.89	64.63±12.52
Inferior	102.94±38.20	105.50±29.49
Average	79.81±23.94	81.38±16.71

Table 3: Theintra-class correlation coefficient alpha between the average RNFL thicknesses as measured by the Stratus and Cirrus OCT machines

Parameter	ICC alpha (RNFL thickness, µm)
Average overall	0.90
Average glaucoma	0.93
Average control	0.84
Temporal	0.81
Superior	0.85
Nasal	0.66
Inferior	0.93

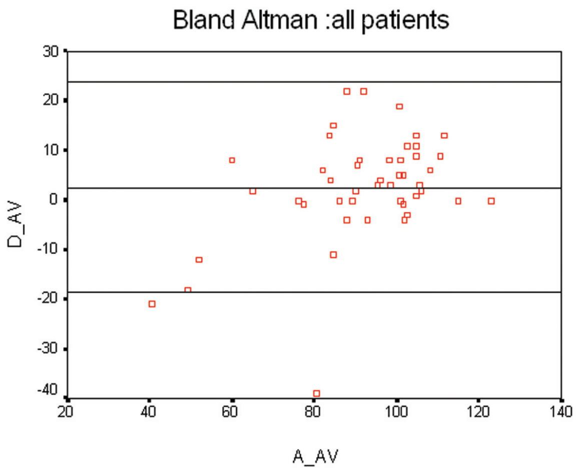

Figure 1

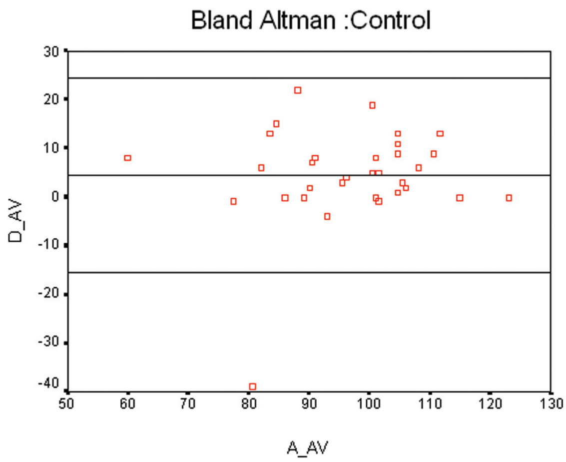

Figure 2

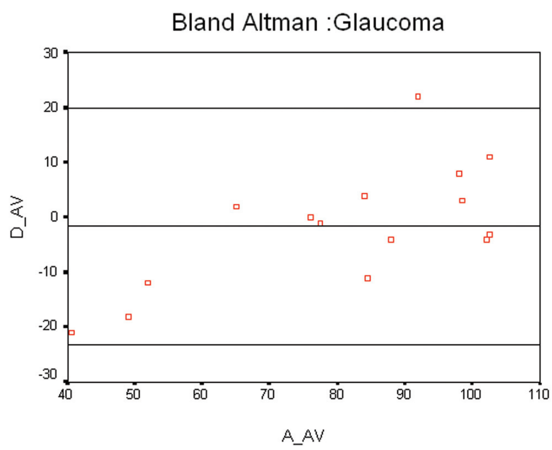

Figure 3

A good correlation, however, is not an index of reproducibility of readings between two instruments. The Bland Altman plots for limits of agreement (95% confidence interval) between the two readings obtained by the Stratus and Cirrus OCT operating systems in the overall population was found to be +22.70 to -19.62microns, in glaucoma patients +23.06 to -18.94 microns and in the control group +24.69 to -15.51microns (Figures 1,2 and 3).

Discussion

As both glaucoma diagnosis and progression are defined by the clinical appearance of the optic nerve and the visual field, high-resolution quantitative assessment of the thickness (?) of the retinal cellular layers by optical coherence tomography is of particular utility (Quigley, 1992; Sommer, 1977; Medeiros, 2005). The Cirrus OCT acquires OCT data about 70 times faster (27,000 Vs 400A-scans per second) and with better resolution (5ìm Vs ~10 ìm axial resolution) than the Stratus OCT does. Because of this, better visualization of the RNFL defects is possible within the 3D data set, and the 3D data cube has much less interpolation between adjacent points than the sparser Time Domain OCT scans have (De Boer, 2003; Fujimoto, 2003; Medeiros et al, 2005; Schuman, 2008). However, as glaucoma is a slowly progressing disease requiring long- term, longitudinal follow-up to monitor its progression, it is also important to assess how the RNFL thickness and optic disc measurements compare with those acquired using (?) previous OCT technology that is currently in use, to ensure smooth transition of patients from one machine to the other (Quigley, 1992; Sommer, 1977; Medeiros et al, 2005).

In our study, the ICC alpha showed a good correlation between the RNFL values acquired by the two imaging systems, though lower than the correlation between the Stratus and RTVue reported elsewhere (Sung et al, 2009). Also, there was a significant variation in this value between those of the glaucoma patients and the control population, with the former showing a better correlation.

The RNFL thickness as estimated by the Cirrus OCT was found to be less than that estimated by the Stratus OCT in the overall subjects (maximum discrepancy in the nasal quadrant, minimum in the inferior). A similar pattern was noticed in the control group, with a difference between the two averages. A similar finding was noted by Sung et al too (2009).

The ICC alpha, however, is not an index of the reliability of an instrument, and even very good correlation does not imply that the two instruments can be used interchangeably. The Bland Altman limits of agreement for a 95% confidence interval were from +22.70 to -19.62,+24.69 to -15.51, and +23.06 to -18.94 microns in the overall, control and glaucomatous subjects, respectively. The Bland Altman plots also revealed that the Cirrus OCT tends to over estimate the RNFL thickness in comparison to the Stratus in case of thicknesses greater than 80 microns. Since these discrepancies are not acceptable clinically, the two imaging systems may not be used interchangeably. It is therefore essential that clinicians switching to the Cirrus OCT be aware of these discrepancies when shifting patients from one imaging system to the other.

Schuman evaluated the existing spectral domain technology in glaucoma management and concluded that the SD-OCT shows a statistically significant improvement in reproducibility in both peripapillary RNFL and macular scan thickness measurements over the clinical standard for the TD-OCT. This is more relevant for sectoral measurements, making it especially important in the cases of focal loss of tissue, as seen in the early stages of glaucoma (Schuman, 2008).

He reported that for RNFL, there is no relative bias between the 2 devices in all measurements except in the 8 and 12 clock hours. Clock hour 12 had a confidence interval of 1.39 to 26.97, indicating that in this sector, the Stratus measurements tended to be thicker than the Cirrus OCT measurements. In clock hour 8, the confidence interval was 5.54 to 26.16, also indicating that in this sector the TD-OCT measurements tended to be thicker than the SD-OCT measurements.

Narrow confidence intervals for the difference between TD-OCT and SD-OCT were found in this study, indicating that the number of patients (21 eyes of 21 patients) was sufficient to make generalized observations about the difference between the 2 device's reproducibility.

Sung et al (2009) noted significant differences in the RNFL thickness and normative classification as determined on the Stratus and Cirrus OCT, despite an excellent correlation of the RNFL thickness measurement. Moreno-Montanes et al (2010) concluded that the Cirrus OCT has a better scan quality than the Stratus does, especially in glaucomatous eyes.

Gonzales Garcia et al (2009) did a comparative evaluation of the RTVue and Stratus OCT imaging systems comprising of thirty healthy participants (60 eyes) and 38 glaucoma patients (76 eyes), and reported that the measurements by both the machines are highly correlated (ICC alpha 0.97). The correlations generally were lower in healthy eyes than patient eyes, particularly for parameters describing disc topography.They reasoned that this may be explained in part by the use of different strategies to identify the RPE tips and to define the optic disc contour line.

In this study, the Bland-Altman plots showed good agreement between RTVue and Stratus OCT RNFL measurements. In healthy eyes, however, the RTVue average, temporal, and inferior RNFL measurements were found to be thicker than those of Stratus OCT by an average of 1.7, 7.5, and 6.4 ìm, respectively. In addition, they reported that RTVue tends to provide average RNFL thickness measurements approximately 3 ìm thicker than the Stratus OCT does and that this effect is more pronounced for the lower values of the average RNFL thickness. The relationship tends to invert (i.e., Stratus OCT provides greater RNFL thickness measurements than RTVue) for RNFL thicknesses greater than 110 microns.

Conclusion

It is evident that the considerable variability in the RNFL thickness measurements made by the Cirrus and Stratus OCT exceeds the limits of resolution afforded by the instruments.

Since the 95%confidence intervals of limits of agreement of the two instruments are not clinically acceptable, the RNFL measurements obtained from the two OCT systems may not be used interchangeably in monitoring progression or clinical trials.

Given the discrepancies in measurements by the two instruments, it is important to remember that patient transition between different practices on different machines also requires careful interpretation.

References:

De Boer JF, Cense B, Park BH, Pierce MC, Tearney GJ, Bouma BE (2003). Improved signal-to-noise ratio in spectral-domain compared with time-domain optical coherence tomography. Opt Lett; 28: 2067-2069.

Fujimoto JG. Optical coherence tomography for ultrahigh resolution in vivo imaging. (2003). Nat Biotechnol; 21:1361-1367.

GonzÁlez-GarcÍa AO, Vizzeri G, Bowd C, Medeiros FA, Zangwill LM, Weinreb RN (2009). Reproducibility of RTVue Retinal Nerve Fiber Layer Thickness and Optic Disc Measurements and Agreement with Stratus Optical Coherence Tomography Measurements. Am J Ophthalmol; 147(6):1067-1074.

Medeiros FA, Zangwill LM, Bowd C, Vessani RM, Susanna R Jr, Weinreb RN (2005). Evaluation of retinal nerve fiber layer, optic nerve head, and macular thickness measurements for glaucoma detection using optical coherence tomography. Am J Ophthalmol; 139:44–55.

Medeiros FA, Zangwill LM, Bowd C, Sample PA, Weinreb RN (2005). Use of progressive glaucomatous optic disc change as the reference standard for evaluation of diagnostic tests in glaucoma. Am J Ophthalmol; 139:1010-1018.

Moreno-Montanes J, Olmo N, Alvarez A, Garcia N, Venturia JZ (2010). Cirrus HDOCT compared with Stratus OCT in Glaucoma Diagnosis. Invest Ophthalmol Vis Sci.; 51:335-343.

Quigley HA, Katz J, Derick RJ, Gilbert D, Sommer A (1992). An evaluation of optic disc and nerve fiber layer examinations in monitoring progression of early glaucoma damage. Ophthalmology; 99: 19-28.

Schuman JS. Spectral Domain Optical Coherence Tomography for Glaucoma (2008). Trans Am Ophthalmol Soc; 106:426-458.

Sommer A, Miller NR, Pollack I, Maumenee AE, George T (1977). The nerve fiber layer in the diagnosis of glaucoma. Arch Ophthalmol; 95:2149-2156.

Sung KR, Kim DY, Park SB, Kook MS. Comparison of RNFL thickness by Cirrus HD and Stratus OCT (2009). Ophthalmology; 116:1264-1270.

Source of support: nil. Conflict of interest: none