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A STUDY TO COMPARE THE RETINAL NERVE FIBER LAYER (RNFL) MEASUREMENTS USING THE TD OCT 'STRATUS' AND THE SD OCT 'RTVUE' IN HEALTHY PARTICIPANTS AND GLAUCOMA PATIENTS

Ophthalomology

Dr. Sarika Dubey Assistant professor, Department of Ophthalmology, SMS Medical College, Jaipur

Dr. Sonal Agrawal* Postgraduate, Department of Ophthalmology, SMS Medical College, Jaipur *Corresponding Author

ABSTRACT

Background: To compare the RNFL measurements using the conventional Time Domain Optical Coherence Tomography (TD-OCT) 'Stratus' and the Spectral Domain Optical Coherence Tomography (SD OCT) 'RTVue' in healthy participants and glaucoma patients. **Methods:** This prospective cross-sectional study included 50 eyes in each of the two study groups as, healthy eyes and eyes of established glaucoma patients. Peripapillary RNFL thickness was measured by both machines in random order by the same operator on the same day with pupils uniformly dilated to over 5.0 mm. Three separate fast RNFL Scans were acquired with Stratus OCT, from which the most reliable scan was chosen for comparison. For RTVue, "RNFL3.45" scan protocol was used, which consists of four sets of 1024 "A-scans" along a 3.45 mm-diameter circle centered on the optic disc. **Results:** There was a significant difference in RNFL measurements between the two methods ,which was maximum in the superior quadrant and minimum in the nasal quadrant in both the groups**. Conclusion:** In both the groups, RTVue RNFL measurements are thicker as compared to that of Stratus with maximum quadrant mean RNFL measurement in the inferior quadrant and minimum in the nasal quadrant. Maximum difference in RNFL measurement between the two machines was at superior quadrant in both the groups.

KEYWORDS

RNFL, SD OCT, TD OCT, Stratus, RTVue.

INTRODUCTION

Glaucoma is a group of diseases characterized by chronic progressive optic nerve damage with loss of retinal ganglion cells, eventually manifesting as RNFL thinning and cupping of the optic disc with corresponding functional visual field defect (VFD). The clinical diagnosis of glaucoma currently is based on documented glaucomatous changes to the optic disc appearance combined with visual field testing such as standard automated perimetry (SAP) pick up VFD when an irreversible loss of 30-50 % RNFL has already occurred. [1,2] But the thinning of the neuroretinal rim due to degeneration of retinal ganglion cell axons is the earliest change in the development of glaucoma. The newer diagnostic modalities like OCT enable us to make a "pre-perimetric" diagnosis of glaucoma.

OCT is a noninvasive technology that can provide real time, objective, cross-sectional measurements of various layers of the retina, including RNFL. It has been used to measure peripapillary RNFL thickness in several diseases, such as glaucoma, optic disk edema, hereditary optic neuropathies, and multiple sclerosis. [3]

OCT technology, with the incorporation of spectral-domain (SD) imaging offers significant advantages over the traditional time-domain (TD) OCT techniques. [4]

Unlike TD-OCT, a stationary reference mirror is used in SD-OCT, and the OCT signal is acquired using a spectrometer as a detector. [5] It is capable of an acquisition speed of up to 29,000 A scans per second with a depth resolution of 5µm.

[6] Also, SD-OCT offers a higher resolution than TD-OCT2 and can provide a significant reduction in motion artifacts and an increased signal-to-noise ratio compared with TD-OCT. [7]

Our study compared peripapillary RNFL measurement between Stratus and RTVue in healthy and glaucomatous eye.

METHODS

The study was a prospective cross-sectional study conducted at the Glaucoma clinic in a tertiary center in North India between January 2012 and September 2012.

Participants

The study has two groups: healthy eyes (defined as having normal findings in a comprehensive ocular examination with intraocular pressure <22 mmHg, open angle on gonioscopy, normal appearance of optic disc and automated perimetry glaucoma hemifield test (GHT) within normal limits) and eyes of established glaucoma patients (defined as showing both glaucomatous optic neuropathy and glaucomatous visual field defect). Fifty eyes were included in each study group. Patients with age: ≥ 20 years, Best corrected visual acquity (BCVA): ≥ 6/12 and refractive error: ≤ -5.0D (spherical), < +3.0D (spherical) and < ± 3.0D (cylindrical) were included in the study. Patients with cataract greater than grade 3 on the Lens Opacities Classification System III, and with other ocular pathology like coexisting retinal disease, uveitis and non-glaucomatous optic neuropathy, vitreous haemorrhage were excluded. Also patients with previous intraocular surgery except uneventful cataract surgery ,disc anomalies, advanced glaucoma and glaucoma suspects were also excluded. Signal strength <6 on Stratus OCT and Signal strength indicator (SSI) <35 on RTVue SD-OCT were also excluded.

Technique

In the eligible eyes, peripapillary RNFL thickness was measured each with Stratus OCT (software version 4.0.7; Carl Zeiss Meditec, Dublin, CA) and the RTVue (Optovue, Inc.Fremont, CA. software version #6,1,0,4) in random order by the same operator on the same day. All pupils were uniformly dilated to over 5.0 mm.

Three separate fast RNFL Scans were acquired with Stratus OCT. The subject was seated and properly aligned. The OCT lens was adjusted for any refractive error. After bringing the optic nerve into view on the live fundus camera using the internal fixation light, the Z-offset and enhancement (polarization) were optimized. The aiming circle was adjusted to be centered over the optic nerve head so that an OCT temporal, superior, nasal, inferior, temporal profile of an even 1.73-mm radius could be obtained. If the subject moved or blinked during the scan, the image is repeated. The scans were discarded and retaken if the signal strength is less than 6. Each Fast RNFL scan captured 3 successive circular scans around the disc with A-scan measurements at 256 points per revolution over a total of 1.92 seconds. The resulting RNFL thickness output is an averaged value computed from a combined set of 768 A-scans. From the exported group of 3 scans, the most reliable scan was chosen for comparison (defined as the highest percentage of acceptable A-scans with the highest signal strength).

For RTVue, "RNFL3.45" scan protocol was used, which consists of 4 sets of 1024 "A-scans" along a 3.45 mm- diameter circle centered on the optic disc. This scan protocol takes 76 milliseconds to complete. To allow for comparison with the Stratus system, the scan circle was also manually centered when using the RTVue-100 in a manner analogous to that required with the Stratus.Eye motion and blinking can cause artifacts. In the maps the eye movement appeared as a break in the blood vessel pattern. If such breaks were seen, the scan was repeated.

Statistical Analysis

The data was presented in terms of mean±S.D. for quantitative variables and frequency (%) for categorical variable under reach group separately. The Pearson's correlation coefficient was determined to see the linear relationship between two quantitative variables along with statistical significance. Measurement of agreement "kappa statistics" was calculated along with statistical significance by chi square test to see the agreement in terms of concordance/discordance between the two machines. "p" value ≤ 0.05 is taken as a level of statistical significance. Data was analyzed by using SPSS statistical software version 16.0.

RESULTS

All participants satisfying the criteria for inclusion participated in the study. A total of 53 individuals (100 eyes) with a mean age ± S.D. of 55.64 ± 13.40 years were included in the study. Of these, 26 subjects (50 eyes) were classified as healthy and 27 subjects (50 eyes) were classified as glaucoma eyes. Healthy participant had a mean age of 49.19 ±

14.57 years and a median age of 44.5 (31-78) years. Glaucoma patient had a mean age of 61.85 ± 8.58 years and a median age of 63.0 (42-76) years. Of the total 26 healthy participants, 16 were females and 10 were males. In glaucoma patients, out of total 27 patients, 14 were females and 13 were males.

The mean average RNFL thicknesses of healthy and glaucoma eyes were 92.14 ± 8.18µm and 73.54 ± 14.57µm as determined by TD OCT (Stratus) measurement and 103.55 ± 8.18µm and 89.27 ± 16.64µm as determined by SD OCT (RTVue) measurement, respectively.

The mean RNFL thickness of glaucoma eyes in temporal, superior, nasal and inferior quadrant as measured by TD- OCT (Stratus) were 59.50±14.59µm, 85.54±21.40µm, 58.88±16.17µm, and 90.16±25.41µm respectively. The mean RNFL thickness of glaucoma eyes in temporal, superior, nasal and inferior quadrant as measured by SD-OCT (RTVue) were 71.38±17.76µm, 109±21.82µm, 65.92±12.74µm, and 111±25.28µm, respectively. [Table 1]

TABLE 1. Mean Retinal Nerve Fibre Layer (RNFL) Thickness Values Measured by TD OCT (Stratus) and SD OCT (RTVue) for Glaucoma eyes

	Mean RNFL Thickness Measured by Stratus (µ) ±SD	Mean RNFL Thickness Measured by RTVue (µ) ±SD	P	Mean Difference (µ)±SD (RTVue-Stratus)	Minimum/Maximum Difference (µ)
Average	73.54±14.57	89.27±16.64	<0.001	15.72±9.67	-0.25/58.44
Temporal	59.50±14.59	71.38±17.76	0.290	11.88±21.19	-22/115
Superior	85.54±21.40	108.98±21.82	<0.001	23.44±13.20	-12/61
Nasal	58.88±16.17	65.92±12.73	<0.001	7.04±12.14	-41/23
Inferior	90.16±25.40	110.96±25.28	<0.001	20.08±19.33	0/129

The mean RNFL thickness of healthy eyes in temporal, superior, nasal and inferior quadrant as measured by TD-OCT (Stratus) were 68.20±10.5µm, 111.2±13.65µm, 68.06±11.76µm, and 121±31.8µm, respectively. The mean RNFL thickness of healthy eyes in temporal, superior, nasal and inferior quadrant as measured by SD-OCT (RTVue) were 77.58±11.98µm, 126±15.3µm, 75.84±10.38µm, and 134±12.9µm, respectively. [Table 2]

TABLE 2. Mean Retinal Nerve Fibre Layer (RNFL) Thickness Values Measured by TD OCT (Stratus) and SD OCT (RTVue) for Healthy eyes

	Mean RNFL Thickness Measured by Stratus (µ) ±SD	Mean RNFL Thickness Measured by RTVue (µ) ±SD	P	Mean Difference (µ)±SD (RTVue-Stratus)	Minimum/Maximum Difference (µ)
Average	92.14±8.18	103.55±8.18	<0.001	11.41±6.25	-1.37/27.45
Temporal	68.16±10.50	77.58±11.98	<0.001	9.42±11.36	-16/34
Superior	111.18±13.64	126.38±15.27	<0.001	15.2±14.46	-16/44
Nasal	68.06±11.76	75.84±10.37	0.001	7.78±11.60	-15/34
Inferior	121.20±13.77	133.56±12.88	<0.001	12.36±10.74	-7/47

The mean average and quadrant RNFL thickness measured by SD OCT (RTVue) was higher than that measured by TD OCT (Stratus) in both healthy and glaucoma eyes.

The difference between RNFL thickness measured by SD OCT (RTVue) and TD OCT (Stratus) was maximum in the superior quadrant (23.44, 15.20) and minimum in the nasal quadrant (7.04, 7.78) in both healthy and glaucoma eyes, respectively.

In Glaucoma eyes, the RNFL thickness measured by TD OCT (Stratus) and SD OCT (RTVue) were correlated in all sectors, including average RNFL thickness (r = 0.82; P<0.001; Table 3). Statistically significant and positive correlation for RNFL measurements was seen in superior, nasal and inferior quadrant. The correlation was weak in the temporal quadrant (r = 0.15; P = 0.290). [Table 3].

TABLE 3. Agreement and Correlation between TD OCT (Stratus) and SD OCT (RTVue) measurement for Glaucoma eyes.

	Mean Difference (µm)±SD (RTVue-Stratus)	95% CI of the difference (lower & upper)	Correlation coefficient (r)	P
Average RNFL	15.72±9.67	-18.47 to -12.98	0.82	<0.001
Temporal RNFL	11.88±21.19	-17.90 to -5.85	0.15	0.290
Superior RNFL	23.44±13.20	-27.19 to -19.68	0.81	<0.001
Nasal RNFL	7.04±12.14	-10.49 to -3.58	0.67	<0.001
Inferior RNFL	20.08±19.33	-26.29 to -15.30	0.70	<0.001

In Healthy eyes, the RNFL thickness measured by TD OCT (Stratus) and SD OCT (RTVue) were correlated in all sectors, including average RNFL thickness (r = 0.70; P<0.001). [Table 4]. All quadrants showed statistically significant and positive correlation.

Statistics also show 92% agreement between TD-OCT (Stratus) and SD-OCT (RTVue) for average RNFL thickness in healthy eye. Kappa value=0.840 with a 'p' value <0.001. There is a 96% agreement between TD-OCT (Stratus) and SD-OCT (RTVue) for average RNFL thickness in glaucoma eyes. Kappa value=0.645 with a 'p' value <0.001.

DISCUSSION

RNFL thickness measurement by OCT is extensively used in several diseases including glaucoma. The OCT technology has changed considerably in recent years with the incorporation of spectral-domain (SD) imaging that offers significant advantages over the traditional time-domain (TD) OCT techniques. [4] The potential advantages of SD-OCT include improved axial resolution, greater flexibility to scan a variety of surface patterns, and improved image realignment, which may improve the accuracy of long-term comparisons.

Though significant clinical experience and research data have been amassed to support TD OCT systems, which greatly expand the utility of this technology in clinical settings [8] similar systematic studies of SD OCT systems are lacking. The studies that has compared SD OCT with TD OCT (Stratus) has shown that Cirrus OCT (SD OCT) tend to measure thinner RNFL than TD- OCT (Stratus), [9] whereas RTVue (SD OCT) tended to have a thicker RNFL than TD-OCT. [10]

Savini et al when compared two SD OCT technology with Cirrus and RTVue in healthy eyes, found that RTVue measure thicker RNFL than the Cirrus. [11] Studies has also shown good correlation between SD-OCT and TD-OCT RNFL measurements; however, systematic and statistically significant differences were reported between two devices. [10] Hence, it is vital to understand the comparability of RNFL thickness measures obtained from these 2 related, yet distinct, technologies.

Our study shows that SD OCT (RTVue) average, and quadrant RNFL measurement tended to be thicker than those of TD OCT (Stratus) measurements in both glaucoma and healthy eyes. Similar results were shown by Gonzalez Garcia et al [10] when they evaluated RTVue measurements and Stratus measurements in glaucoma eyes. In healthy eyes RTVue measured thicker RNFL than Stratus at average, temporal and inferior quadrant and cited reasons for the discrepancies' in the measurements in healthy eyes. [10]

Johnson et al [12] noted thicker RNFL measurement by RTVue than Stratus (TD OCT) at average and all 4 quadrants in healthy eyes.

Lee et al [13] also noted thicker RNFL measurements by RTVue in a study that has compared the three machines namely Cirrus, RTVue and Stratus simultaneously in healthy and glaucoma eyes. Studies has analyzed clock hour RNFL thickness measurements between the

Stratus (TD OCT) and Cirrus (SD OCT), [14] [15] it is not possible in our study as RTVue does not give clock hour wise RNFL thickness measurement.

Analysis of difference between the quadrant RNFL measurements obtained from RTVue and Stratus showed maximum difference at the superior quadrant. Similar result was noted by other studies analyzing RTVue and Stratus OCT. [12] [13] They also noted that the difference was reverse in nasal quadrant, means Stratus OCT measures slightly thicker RNFL than RTVue. [12] [13] Our study has not shown such result at nasal quadrant in favor of Stratus OCT. Though the difference between the RNFL measurements was minimum in nasal quadrant, still RTVue measured thicker RNFL at nasal quadrant than Stratus. More comparative studies from Indian population will be able validate this analysis.

There are many explanations for thick RNFL measurements by SD OCT (RTVue). First, the thicker RNFL measurements made by the RTVue may have resulted from the different method of data acquisition employed in this instrument. The two OCT instruments measure RNFL thickness at different peripapillary locations; namely 3.46 mm for Stratus and 3.45 mm for the RTVue. Thus an exact anatomical comparison is difficult as the RNFL thins with increasing distance from the center of the disc. Second, the differences in RNFL thickness measurements are more likely to be due to algorithmic differences in retinal segmentation for each instrument. Third, the SD OCT (RTVue) has significantly higher scanning resolution than TD OCT (Stratus). Earlier studies have found that the scanning resolution affects RNFL thickness measurement. [16] [17]

In our study, Pearson correlation coefficient shows positive and strong correlation between TD OCT (Stratus) and SD OCT (RTVue) measurements for average RNFL thickness in glaucoma and healthy eyes. Correlation was positive and medium to strong between TD OCT (Stratus) and SD OCT (RTVue) measurements for quadrant RNFL thickness in glaucoma and healthy eyes except for temporal quadrant in glaucoma eyes. As per the kappa statistics the two OCT machine (Stratus and RTVue) showed good agreement between the instruments for average RNFL thickness. These results suggest the ability for the SD OCT (RTVue) to detect glaucomatous structural damage is likely as good as that of the TD OCT (Stratus). Gonzalez et al in their study found good correlation and agreement between RTVue and Stratus OCT in both healthy and glaucoma groups. [10] Lee et al compared the RNFL thickness measurements between the Stratus and RTVue OCT in both healthy and glaucoma eyes. [13] Study revealed considerable agreement among the instruments.

Our study also showed that the current algorithms for RNFL thickness measurement by SD OCT (RTVue) and TD OCT (Stratus) generate mean values that are significantly different and therefore cannot be considered interchangeable. Thus, clinicians incorporating RTVue in their clinical practice should be aware of the discrepancies in the measurements between RTVue and Stratus OCT.

As discussed, earlier studies have also shown good correlation between SD-OCT and TD-OCT RNFL measurements; however, systematic and statistically significant differences were reported between two devices. [10]

One limitation of our study was that there was a significant difference in the age of the enrolled participants. Namely, the glaucomatous group was significantly older than the control group. Second limitation was the small sample size of the study groups. Studies with larger sample size from Indian population will be able to validate the results of our study.

To conclude, direct comparison of the measurements may be misleading because there were significant differences between the RNFL thickness measurements between the TD OCT (Stratus) and SD OCT (RTVue). SD OCT (RTVue)average RNFL measurements generally were thicker than TD OCT (Stratus) measurements, suggesting that RNFL measurements obtained with TD OCT (Stratus) and SD OCT (RTVue) are not interchangeable.

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