Quantification of retinal nerve fiber layer thickness using spectral domain optical coherence tomography in normal Indian population

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The purpose of this study was to measure peripapillary retinal nerve fiber layer thickness (RNFLT) using spectral domain optical coherence tomography (SD-OCT) in normal Indian eyes, for which, 210 normal volunteers were recruited. One eye of each subject underwent RNFL scanning at 3.4 mm circle diameter around optic nerve using SD OCT. The data were analyzed to determine RNFLT in the sample population and its variation with age and gender. The average peripapillary RNFLT was 114.03 ± 9.59 µm. There was no effect of gender on RNFLT parameters. Age had significant negative correlation with average (P = 0.005), superior (P = 0.04), temporal (P = 0.049), and nasal quadrants (P = 0.01) RNFLT. Inferior quadrant RNFLT also had a negative correlation with age, but it was not statistically significant (P = 0.15).

Key words: Indian eyes, normative database, retinal nerve fiber layer thickness, spectral domain optical coherence tomography.

Optical coherence tomography (OCT) is an imaging device, which produces high resolution, cross-sectional images of retinal nerve fiber layer (RNFL) and optic nerve head (ONH).

Spectral OCT/SLO (spectral OCT/scanning laser ophthalmoscope, OFKO/OTI, V 2.26, Florida) is a commercially available spectral domain (SD) OCT, which has axial resolution of 5 µm and a scan velocity of 27,000 axial scans/second as opposed to Stratus OCT (Carl Zeiss Meditec, Inc., Dublin, CA), which has an axial resolution of 15 µm and a scan velocity of 400 axial scans/second. SD OCT records the interferometric information with a Fourier-domain spectrometric method instead of adjusting the position of a reference mirror as in Stratus OCT.¹ This permits high-density raster scanning of retinal tissue while minimizing eye motion artifacts. Reproducibility of RNFL thickness (RNFLT) measurements obtained with spectral OCT/ SLO has been established.²

RNFLT has shown to have interindividual variation, which could be age or race related.³-⁷ We estimated peripapillary RNFLT and the effect of age and gender on RNFLT in normal Indian eyes using SD-OCT.

Materials and Methods

For this observational, cross-sectional study, 210 volunteers were recruited from the institute staff and patients with refractive error, from May 2008 to December 2009.

Assuming 95% (Zα/2 = 1.96) confidence interval, 90% (Zβ = 1.24) power, and margin of error (d) of 5 µm and SD of 21 using sample size formula

\[ n = \left[ \frac{Z_{\alpha/2} + Z_{\beta}}{d} \right]^2 \times \sigma^2 \]

the minimum sample size calculated was 181. After informed consent, all participants underwent comprehensive ophthalmic examination, achromatized automated perimetry using Swedish Interactive Threshold Algorithm, Standard 24-2 program with Humphrey visual field analyzer (Carl Zeiss Meditec, Dublin, CA).

Subjects were classified as having normal eyes if they had best corrected visual acuity of > 20/30, refractive error within ± 3 diopters (D) of sphere and ± 1.5D of cylinder, intraocular pressure < 21 mmHg, clear ocular media on lens opacities classification

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system III, open angles on gonioscopy, healthy optic disc and normal visual field, which were defined as mean deviation and pattern standard deviation within 95% confidence limits and glaucoma hemifield test within normal limits. Subjects with ocular pathology and previous intraocular surgery were excluded.

After dilation, one randomly selected eye of participant underwent RNFL scanning with spectral OCT/SLO. Using internal fixation target, a circular scan with 3.4 mm circle diameter was centered around ONH and the location for proper positioning of scan in relation to the ONH was observed on the SLO image. The RNFL analysis uses an automated OCT software algorithm to identify anterior and posterior margins of RNFL. RNFL parameters evaluated were: average peripapillary RNFL, four quadrant, and eight sectors RNFL. The sectors were defined in clockwise order for right eye and counterclockwise order for the left eye. Only scans with signal strength of > 7 and no segmentation algorithm failures were included for analysis.

Statistical analysis was performed using SPSS version 15 (SPSS Inc., Chicago, IL). Effect of age on RNFLT was analyzed by linear regression analysis and Pearson coefficient of correlation. Student’s t-test was used to compare RNFLT between gender. Analysis of variance (ANOVA) with post-hoc test of Tukey was used to compare differences in RNFLT parameters among various age groups.

Results

There were 110 males (age, 41.27 ± 19.9 years) and 100 females (age, 41.7 ± 16.4 years). Mean spherical equivalent was 0.59 ± 2.11 D.

The average peripapillary RNFLT was 114.03 ± 9.6 µm (range, 90–139). RNFLT was thickest in inferior quadrant, followed by superior quadrant, nasal quadrant, and thinnest in temporal quadrant [Table 1].

Various RNFL parameters obtained were compared between males and females but none showed statistical significance [Table 2].

The subjects were divided into seven age groups according to age [Table 3]. Mean values of superior quadrant and sector (age groups of 20–29, 30–39 years), nasal quadrant and sector (age groups of 20–29, 40–49 years), superior temporal sector (age groups of 20–29, 60–69 years), inferior nasal sector (age groups of 10–19, 20–29, 40–49 years), and inferior temporal sector (age groups of 10–19, 40–49 years) were significantly different across the age groups [Table 3]. Age had a statistically significant negative correlation with average RNFLT. On applying the regression equation, average RNFLT showed negative slope of 0.116 µm/year (Average RNFLT = 119.06 – 0.116 age, correlation coefficient (r) = -0.20, p = 0.005). Except for inferior quadrant RNFLT, other quadrants showed statistically significant inverse correlation with age [Table 3].

Discussion

Previous studies using OCT have shown variable RNFLT

| Table 1: Descriptive statistics of retinal nerve fiber layer thickness in the sample population |
|---------------------------------|--------|--------|------------------|
| **RNFL parameters**         | **Mean (SD)** | **Range** | **95% confidence interval** |
| Average                        | 114.03 (9.59) | 90–139 | 112.7–115.4 |
| Quadrants                      |        |        |                  |
| Superior                       | 138.1 (16.7) | 98–194 | 135.8–140.5 |
| Temporal                      | 70.2 (10.3)  | 49–105 | 68.8–71.7  |
| Inferior                       | 142.4 (16.7) | 100–189 | 139.9–144.7 |
| Nasal                          | 104.8 (14.6) | 60–143 | 102.8–106.9 |
| Sectors                        |        |        |                  |
| Superior                       | 142.2 (22.5) | 95–215 | 138.9–145.3 |
| Superior temporal              | 110.5 (16.8) | 74–152 | 108.1–112.9 |
| Temporal                      | 57.6 (7.4)  | 43–80  | 56.6–58.6  |
| Inferior temporal              | 103.3 (20.5) | 61–178 | 100.4–106.2 |
| Inferior                       | 155.9 (25)  | 11–216 | 152.4–159.5 |
| Inferior nasal                 | 116.7 (19.8) | 78–171 | 113.8–119.5 |
| Nasal                          | 95.3 (15.4)  | 51–132 | 93.1–97.5  |
| Superior nasal                 | 130.8 (17.4) | 89–177 | 128.4–133.3 |

**Note:** RNFL: Retinal nerve fiber layer; SD: Standard deviation.
measurements in normal eyes of different population [Table 4]. Our results showed significantly higher values of RNFLT when compared to White eyes,[4] Indian eyes using Stratus OCT,[5,6] RTVue SD OCT (Optovue Inc., Fremont, CA)[7] and lower value when compared to RNFLT in normal Latino population. [8] This discrepancy could be due to the population age studied, difference in sample size, racial difference, and different generation of OCT used for the study. Hence, it is important to have a database for each ethnic group in the OCT software.

Schuman et al.[9] showed that RNFLT of men were usually thinner than that of women but not statistically significant. Our results agree with previous reports[5,7] that have shown no significant gender-related difference in RNFLT.

Some studies have shown a significant decline in average RNFLT measurement with advancing age using OCT,[5,10] while others have failed to show correlation between age and RNFLT.[5,7] Parikh et al.[10] reported statistically significant linear decrease of average RNFLT with age, with a negative slope of 0.16 µm/year in normal Indian eyes. We found that the age had statistically significant negative correlation with average, superior, nasal, and temporal quadrant RNFLT, and average RNFLT demonstrated a negative slope of 0.116 µm/year.

Limitation of this study is that it was based on cross-sectional data and to know the effect of age on RNFLT, it would be ideal to measure RNFLT longitudinally over a period of time. Also, the disc size of the subjects was not estimated; however, in a recent study[7] on Indian eyes reported that ONH size did not influence RNFLT.

To conclude, the study provides normative database for RNFLT using SD-OCT in Indian eyes. Age-related and regional differences of RNFLT should be considered when evaluating structural changes in glaucoma.

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A very rare congenital neurological disorder characterized by bilateral facial and abducens nerve paralysis, thickening of lower lip and inability to close the mouth, along with other common musculoskeletal abnormalities. This is a typical presentation of Moebius syndrome which is a very rare congenital neurological disorder characterized by bilateral facial and abducens nerve paralysis. Most patients usually present in infancy or early childhood. However, some cases may not be diagnosed until adulthood, as in this case. The patient had bilateral complete lateral rectus muscle weakness and inability to move both eyes outward. There was also bilateral incomplete medial rectus palsy, left-sided facial nerve paralysis, and bilateral moderate restriction of medial rectus muscle movements. The patient had difficulty in closing the left eye completely since 6 months, along with associated limb deformities, and inability to completely close the mouth, along with other musculoskeletal abnormalities.

The patient was referred to the Department of Ophthalmology, Dr SM CSI Medical College, Khammam, Trivandrum, and Department of Ophthalmology, Mamata Medical College, Trivandrum, for evaluation. The patient had a history of restricted outward movements of the eyes since January 2010 and unable to form facial expressions and to close the eyes since childhood. Ocular, facial, and systemic examination revealed that the patient had bilateral complete lateral rectus muscle weakness and inability to move both eyes outward and to close the left eye completely since 6 months and inability to move both eyes outward and to close the left eye since 6 months. The patient was subjected to various imaging techniques including optical coherence tomography to evaluate the retinal nerve fiber layer thickness in normal Indian population.

Key words: Moebius syndrome, congenital neurological disorder, bilateral facial and abducens nerve paralysis, thickening of lower lip, inability to close the mouth.

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