



Original Research Article

Comparison of RNFL thickness in glaucoma patients and non-glaucomatous patients

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ABSTRACT

Glaucoma is the leading cause of irreversible blindness worldwide, especially in developing countries. In countries like India, late presentation and lack of awareness contribute to blindness caused by glaucoma. The only way to reduce the burden of blindness due to glaucoma is early diagnosis. The Fourier Domain OCT (FD-OCT) has evolved into one of the best techniques for early diagnosis and monitoring the progress of glaucoma. The measurement of the retinal nerve fiber layer (RNFL) is of paramount importance in glaucoma. We, at a tertiary eye institute, undertook the present study on a FD-OCT to compare the retinal nerve fiber layer in 50 eyes each of glaucoma patients (Group A) and non-glaucomatous volunteers (Group B). An informed consent was taken from all candidates. In Group A a mean \pm SD of average, superior, inferior retinal nerve fiber layer thickness (μm) were 94.26 ± 13.436 , 96.08 ± 15.485 , 92.45 ± 13.179 respectively and in Group B mean \pm SD of average, superior, inferior retinal nerve fiber layer thickness (μm) were 114.9 ± 8.022 , 116.7 ± 8.058 , and 113.1 ± 10.692 respectively. Using independent t-test the difference between both the groups was found to be highly significant in all the sectors. This demonstrates the need for a baseline RNFL in all glaucomatous and glaucoma suspect eyes. Using independent t-test the difference between both the groups was found to be highly significant for all the GCC parameters. The focal loss of volume (FLV)% was 3.692 ± 3.533 in the glaucomatous eyes and 0.856 ± 1.211 in the non-glaucomatous eyes, $p < 0.0001$. The global loss of volume (GLV) % or diffuse loss of volume was 13.849 ± 8.485 for the glaucoma group and 2.031 ± 1.681 for the healthy eyes ($p < 0.0001$). This clearly demonstrates that the GCC plays a vital role in the diagnosis and follow-up of all cases of glaucoma and cases suspected of having glaucoma.

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1. Introduction

Glaucoma is the leading cause of irreversible blindness in the world.¹ Early detection of glaucoma has focused on evaluation of the retinal nerve fiber layer (RNFL) and the optic nerve head (ONH), because both the retinal nerve fiber layer and the optic nerve head can be imaged and have been shown to undergo structural changes prior to clinically detectable visual field loss. Many studies have shown the utility of measuring the peripapillary RNFL thickness for

early diagnosis and monitoring of glaucoma. The RNFL assessment with SD-OCT can detect glaucomatous damage before visual field defects occur in glaucoma suspects.²

Glaucoma causes progressive degeneration of retinal ganglion cells due to ganglion cell apoptosis, which then leads to retinal nerve fiber layer thinning and optic nerve head (ONH) cupping. Since these structural changes in the retinal nerve fiber layer (RNFL) and optic nerve head may result in irreversible visual field (VF) loss, the early diagnosis of glaucoma is vital for the early initiation of treatment that may stop or slow down further permanent vision loss.^{3,4}

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Retinal nerve fiber layer analysis is more sensitive than optic nerve head evaluation, because optical coherence tomography has shown thinning of the nerve fiber layer due to aging without detectable changes in the Optic Nerve Head appearance.⁵ Nerve fiber layer thinning is seen in glaucoma, because it is directly correlated with loss of ganglion cells, which is the primary event in glaucomatous damage.⁶

Potential advantages of Spectral/ Fourier domain optical coherence tomography are its faster acquisition times and its higher resolutions imaging (i. e, 2-5micrometer axial resolution).⁷⁻¹⁰The higher acquisition speeds in Spectral/Fourier domain optical coherence tomography allow for the transition from 2-dimensional to 3-dimensional and video ophthalmic imaging.¹¹It can measure 3D Scan (Disk and Macular) in 2 seconds and depth resolution (in tissue) of 5 micrometer and transverse resolution of 15 micrometer, scan range in depth 2-2.3 millimeter and transverse 2-12 millimeter.⁸

With the ultrahigh acquisition speeds of Spectral/Fourier domain optical coherence tomography, realignment of A-lines within a single image becomes unnecessary.¹²

2. Materials and Methods

The present study was conducted using the Fourier-domain optical coherence tomography (RTVue-100) which directly measures the thickness of retinal nerve fiber layer and provides unique analysis of the percent loss compared to extensive normative database.

Total of 100 consecutive eyes were assigned into two groups:

Group A: 50 eyes of 33 patients of primary open angle glaucoma randomly selected from patients visiting the Glaucoma Unit of the Regional Institute of Ophthalmology, Pandit/Bhagwat/Dayal Sharma, Post Graduate Institute of Medical Sciences, Rohtak.

Group B: 50 eyes of 35 non-glaucomatous age and sex-matched healthy volunteers were also enrolled in the study.

2.1. Inclusion criteria

1. Group A: Established cases of Primary Open Angle Glaucoma fulfilling the following criteria: Open anterior chamber angle, glaucomatous visual field loss (defined as a Pattern Standard Deviation [$P < 0.05$] or Glaucoma Hemi field Test result [$P < 0.01$] outside the normal limits in a consistent pattern on three qualifying Visual Fields, optic nerve head changes such as diffuse or localized rim thinning, disc (splinter hemorrhage), notch in the rim, vertical cup disc ratio more than fellow eye by more than .2 or previous photographic documentation of progressive excavation of the disc, progressive thinning of neuroretinal rim or nerve fiber layer defects visible on slit-lamp bio microscopy, or progressive loss of nerve fiber layer,

corrected intraocular pressure > 21 at presentation.

2. Group B: Both eyes had corrected intraocular pressure of less than 21 mm of Hg, normal visual fields as obtained using Humphrey Swedish interactive thresholding algorithm 30-2 [Defined as having a Mean Deviation and Pattern Standard Deviation within 95% limits of normal reference and glaucoma hemi field test results within 97% limits], an open anterior chamber angle, a normal appearing optic nerve head, a normal nerve fiber layer and no history of ocular disease, surgery or systemic corticosteroid use.

An informed consent was taken from all participants.

2.2. Exclusion criteria

Patients with intraocular surgery, retinal or ocular disease or optic atrophy, corneal disease, myopia $> -6.0D$ or hypermetropia $> 3.0D$, age < 40 years or > 79 years, cataract and diabetes mellitus were excluded from the study.

A detailed history taking and clinical examination including vision testing, central corneal thickness measurement, applanation tonometry, gonioscopy, automated perimetry and ophthalmoscopic examination was done in all patients.

In the current study, only images with Signal Strength Index of more than 45 were used. The results within both the groups were analysed using Graph pad prism version 5 and SPSS 17.

In Group a mean \pm SD of average, superior, inferior retinal nerve fiber layer thickness (μm) were 94.26 ± 13.436 , 96.08 ± 15.485 , 92.45 ± 13.179 respectively and in Group B mean \pm SD of average, superior, inferior retinal nerve fiber layer thickness (μm) were 114.9 ± 8.022 , 116.7 ± 8.058 , 113.1 ± 10.692 respectively.

In Group A mean \pm SD of retinal nerve fiber layer thickness (μm) in all the 16 segments ST1, ST2, TU2, TU1, TL1, TL2, IT2, IT1, IN1, IN2, NL2, NL1, NU1, NU2, SN2, SN1 were 129.26 ± 28.168 , 112.2 ± 25.107 , 77.8 ± 15.296 , 55.56 ± 11.723 , 52.42 ± 10.184 , 71.68 ± 16.966 , 112.38 ± 22.836 , 133.88 ± 28.757 , 126.38 ± 26.516 , 112.62 ± 18.657 , 75.50 ± 16.357 , 62.36 ± 13.922 , 66.54 ± 15.101 , 93.72 ± 19.496 , 116.58 ± 20.398 , 116.56 ± 24.455 respectively and in Group B mean \pm SD of retinal nerve fiber layer thickness (μm) in all the 16 segments ST1, ST2, TU2, TU1, TL1, TL2, IT2, IT1, IN1, IN2, NL2, NL1, NU1, NU2, SN2, SN1 were 152.76 ± 18.502 , 145.94 ± 19.622 , 104.44 ± 13.649 , 76.42 ± 7.565 , 66.70 ± 7.265 , 90.32 ± 12.417 , 142 ± 18.333 , 164.86 ± 19.461 , 149.50 ± 23.644 , 126.48 ± 19.692 , 91.58 ± 12.977 , 70.56 ± 8.498 , 76.76 ± 10.773 , 108.36 ± 16.196 , 132.28 ± 14.374 , 133.46 ± 18.227 respectively.

The difference in retinal nerve fiber layer thickness (Average, Superior, Inferior and 16 Sectors) in the primary open angle glaucoma and control group was very highly

Table 1: RNFL thickness in Group A and B

Parameters	Group A (Mean ± SD)	Group B (Mean ± SD)	p-Value
Average	94.26 ± 13.436	114.9 ± 8.022	<0.0001(VHS)
Superior	96.08 ± 15.485	116.7 ± 8.058	<0.0001(VHS)
Inferior	92.45 ± 13.719	113.1 ± 10.692	<0.0001(VHS)
ST1	129.26 ± 28.168	152.76 ± 18.502	<0.0001(VHS)
ST2	112.2 ± 25.107	145.94 ± 19.622	<0.0001(VHS)
TU2	77.8 ± 15.296	104.44 ± 13.649	<0.0001(VHS)
TU1	55.56 ± 11.723	76.42 ± 7.565	<0.0001(VHS)
TL1	52.42 ± 10.184	66.70 ± 7.265	<0.0001(VHS)
TL2	71.68 ± 16.966	90.32 ± 12.417	<0.0001(VHS)
IT2	112.38 ± 22.836	142 ± 18.333	<0.0001(VHS)
IT1	133.88 ± 28.757	164.86 ± 19.461	<0.0001(VHS)
IN1	126.38 ± 26.516	149.50 ± 23.644	<0.0001(VHS)
IN2	112.62 ± 18.657	126.48 ± 19.692	<0.0001(VHS)
NL2	5.50 ± 16.357	91.58 ± 12.977	<0.0001(VHS)
NL1	62.36 ± 13.922	70.56 ± 8.498	0.001(S)
NU1	66.54 ± 15.101	76.76 ± 10.773	<0.0001(VHS)
NU2	93.72 ± 19.496	108.36 ± 16.196	<0.0001(VHS)
SN2	116.58 ± 20.398	132.28 ± 14.374	<0.0001(VHS)
SN1	116.56 ± 24.455	133.46 ± 18.227	<0.0001(VHS)

Table 2: Area under receiver operating characteristic curve (AROC) of retinal nerve fiber layer (RNFL)

Parameters	AROC (95% Confidence Interval- CI)	Standard Error	p-Value	Sensitivity	
				Specificity>85%	Specificity>95%
RNFL Average	0.9252 (0.877-0.973)	0.02442	<0.0001(VHS)	82	66
RNFL Superior	0.8876 (0.822-0.953)	0.03341	<0.0001(VHS)	74	62
RNFL Inferior	0.8852 (0.823-0.947)	0.03169	<0.0001(VHS)	72	66
ST1	0.722 (0.621-0.824)	0.052	<0.0001(VHS)	56	46
ST2	0.848 (0.773-0.923)	0.038	<0.0001(VHS)	66	56
TU2	0.91 (0.854-0.965)	0.028	<0.0001(VHS)	82	64
TU1	0.942 (0.899-0.985)	0.022	<0.0001(VHS)	84	80
TL1	0.881 (0.807-0.955)	0.038	<0.0001(VHS)	82	76
TL2	0.833 (0.746-0.920)	0.044	<0.0001(VHS)	72	62
IT2	0.859 (0.782-0.937)	0.04	<0.0001(VHS)	78	68
IT1	0.819 (0.734-0.904)	0.043	<0.0001(VHS)	74	50
IN1	0.746 (0.649-0.843)	0.05	<0.0001(VHS)	44	26
IN2	0.685 (0.582-0.788)	0.052	0.001(S)	38	22
NL2	0.776 (0.685-0.867)	0.046	<0.0001(VHS)	56	42
NL1	0.717 (0.615-0.819)	0.052	<0.0001(VHS)	50	42
NU1	0.702 (0.598-0.806)	0.053	<0.0001(VHS)	44	28
NU2	0.709 (0.609-0.810)	0.051	<0.0001(VHS)	40	36
SN2	0.743 (0.645-0.841)	0.05	<0.0001(VHS)	52	42
SN1	0.703 (0.600-0.805)	0.052	<0.0001(VHS)	44	36

significant ($p < 0.0001$) except in NL 1 in which difference in both the groups was significant.

The highest retinal nerve fiber layer thickness was in IT1 ($133.88 \pm 28.757 \mu\text{m}$ and $164.86 \pm 19.461 \mu\text{m}$) in Group A and Group B respectively.

The lowest retinal nerve fiber layer thickness was in TL1 ($52.42 \pm 10.184 \mu\text{m}$ and $66.7 \pm 7.265 \mu\text{m}$) in Group A and Group B respectively.

Comparison of retinal nerve fiber layer thickness in Group A (POAG) and Group B (Control) shows a very highly significant difference in the POAG and control

groups. These results were consistent in average, superior, inferior, and all the 16 segments of retinal nerve fiber layer thickness.

Table 1 shows comparison between RNFL thickness of Group A and Group B in different sectors, using independent t-test the difference between both the groups was found to be very highly significant in all the sectors except in NL 1 in which difference in both the groups was significant.

Table 2 depicts AROC of RNFL parameters in Group A and Group B. Among all the parameters most significant

were the value of Average RNFL, Upper Temporal RNFL, Superior RNFL, and Inferior RNFL.

3. Results

In the present study, mean age of the patients in Group A was 51.78 ± 1.36 years (range 40-71 years), mean age of patients in Group B was 50.86 ± 1.199 years (range 40-72 years).

There were 46% males and 54% females in Group A and 54% males and 46% females in Group B.

Signal strength index of retinal nerve fiber layer of Group A and Group B was 53.56 ± 10.137 and 61.838 ± 11.436 respectively.

4. Discussion

Glaucoma causes irreversible blindness worldwide. Early detection and monitoring to prevent loss of vision is essential.¹ Glaucoma is the number one cause of irreversible blindness throughout the world.¹ The SD/ FD-OCT can detect early glaucoma and help to save sight.⁴ It is non-invasive and easy to perform. Our study was carried in 100 patients to compare the RNFL thickness between glaucoma patients and normal age and sex matched controls.

The difference in retinal nerve fiber layer thickness (Average, Superior, Inferior and 16 Sectors) in the Primary Open Angle Glaucoma and Control Group was very highly significant ($p < 0.0001$) except in NL 1 in which difference in both the groups was significant.

The use Spectral domain OCT for the diagnosis of glaucoma has been well established. Studies have shown that RNFL parameters are consistent and reproducible, with high diagnostic sensitivity and specificity in discriminating between healthy and glaucomatous eyes.¹³ In agreement with the present study, a study on the comparison between early glaucoma and healthy subjects demonstrated that RNFL thickness was better than any other tested ONH parameter.¹⁴

In our study, regarding the AROC of RNFL parameters in Group A and Group B., the parameters most significant were the value of Average RNFL, Upper Temporal RNFL, Superior RNFL, and Inferior RNFL. In the present study Area Under Receiver Operating Characteristic Curve (AROC) of average retinal nerve fiber layer thickness (RNFL) was (0.9252 ± 0.024) . The proven diagnostic use of SD-OCT for distinguishing between healthy and glaucomatous eyes using average RNFL thickness have been reported to have an AROC curve value of around 0.9, which is similar to our study.¹⁵ The factors which can affect the discrimination ability are the severity stage of glaucoma, with better accuracy in comparison between healthy and more advanced disease compared with discrimination of early stages of glaucoma.¹⁶

5. Conclusion

RNFL thickness measurement by the FD-OCT is of paramount importance in all cases of glaucoma and glaucoma suspects. In our study, there was significant RNFL thinning in the glaucoma group, as compared the healthy non-glaucomatous eyes. FD-OCT can be used to detect glaucoma as well as its monitor its progression. A baseline FD-OCT reading of all glaucoma patients as well as glaucoma suspect patients should be taken and repeated every 6 months/one year to look for progression so that sight can be preserved. The FD-OCT is a valuable tool to reduce the magnitude of glaucoma blindness worldwide.

6. Source of Funding

None.

7. Conflict of Interest

None.

References

- Weinreb RN, Aung T, Medeiros FA. The Pathophysiology and Treatment of Glaucoma. *JAMA*. 2014;311(18):1901–11.
- Sommer A, Katz J, Quigley HA. Clinically detectable nerve fiber atrophy precedes the onset of glaucomatous field loss. *Arch*. 1991;109(1):77–83.
- Buskirk EMV, Cioffi GA. Glaucomatous Optic Neuropathy. *Am J Ophthalmol*. 1992;113(4):447–52.
- Lin SC, Singh K, Jampel HD, Hodapp EA, Smith SD, France BA, et al. Optic nerve head and retinal nerve fibre layer analysis. A report by American Academy of Ophthalmology. *Ophthalmology*. 2007;114(10):1937–49.
- Schuman JS, Hee MR, Puliafito CA, Wong C, Kloizman TP, Lin CP. Quantification of nerve fiber layer thickness in normal and glaucomatous eyes using optical coherence tomography. *Arch Ophthalmol*. 1995;113(5):586–96.
- Blumenthal EZ, Weinreb RN. Assessment of the retinal nerve fiber layer in clinical trials of glaucoma neuroprotection. *Surv Ophthalmol*. 2001;45(3):S305–12.
- Chen HY, Huang ML, Hung PT. Logistic regression analysis for glaucoma diagnosis using Stratus optical coherence tomography. *Optom Vis Sci*. 2006;83(7):527–34.
- Cense B, Nassif NA, Chen TC, Pierce MC, Yun SH, HPark B, et al. Ultrahigh-resolution high-speed retinal imaging using spectral-domain optical coherence tomography. *Optics Express*. 2004;12(11):2435–47.
- Wojtkowski M, Srinivasan VJ, Ko TH, Fujimoto JG, Kowalczyk A, Duker JS, et al. Ultrahigh-resolution, high-speed, Fourier domain optical coherence tomography and methods for dispersion compensation. *Optics Express*. 2004;12(11):2404–22.
- Wojtkowski M, Srinivasan V, Fujimoto JG, Ko T, Schuman JS, Kowalczyk A, et al. Three-dimensional Retinal Imaging with High-Speed Ultrahigh-Resolution Optical Coherence Tomography. *Ophthalmology*. 2005;112(10):1734–46.
- Wojtkowski M, Leitgeb R, Kowalczyk A, Bajraszewski T, Fercher AF. In vivo human retinal imaging by Fourier domain optical coherence tomography. *J Biomed Opt*. 2002;7(3):457–63.
- Chen TC, Cense B, Pierce MC, Nassif NA, Park BH, Yun SH, et al. Spectral Domain Optical Coherence Tomography: ultrahigh-speed, ultrahigh-resolution ophthalmic imaging. *Arch Ophthalmol*. 2005;123(12):1715–20.
- Bussell II, Wollstein G, Schuman JS. OCT for glaucoma diagnosis, screening and detection of glaucoma progression. *Br J Ophthalmol*.

- 2014;98(2):ii15–9.
14. Sung KR, Na JH, Lee Y. Glaucoma diagnostic capabilities of optic nerve head parameters as determined by Cirrus HD optical coherence tomography. *J Glaucoma*. 2012;21(7):498–504.
 15. Ervin AM, Boland MV, Myrowitz EH. Screening for glaucoma: comparative effectiveness. Comparative effectiveness reviews. *Agency Healthc Res Qual*. 2012;.
 16. Bengtsson B, Andersson S, Heijl A. Performance of time-domain and spectral-domain Optical Coherence Tomography for glaucoma screening. *Acta Ophthalmol*. 2012;90(4):310–5.

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