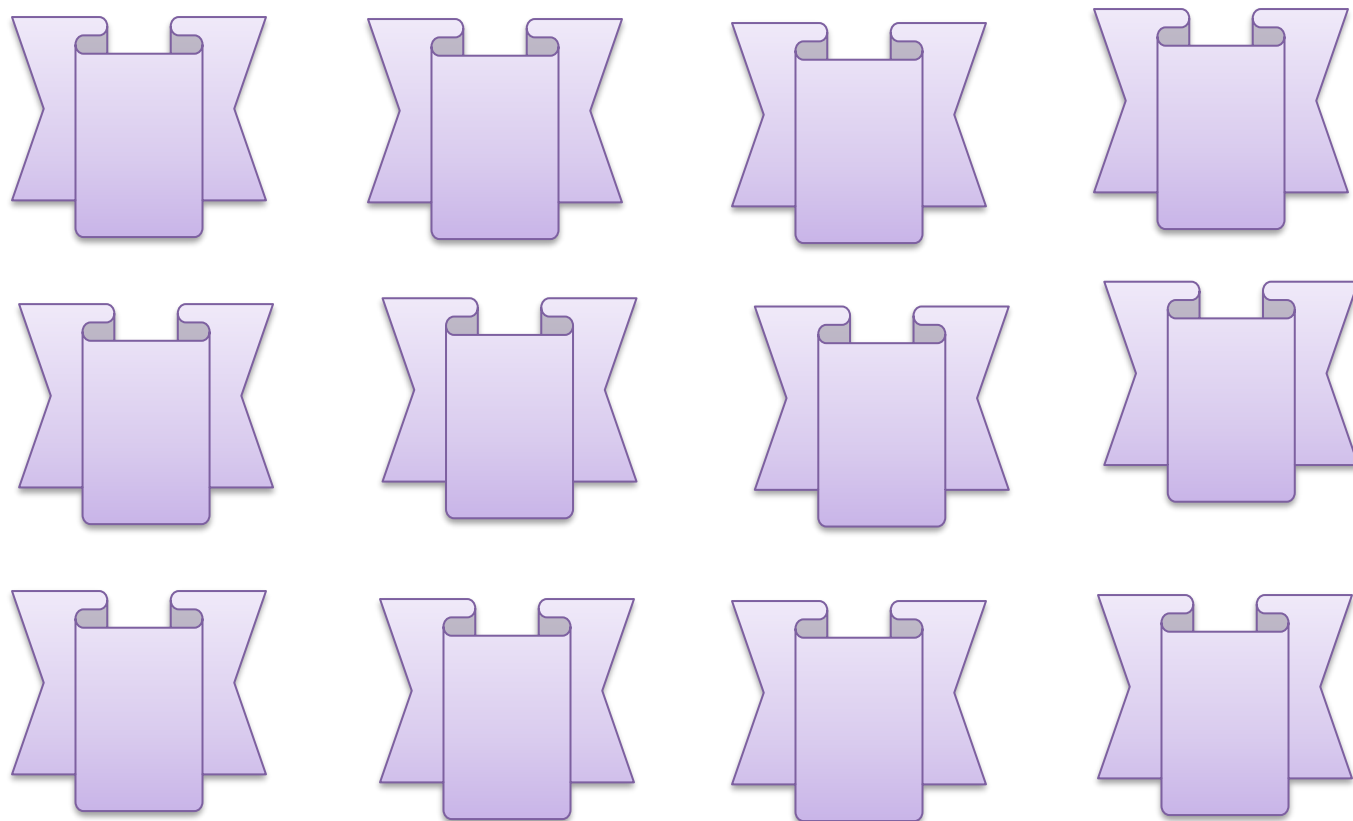


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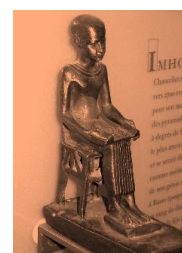
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## Original Article

### Primary Open-angle Glaucoma and Normal Tension Glaucoma Diagnosis: The Role of Macular Thickness Asymmetry

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## ABSTRACT

#### Article information

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**Background:** According to reports, the macula provides a number of potential physiological and anatomical benefits for glaucoma detection and management.

**The Aim of the work:** This study aims to determine if spectral domain optical coherence tomography [SD-OCT] measures of macular and peripapillary retinal nerve fiber layer [RNFL] thickness can reliably differentiate between primary open-angle glaucoma [POAG] and normal-tension glaucoma [NTG].

**Patients and Methods:** A prospective study enrolled 10 healthy participants, 29 glaucomatous patients: 13 with POAG and 16 with NTG. Diagnosis based on intraocular pressures, visual fields, and optic nerves. The following parameters were measured by SD-OCT B-scans: RNFL thickness [circumpapillary scan] and macular thickness [posterior pole asymmetry scan] in both eyes and then recorded in addition to the calculated inter-eye and intra-eye differences [asymmetry parameters]. Receiver operator characteristic [ROC] analysis was used to determine the optimum cut off value for the studied diagnostic markers [RNFL and macular thickness].

**Results:** Inferior macular thickness asymmetry [intereye] had the highest discrimination for normal-POAG [AUC=0.838, sensitivity = 61.5% at 80% specificity], followed by inferior RNFL thickness [intereye] asymmetry [AUC=0.808, sensitivity = 61.5% at 80% specificity]. For normal-NTG total macular thickness asymmetry [intereye] had the highest discrimination [AUC=0.756, sensitivity = 68.8 % at 80% specificity], followed by inferior RNFL thickness [intereye] asymmetry [AUC=0.700, sensitivity = 62.5 % at 80% specificity].

**Conclusion:** For the discriminating of NTG and POAG, the macular parameters function is comparable to the RNFL parameters. The top SD-OCT metrics with the best discriminating skills were intereye Inferior macular thickness asymmetry, the total retinal nerve fibre layer thickness, the intereye inferior retinal nerve fibre thickness, and the inferior macular thickness

**Keywords:** Primary Open-angle Glaucoma; Normal Tension Glaucoma; SD-OCT; RNFL.



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## INTRODUCTION

Glaucoma manifests as a progressive optic neuropathy, wherein there is a gradual deterioration of retinal ganglion cells [RGCs] and their axons. This degenerative process leads to the loss of nerve fiber layer, the development of optic disc cupping, and ultimately, the emergence of glaucomatous visual field alterations [1].

Although glaucomatous retinal ganglion cell loss and optic nerve atrophy can occur in the absence of elevated Intraocular pressure [IOP], IOP is widely considered a risk factor for glaucoma [2]. Although there is considerable overlap between the causes of NTG and POAG, the mechanism of optic neuropathy changes from IOP-dependent variables in POAG to additional pressure-independent mechanisms in NTG [3]. Therefore, NTG is sometimes considered to be a subset of POAG due to its shared characteristics [4]. Scanning laser ophthalmoscopy, scanning laser polarimetry, and optical coherence tomography are established imaging modalities employed in the diagnostic evaluation of glaucoma. These techniques enable the meticulous analysis of the optic nerve head's structural characteristics and facilitate the assessment of RNFL thickness [5].

The identification of optic nerve head [ONH] impairment, characterized by the presence of cupping and the attenuation of the peripapillary RNFL, has conventionally served as the basis for glaucoma diagnosis. Nevertheless, the exclusive reliance on these conventional indicators fails to provide a precise and reliable determination of glaucoma [6,7]. Several physiological and anatomical advantages of the macula for detecting and managing glaucoma have been reported [8,9].

The use of optical coherence tomography [OCT] for macular imaging in the treatment of glaucoma is becoming increasingly well documented. High-resolution imaging of the full macula and individual macular segments is now possible with the help of spectral domain OCT [SD-OCT]. The utilization of asymmetry analysis facilitates the assessment of macular thickness, a metric that holds significant value in the identification and monitoring of glaucoma. Certain artifacts observed on RNFL scans may be mitigated through the utilization of macular SD-OCT imaging. Furthermore, it is worth noting that the identification of non-glaucomatous optic neuropathies can potentially be facilitated through the utilization of macular thickness plots, as RNFL scans. Enhanced glaucoma monitoring utilizing macular

SD-OCT may yield favorable outcomes in specific demographic subsets, including pediatric patients and individuals with myopia [5].

The primary objective of this study is to evaluate the efficacy of SD-OCT in discerning between POAG and NTG by means of macular and peripapillary RNFL thickness measurements.

## PATIENTS AND METHODS

Seventy-eight eyes of 39 subjects were included in this prospective cross-sectional study. The study was approved by the Ethics Board of Al-Azhar University. We followed the Helsinki declaration principals. Informed written consent was obtained from every participant. We recruited the participants from the Al-Zahraa University Hospital. We recruited the patients according to the following criteria:

**The inclusion criteria were:** 1] Individuals older than 30 years; 2] patients diagnosed as NTG or POAG; 3] open angles; 4] OCT scans with a signal-to-noise ratio of greater than 35; 5] Reliable SAP carried out in less a month after OCT imaging; 6] refractive error of no more than 5 dioptre for a sphere and 3 dioptre for a cylinder.

**The Criteria for exclusion of a patient from the study were:** 1] BCVA < 20/60 on the Snellen chart, 2] any corneal and vitreoretinal disorders that might make it difficult to get accurate VFs and scans of the retina, 3] significant parapapillary atrophy, 4] Patients who were unable to undergo a valid visual field [VF] test after three attempts, as well as those presenting with any additional ophthalmic or neurologic disorders that may lead to defects in standard automated perimetry [SAP].

**Data collection:** All study participants were subjected to a thorough ophthalmic evaluation, which encompassed various assessments. These included measurements of visual acuity, determination of refractive errors, and evaluation of intraocular pressure using the Goldmann tonometry technique. Additionally, a dilated fundus examination was performed using a slit lamp and binocular indirect ophthalmoscopy to examine the optic nerve head in a stereoscopic manner. Furthermore, standard white on white automated perimetry [SAP] was conducted using the Octopus 301 Haag-Streit device manufactured by Interzeag International- AG, located in Schlieren, Switzerland. Lastly, SD-OCT imaging was carried out using the SD-OCT Spectralis HRA + OCT

system developed by Heidelberg Engineering in Germany. Glaucomatous eyes were characterized as those exhibiting verified glaucomatous visual field impairments on two dependable visual field assessments, along with the manifestation of a glaucomatous optic disc on slit-lamp biomicroscopy by a cup-to-disc ratio exceeding 0.7, Asymmetrical cup-to-disc ratio, or the presence of disc hemorrhage, notching of the neuroretinal rim, vertical elongation of the optic cup or focal thinning. The eyes afflicted with glaucoma were classified into two distinct subgroups based on the IOP level. The NTG cohort was delineated as individuals exhibiting untreated peak IOP values of 21 mmHg or below, ascertained through three distinct measurements conducted at different time points during separate visits throughout the clinical monitoring period. Patients are consisted of individuals who presented with a documented ocular hypertension [OHT] condition, characterized by IOP readings consistently surpassing the threshold of 21 mmHg, as confirmed by three separate measurements conducted on distinct days. The control group consisted of individuals who were selected from patients referred for routine ophthalmic examination and hospital staff members. These individuals were carefully matched in terms of age and sex to ensure comparability. Importantly, they had no history of ocular disease or prior intraocular or laser surgery, with the exception of uncomplicated cataract surgery.

The individuals comprising the healthy control group exhibited an unremarkable anterior segment, unobstructed angles, and unremarkable posterior segment observations. Furthermore, their ophthalmic examinations revealed a normal appearance of the ONH. In the absence of pharmacological intervention, IOP measurements were observed to be below the threshold of 21 mmHg. Furthermore, the results obtained from standard automated perimetric assessment of the visual field exhibited no abnormalities.

**Standard automated perimetry:** With the participant being dark-adapted for three to five minutes prior to the test, standard automated perimetry was carried out utilising the usual method on making VF tests. As determined by less than 33% focus loss and less than 20% positive and negative catch trials, all visual field tests were trustworthy. According to the standards established by **Hodapp *et al.*** <sup>[10]</sup>, a glaucomatous visual field defect was defined as having a mean deviation greater than +2.0 dB, loss variance greater than 6.0 dB, or both; at least 25% of points depressed below five percent

level, 15% of points depressed below one percent level, with or without points within the central five degrees and one or both hemifields with sensitivity 15 dB or less <sup>[11]</sup>.

### **Spectral domain optical coherence tomography**

The commercially available SD-OCT Spectralis HRA + OCT was used to scan each subject [Heidelberg Engineering]. In scanning laser ophthalmoscopy [SLO] mode, this device operates at an 820 nm wavelength in the near infrared spectrum. A super-luminescent diode with a peak wave-length of 870 nm serves as the SD-light OCT's source. The dual laser scanning systems' OCT scans [40,000 A-Scans per second] and infrared images are obtained simultaneously. For the purpose of reducing speckle noise, 16 successive circular B-scans [3.4 mm in diameter; 768 A-scans] centred at the optic disc were automatically averaged.

Online tracking software was used to account for eye movements. The thickness of the RNFL and the whole retina can be measured separately using the Spectralis software version 3.2.1. The segmentation software successfully located and automatically designated the limits of the nerve fibre layer. The nerve fibre layer was thought to include the retinal vessels that are found within the RNFL. Four sectors of the thickness data from the circular scans were averaged to reveal the distribution of RNFL thickness around the optic disc [45 degrees each]. In each example, a single user did at least two retinal scans, and the scans with the best image quality were taken into consideration. The macular thickness was measured using a posterior pole high speed 12 degrees diameter volume scan, and the findings were produced by dividing the macular area into nine areas containing three circles each by retinal map analysis system. A good-quality scan was defined as the presence of homogeneous signal strength, high reflectance signals from the RNFL and the retinal pigment epithelium, and unambiguous delineation of both layers without the lack of any section of the image.

**Statistical analysis:** SPSS [Statistical Package for the Social Science; SPSS Inc., Chicago, IL, USA] version 17 for Microsoft Windows was used to do the statistical analyses. Qualitative data were presented as frequency and percentages. Quantitative data were presented as mean and SD. Kruskal-Wallis test was used to compare between the three study groups, followed by post hoc multiple 2-group

comparisons. The quantification of accuracy was conveyed through the utilization of the sensitivity and specificity. Receiver operator characteristic [ROC] analysis was employed to ascertain the optimal threshold value for the diagnostic markers under investigation. Statistical significance was determined by considering p-values that were less than 0.05.

### RESULTS

A total of 39 subjects were included in this study [13 patients with POAG, 16 patients with NTG and 10 normal subjects]. The three groups were matched for the age with no significant difference between them [P = 0.76]. The mean age of the POAG, NTG, and normal subjects was  $50.0 \pm 6.8$ ,  $48.38 \pm 14.6$ ,  $47.5 \pm 14.2$  years respectively. The POAG group had significantly worse visual field indices [MD, VD] than the NTG group, and the normal group [p-value 0.001, and 0.0001 respectively]. The mean values for MD and LV in the POAG group were [ $6.1 \pm 2.21$ ,  $9.3 \pm 5.6$  dB] OD and OS, respectively. The mean values for MD in the NTG group were [ $3.7 \pm 2.06$ ,  $2.9 \pm 1.79$  dB] and LV [ $9.75 \pm 4.78$ , and  $7.57 \pm 5.64$  dB] OD and OS, respectively. The difference between the three groups and also between each two groups regarding the MD and LV was significant statistically [P value > 0.05 for all] except for the difference between the difference between the normal and NTG groups regarding the MD and LV of the left eye in which the difference was not significant statistically [P = 0.1, and 0.06 respectively] [Table 1].

As regards the total NFL thickness, the difference between the POAG and NTG was not significant statistically in both eyes [P > 0.05], however we found a significant difference between the POAG and control patients in the left eyes in which the total RNFL was significantly lower in the POAG [P = 0.02]. In terms of the inferior NFL thickness, in the right

eyes we found no significant difference between the three groups. However, in the left eyes it was significantly lower in the POAG group than the control and NTG groups [P = 0.03] [Table 2].

According to the macular thickness, the three groups were comparable regarding the total, superior, and inferior macular thickness [P value > 0.05 for all] [Table 2]. As regards the Inter eye Comparison of the three studied groups, we found no significant difference between the three groups regarding the total and superior RNFL thickness, however the inter eye difference of the inferior RNFL thickness was significantly higher in POAG group than the other two groups [P =0.04]. The inter eye total macular thickness was significantly higher in POAG and NTG groups than the control group [P = 0.02, and 0.05 respectively]. Also, the inter eye difference of the inferior macular thickness was significantly higher in POAG group than the NTG and control groups [P = 0.03] [Table 3].

Inferior macular thickness asymmetry [intereye] had the highest discrimination for normal-POAG [AUC=0.838, sensitivity = 61.5% at 80% specificity], and normal - NTG [AUC=0.694, sensitivity = 50 % at 80% specificity]. These followed by total RNFL thickness that has the sensitivity [69.2% at 80% specificity] and the area under ROC [0.781] in discriminating POAG and control groups and 50 % sensitivity at 80% specificity and the area under ROC 0.650 in discriminating NTG and control groups. Intereye Inferior RNFL has the area under ROC [0.808] with sensitivity [61.5% at 80% specificity] in discriminating POAG and control groups and 62.5 sensitivity at 80% specificity and the area under ROC 0.700 in discriminating NTG and control groups. The area under ROC curve was significantly higher in total macular thickness than the area under ROC curve for total RNFL thickness. Inferior minus superior RNFL thickness had the lowest sensitivity [30.5% at 80% specificity] and the smallest area under ROC curve [Table 4].

**Table [1]:** Baseline clinical data of the studied patients

		Controls	POAG	NTG	Kruskal-Wallis Test	Mann-Whitney Test		
		Mean ± SD	Mean ± SD	Mean ± SD	P <sub>1</sub>	P <sub>2</sub>	P <sub>3</sub>	P <sub>4</sub>
<b>Age</b>		47.5 ± 14.261	50.0 ± 6.807	48.38 ± 14.67	0.705	-	-	-
<b>MD</b>	OD	1.740 ± 2.2172	6.19 ± 2.21	3.71 ± 2.06	0.001	0.006	0.031	0.001
	OS	1.950 ± 1.7552	9.34 ± 5.60	2.938 ± 1.79	0.000	0.000	0.155	0.000
<b>LV</b>	OD	4.270 ± 1.7269	18.446 ± 7.16	9.75 ± 4.788	0.000	0.001	0.001	0.000
	OS	5.010 ± 2.7566	22.11 ± 13.95	7.575 ± 5.641	0.000	0.000	0.069	0.000

P<sub>1</sub>; P- value [Kruskal-Wallis Test, comparing the 3 independent groups]. P<sub>2</sub>; P- value [Mann-Whitney Test, POAG Vs NTG]. P<sub>3</sub>; P- value [Mann-Whitney Test, Control Vs NTG]. P<sub>4</sub>; P- value [Mann-Whitney Test, POAG Vs control]

**Table [2]:** Retinal nerve fiber layer thickness and macular thickness categorized by diagnosis and by eye

		Controls	POAG	NTG	Kruskal-Wallis Test	Mann-Whitney Test		
		Mean ± SD	Mean ± SD	Mean ± SD	P <sub>1</sub>	P <sub>2</sub>	P <sub>3</sub>	P <sub>4</sub>
<b>Global NFL thickness</b>	OD	99.8 ± 11.87	93.00 ± 9.39	93.44 ± 13.47	0.391	0.809	0.316	0.162
	OS	99.1 ± 11.22	86.85 ± 16.7	93.88 ± 9.06	0.065	0.187	0.170	0.028
<b>Inferior NFL thickness</b>	OD	132.4 ± 23.59	121.46±12.22	120.6±20.3	0.445	0.982	0.268	0.251
	OS	131.0 ± 15.87	110.2±22.5	123.94±12.96	0.039	0.091	0.196	0.020
<b>Superior NFL thickness</b>	OD	118.5 ± 13.62	108.0±12.416	113.81±18.87	0.224	0.357	0.370	0.082
	OS	122.2±18.08	108.2±22.8	115.6±14.94	0.274	0.357	0.356	0.129
<b>Inferior minus superior RNFL thickness</b>	OD	13.9±23.33	13.46±15.72	6.81 ± 19.6	0.872	0.629	0.771	0.780
	OS	8.80±15.288	2.00 ± 14.88	8.38±16.85	0.444	0.263	0.874	0.291
<b>Inferior/superior RNFL thickness difference</b>	OD	18.9±19.03	14.5±14.65	17.9±9.6	0.410	0.167	0.561	0.641
	OS	14.8±8.741	12.0±8.34	15.63 ± 9.912	0.551	0.334	0.895	0.367
<b>Total macular thickness</b>	OD	283.0±11.53	279.±11.07	278.0±16.06	0.634	0.930	0.356	0.456
	OS	283.9±12.31	276.0±12.16	279.38±15.06	0.317	0.568	0.234	0.172
<b>Inferior macular thickness</b>	OD	281.9±12.78	278.8±11.62	277.9±17.02	0.705	0.930	0.370	0.598
	OS	284.9±13.63	275.4±15.83	279.06±16.32	0.306	0.443	0.303	0.153
<b>Superior macular thickness</b>	OD	283.8±10.84	279.4±10.8	278.6±15.4	0.482	0.947	0.215	0.385
	OS	282.6±11.21	276.5 ± 9.5	279.2±15.02	0.406	0.429	0.460	0.203
<b>Inferior/superior macular thickness difference</b>	OD	4.10 ± 3.11	3.69 ± 3.35	4.69 ± 3.591	0.613	0.287	0.710	0.754
	OS	3.70 ± 2.497	6.31 ± 7.46	6.38 ± 5.084	0.422	0.508	0.176	0.593

Inferior minus superior RNFL thickness: Calculated as inferior minus superior RNFL thickness to account for normal anatomic configuration. Inferior/superior RNFL thickness difference: Absolute difference between superior and inferior RNFL thickness. Inferior/superior macular thickness difference: Absolute difference between superior and inferior macular thickness. P<sub>1</sub>; P- value [Kruskal-Wallis Test, comparing the 3 independent groups]. P<sub>2</sub>; P- value [Mann-Whitney Test, POAG Vs NTG]. P<sub>3</sub>; P- value [Mann-Whitney Test, Control Vs NTG]. P<sub>4</sub>; P- value [Mann-Whitney Test, POAG Vs control].

**Table [3]:** Inter eye comparison of retinal nerve fiber layer thickness and macular thickness between subjects diagnosed with early primary open-angle glaucoma and normal subjects

	Controls	POAG	NTG	Kruskal-Wallis Test	Mann-Whitney Test		
	Mean ± SD	Mean ± SD	Mean ± SD	P <sub>1</sub>	P <sub>2</sub>	P <sub>3</sub>	P <sub>4</sub>
<b>Global RNFL thickness: right eye vs left eye difference</b>	4.10 ± 1.792	9.08 ± 14.546	4.69 ± 6.916	0.498	0.376	0.277	0.876
<b>Inferior RNFL thickness: right eye vs left eye difference</b>	5.40 ± 7.662	18.62 ± 22.176	11.19 ± 11.714	0.046	0.403	0.090	0.013
<b>Superior RNFL thickness: right eye vs left eye difference</b>	9.30 ± 6.056	10.23 ± 12.853	9.00 ± 10.850	0.663	0.495	0.475	0.576
<b>Inferior minus superior RNFL thickness: right eye vs left eye</b>	12.50 ± 10.512	15.62 ± 11.340	11.06 ± 10.129	0.555	0.322	0.833	0.402
<b>Inferior/superior RNFL thickness difference: right eye vs left eye</b>	11.70 ± 10.520	11.62 ± 9.588	10.19 ± 7.918	0.954	0.982	0.958	0.641
<b>Total macular thickness: right eye vs left eye difference</b>	2.30 ± 4.218	4.54 ± 5.190	5.13 ± 4.843	0.063	0.550	0.029	0.059
<b>Inferior macular thickness: right eye vs left eye difference</b>	3.60 ± 6.569	7.54 ± 7.367	5.75 ± 5.779	0.031	0.376	0.099	0.006
<b>Superior macular thickness: right eye vs left eye difference</b>	2.80 ± 2.616	3.54 ± 3.992	5.44 ± 5.228	0.344	0.258	0.200	0.749
<b>Inferior/superior macular thickness difference: right eye vs left eye</b>	3.00 ± 2.404	6.77 ± 6.585	4.94 ± 4.905	0.333	0.378	0.422	0.160

P<sub>1</sub>; P- value [Kruskal-Wallis Test, comparing the 3 independent groups]. P<sub>2</sub>; P- value [Mann-Whitney Test, POAG Vs NTG]. P<sub>3</sub>; P- value [Mann-Whitney Test, Control Vs NTG]. P<sub>4</sub>; P- value [Mann-Whitney Test, POAG Vs control].

**Table [4]:** ROC analysis for retinal nerve fiber layer parameters for comparing normal and POAG, normal and NTG

	POAG Vs Control				NTG Vs Control			
	AUC	95% CI	Diagnostic Threshold Value [ $\mu$ m]	Sensitivity at 80% Specificity [%]	AUC	95% CI	Diagnostic Threshold Value [ $\mu$ m]	Sensitivity at 80% Specificity [%]
Global NFL thickness	0.781	0.582 - 0.979	90.50	69.2	0.650	0.433 - 0.867	90.50	50.0
Inferior NFL thickness	0.792	0.595 - 0.989	111.50	61.5	0.681	0.466 - 0.897	112.00	37.5
Superior NFL thickness	0.712	0.488 - 0.935	102.50	46.2	0.628	0.387 - 0.869	103.50	31.3
Inferior minus superior RNFL thickness	0.588	0.342 - 0.835	-5.50	30.8	0.538	0.310 - 0.765	-7.50	31.3
Inferior/superior RNFL thickness difference	0.619	0.381 - 0.857	5.50	53.8	0.484	0.250 - 0.718	5.50	25.0
Total macular thickness	0.662	0.428 - 0.895	272.00	46.2	0.641	0.410 - 0.871	270.00	25.0
Inferior macular thickness	0.681	0.459 - 0.903	268.50	38.5	0.656	0.432 - 0.881	268.50	31.3
Superior macular thickness	0.638	0.397 - 0.880	272.00	46.2	0.656	0.429 - 0.883	272.50	31.3
Inferior/superior macular thickness difference	0.358	0.125 - 0.591	3.50	7.7	0.353	0.138 - 0.568	2.50	6.3
Global RNFL thickness: right eye vs left eye difference	0.519	0.271 - 0.768	2.50	46.2	0.628	0.410 - 0.847	2.50	56.3
Inferior RNFL thickness: right eye vs left eye difference	0.808	0.610 - 1.006	9.50	61.5	0.700	0.483 - 0.917	6.50	62.5
Superior RNFL thickness: right eye vs left eye difference	0.569	0.317 - 0.821	3.50	30.8	0.584	0.349 - 0.820	3.50	37.5
Inferior minus superior RNFL thickness: right eye vs left eye	0.604	0.362 - 0.845	16.50	30.8	0.525	0.295 - 0.755	7.00	43.8
Inferior/superior RNFL thickness difference: right eye vs left eye	0.558	0.311 - 0.804	11.50	38.5	0.506	0.273 - 0.739	11.50	50.0
Total macular thickness: right eye vs left eye difference	0.727	0.510 - 0.944	2.50	46.2	0.756	0.550 - 0.962	2.50	68.8
Inferior macular thickness: right eye vs left eye difference	0.838	0.656 - 1.021	3.50	61.5	0.694	0.475 - 0.912	3.50	50.0
Superior macular thickness: right eye vs left eye difference	0.538	0.292 - 0.785	4.50	30.8	0.650	0.436 - 0.864	4.50	43.8
Inferior/superior macular thickness difference: right eye vs left eye difference	0.673	0.449 - 0.897	4.50	46.2	0.594	0.370 - 0.817	4.50	43.8

AUC: Area under the curve

## DISCUSSION

The goal of this study was to assess how well the RNFL and macular parameters of SD-OCT could distinguish between NTG and POAG. It has been reported in 60% of eyes that detectable RNFL loss occurs six years or more before any

detectable visual field deficits in glaucoma; which can occur before measurably damaged optic nerve heads and visual field loss [12]. Yet, additional research has discovered that functional visual field loss could occur before visible anatomical loss of the optic nerves [13].



The predominant approach to glaucoma management revolves around the utilization of visual field tests as a primary diagnostic tool. However, there is a shifting paradigm that favors the identification of structural alterations, as they have been postulated to contribute significantly to the early detection of glaucoma. An assortment of novel technologies has emerged, offering the capability to objectively and non-invasively quantify structural alterations resulting from retinal ganglion cell impairment. The utilization of SD-OCT has experienced a notable surge in popularity within the last decade, primarily attributed to its remarkable advantages in facilitating observer-independent diagnosis and monitoring of glaucoma [14].

In our study, it was observed that the thickness of the Inferior Retinal Nerve Fiber Layer [RNFL] exhibited a notable reduction in eyes affected by Primary Open-Angle Glaucoma [POAG] when contrasted with the eyes of individuals in the healthy control group. Furthermore, it was determined that the eyes afflicted with POAG displayed the most diminished measurements of the nerve fiber layer. The retinal nerve fiber layer [RNFL] thickness exhibited no statistically significant differences between subjects diagnosed with primary open-angle glaucoma [POAG] and those diagnosed with normal-tension glaucoma [NTG]. Previous studies have indicated that there is no significant variation in the optical coherence tomography [OCT] retinal nerve fiber layer [RNFL] parameters between individuals diagnosed with high-tension glaucoma and normal-tension glaucoma [NTG] [15]. Other studies showed difference between POAG and NTG in RNFL thickness [2].

Regarding the macular thickness we noted a considerable decrease in the intereye difference in total macular thickness in NTG and POAG compared to healthy eyes, with NTG exhibit the largest difference compared to the other groups. Also, intereye difference in inferior macular thickness in POAG showed a significant difference compared to other groups.

In a study conducted by **Khanal et al.** [2], notable findings were observed regarding the macular thickness and volume in individuals with normal-tension glaucoma [NTG] and primary open-angle glaucoma [POAG] when compared to those with healthy eyes. Specifically, it was observed that both NTG and POAG patients exhibited a significant decrease in macular thickness and volume. Furthermore,

the POAG group displayed the lowest macular thickness and volume among all the groups under investigation. For all macular thickness parameters, there was a significant difference between groups.

To find the diagnostic capacity for NTG and POAG, we generated AROCs for each of the RNFL thicknesses and macular thickness parameters and estimated the sensitivities at a high specificity of greater than 80%. The ideal macular thickness values for the normal-NTG comparison group were intereye inferior macular thickness. Inter-eye inferior macular thickness also exhibited improved ability to distinguish between normal and POAG groups.

**Khanal et al.** [2] reported that the most optimal parameters for macular thickness and volume are inclusive of total volume, as well as the thickness and volume of the inferior outer macular region.

Given that the inferior arcuate fibers will actually converge towards the inferior part of the optic disc as they follow the route of nerve fiber topography, these findings are consistent with the facts that certain regions of the optic disc are more susceptible to glaucomatous damage [16]. Similar results from other investigations regarding prototype OCT-based glaucomatous damage to the inferior macular areas were also noted [17].

Regarding RNFL, total RNFL thickness and inferior RNFL thickness had the best discriminating power for both normal-NTG comparison group, as well as for normal and POAG groups. The discriminating power of RNFL was higher than macular thickness, however AUC was higher for intereye inferior macular thickness.

According to **Guedes et al.** [18], RNFL thickness had greater discrimination power between early glaucoma and normal eyes [AUC: 0.94] than macular thickness [AROC: 0.77]. In a different investigation by **Medeiros et al.** [19], the comparative analysis revealed that the optimal RNFL thickness parameter, specifically in the inferior quadrant, exhibited a notably superior area under the curve [AUC] of 0.91. In contrast, the most favorable macular thickness value, specifically pertaining to the inferior outer macular region, demonstrated a comparatively lower AUC of 0.81. In the study conducted by **Leung et al.** [20], a comparison was made between the macular nerve fiber layer and the total macular thickness. They observed that there was no significant disparity in the area under the

curve [AUC] values when it came to detecting glaucoma or glaucoma suspects. However, it was noted that the retinal nerve fiber layer [RNFL] thickness exhibited superior discriminatory performance compared to both the total macular thickness and the thickness of the macular nerve fiber layer.

**Conclusion:** For the purpose of distinguishing NTG and POAG from the healthy population, this study's findings show that macular metrics perform similarly to RNFL parameters. In particular, our findings imply that glaucoma is probable when there is an intra eye macular thickness asymmetry and when total RNFL thickness asymmetry.

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