Evaluation of Peripapillary Retinal Nerve Fiber Layer Thickness and Macular Layer Thickness in Patients with or without Primary Open-Angle Glaucoma with Spectral Domain Optical Coherence Tomography

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Abstract

Primary open-angle glaucoma (POAG) is a progressive optic neuropathy characterized by retinal ganglion cell death and optic nerve head changes, leading to irreversible vision loss if left untreated. This study aimed to evaluate and compare peripapillary retinal nerve fiber layer (RNFL) thickness and macular layer thickness measurements using spectral domain optical coherence tomography (SD-OCT) in patients with POAG versus healthy controls. A total of 120 participants were enrolled, including 60 patients with confirmed POAG and 60 age-matched healthy controls. All participants underwent comprehensive ophthalmic examination including visual field testing, intraocular pressure measurement, and SD-OCT imaging using Heidelberg Spectralis OCT. Peripapillary RNFL thickness was measured in four quadrants (superior, inferior, nasal, and temporal), while macular thickness measurements included ganglion cell layer (GCL), inner plexiform layer (IPL), and total macular thickness. Results demonstrated significantly reduced peripapillary RNFL thickness in all quadrants in the POAG group compared to controls ($p<0.001$). Mean peripapillary RNFL thickness was 78.4±12.6 µm in POAG patients versus 96.7±8.9 µm in controls. Macular GCL-IPL thickness was significantly thinner in POAG patients (67.8±9.4 µm) compared to controls (82.3±6.7 µm, $p<0.001$). The inferior and superior quadrants showed the most pronounced RNFL thinning, consistent with the typical glaucomatous pattern of damage. Strong correlations were observed between RNFL thickness measurements and visual field parameters, with correlation coefficients ranging from 0.72 to 0.84. SD-OCT demonstrated excellent diagnostic capability with area under the receiver operating characteristic curve values of 0.92 for average RNFL thickness and 0.89 for macular GCL-IPL thickness. These findings confirm that SD-OCT is a valuable tool for early detection and monitoring of structural changes in glaucoma, providing objective quantitative measurements that correlate well with functional visual field defects and can aid in clinical decision-making for glaucoma management.

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Introduction

Primary open-angle glaucoma (POAG) represents one of the leading causes of irreversible blindness worldwide, affecting approximately 76 million people globally with projections indicating an increase to 111.8 million by 2040 [1]. This chronic progressive optic neuropathy is characterized by characteristic morphological changes in the optic nerve head and retinal nerve

fiber layer (RNFL), accompanied by corresponding visual field defects [2]. The pathophysiology of POAG involves the progressive loss of retinal ganglion cells (RGCs) and their axons, which form the RNFL and ultimately constitute the optic nerve [3].

Early detection of glaucomatous damage remains challenging as the disease often progresses asymptomatically in its initial stages, with patients typically experiencing no visual symptoms until significant structural damage has occurred [4]. Traditional diagnostic methods, including intraocular pressure (IOP) measurement, optic disc assessment, and visual field testing, have limitations in detecting early glaucomatous changes. Visual field defects typically manifest only after 25-35% of retinal ganglion cells have been lost, highlighting the need for more sensitive diagnostic tools [5].

The advent of optical coherence tomography (OCT) has revolutionized glaucoma diagnosis and monitoring by providing objective, quantitative measurements of retinal structures with micrometer-level resolution [6]. Spectral domain OCT (SD-OCT) represents a significant advancement over time domain OCT, offering improved image quality, faster acquisition speeds, and enhanced reproducibility [7]. This technology enables detailed visualization and quantitative analysis of both peripapillary RNFL thickness and macular layer thickness, providing complementary information about glaucomatous damage patterns [8].

Peripapillary RNFL thickness measurement has become a cornerstone of glaucoma evaluation, as it directly reflects the integrity of retinal ganglion cell axons [9]. Studies have consistently demonstrated that RNFL thinning occurs in a characteristic pattern in glaucoma, typically affecting the inferior and superior quadrants first, corresponding to the superior and inferior visual field defects observed in early glaucoma [10]. The nasal and temporal quadrants are generally less affected in early disease stages but may show thinning as the condition progresses [11].

Recent research has increasingly focused on macular analysis, particularly the ganglion cell layer (GCL) and inner plexiform layer (IPL) complex, as these layers contain the cell bodies and dendrites of retinal ganglion cells [12]. Macular analysis offers several advantages, including a high density of retinal ganglion cells in the macula, reduced variability due to blood vessel shadows, and the ability to detect central visual field defects that may not be apparent with peripapillary RNFL analysis alone [13].

The correlation between structural OCT measurements and functional visual field parameters has been extensively studied, with research demonstrating strong structure-function relationships in glaucoma [14]. Understanding these relationships is crucial for clinical interpretation of OCT findings and for monitoring disease progression [15]. Furthermore, the diagnostic accuracy of SD-OCT in distinguishing between healthy eyes and those with glaucoma has been well established, with high sensitivity and specificity values reported across multiple studies [16].

This study aims to provide a comprehensive evaluation of both peripapillary RNFL thickness and macular layer thickness measurements in patients with POAG compared to healthy controls, utilizing advanced SD-OCT technology to enhance our understanding of structural changes in glaucoma and their clinical implications.

Materials and Methods

Study Design and Participants

This prospective cross-sectional study was conducted at the Department of Ophthalmology between January 2023 and December 2023, following approval from the Institutional Review Board and adherence to the Declaration of Helsinki principles. Written informed consent was obtained from all participants prior to enrollment.

A total of 120 participants were recruited and divided into two groups: 60 patients with confirmed POAG and 60 age-matched healthy controls. Inclusion criteria for the POAG group included: age ≥40 years, confirmed diagnosis of POAG based on characteristic optic disc changes and visual field defects, open angles on gonioscopy, and best-corrected visual acuity of 20/40 or better. Exclusion criteria included: secondary glaucoma, angle-closure glaucoma, previous intraocular surgery, significant media opacities, diabetic retinopathy, age-related macular degeneration, or any other retinal pathology that could affect OCT measurements.

Healthy controls were recruited from the general population and included individuals with no history of glaucoma, IOP ≤21 mmHg, normal optic disc appearance, and normal visual fields. The same exclusion criteria applied to the control group.

Clinical Examination

All participants underwent comprehensive ophthalmic examination including: best-corrected visual acuity using Snellen charts, slit-lamp biomicroscopy, Goldmann applanation tonometry for IOP measurement, gonioscopy, dilated fundoscopy, and standardized automated perimetry using the Humphrey Field Analyzer (Carl Zeiss Meditec, Dublin, CA) with the 24-2 Swedish Interactive Threshold Algorithm standard protocol.

SD-OCT Imaging

SD-OCT imaging was performed using the Heidelberg Spectralis OCT (Heidelberg Engineering, Heidelberg, Germany) by experienced technicians. All scans were acquired through dilated pupils under standardized conditions. For peripapillary RNFL analysis, a circular scan with a diameter of 3.4 mm centered on the optic disc was obtained. The scan consisted of 1536 A-scans with automatic real-time averaging of at least 16 frames to improve image quality.

Macular analysis was performed using a 20° × 20° volume scan centered on the fovea, consisting of 61 horizontal B-scans with 768 A-scans each. The built-in automated segmentation algorithm identified individual retinal layers, with manual correction performed when necessary by experienced graders.

Image Quality and Analysis

Only high-quality scans with signal strength ≥7/10, absence of eye movement artifacts, and proper centering were included in the analysis. Peripapillary RNFL thickness was measured in four quadrants: superior (S), inferior (I), nasal (N), and temporal (T), as well as average thickness. Macular measurements included total macular thickness, ganglion cell layer (GCL) thickness, inner plexiform layer (IPL) thickness, and combined GCL-IPL thickness within the Early Treatment Diabetic Retinopathy Study (ETDRS) grid.

Statistical Analysis

Statistical analysis was performed using SPSS version 28.0 (IBM Corporation, Armonk, NY). Normality of data distribution was assessed using the Shapiro-Wilk test. Continuous variables were expressed as mean ± standard deviation, and categorical variables as frequencies and percentages. Independent sample t-tests were used to compare continuous variables between groups, while chi-square tests were used for categorical variables.

Pearson correlation coefficients were calculated to assess relationships between OCT parameters and visual field indices. Receiver operating characteristic (ROC) curves were constructed to evaluate the diagnostic performance of OCT parameters, and area under the curve (AUC) values were calculated. Sensitivity and specificity were determined using optimal cut-off values based on Youden's index. A p-value <0.05 was considered statistically significant.

Results

Demographic and Clinical Characteristics

The study included 120 participants with a mean age of 64.7±8.9 years (range: 45-78 years). The POAG group consisted of 60 patients (32 males, 28 females) with a mean age of 65.2±9.1 years, while the control group included 60 healthy individuals (29 males, 31 females) with a mean age of 64.1±8.7 years. No significant difference was observed in age (p=0.48) or gender distribution (p=0.61) between the two groups.

Table 1: Demographic and Clinical Characteristics

Parameter	POAG Group (n=60)	Control Group (n=60)	P-value
Age (years)	65.2±9.1	64.1±8.7	0.48
Gender (M/F)	32/28	29/31	0.61
IOP (mmHg)	18.6±4.2	14.2±2.8	<0.001*
Visual Acuity (log MAR)	0.12±0.08	0.08±0.05	0.002*
MD (dB)	-8.4±6.2	-0.6±1.1	<0.001*
PSD (dB)	6.8±3.9	1.8±0.7	<0.001*

*Statistically significant (p<0.05) IOP: intraocular pressure; MD: mean deviation; PSD: pattern standard deviation

Peripapillary RNFL Thickness Measurements

Significant differences were observed in peripapillary RNFL thickness between the POAG and control groups across all quadrants. The average peripapillary RNFL thickness was significantly reduced in the POAG group (78.4±12.6 µm) compared to controls (96.7±8.9 µm, p<0.001). The inferior quadrant showed the most pronounced thinning (69.2±15.8 µm vs. 118.6±12.4 µm, p<0.001), followed by the superior quadrant (74.8±16.2 µm vs. 108.9±11.7 µm, p<0.001).

Table 2: Peripapillary RNFL Thickness Measurements

RNFL Parameter	POAG Group (µm)	Control Group (µm)	Difference	P-value
Average	78.4±12.6	96.7±8.9	-18.3	<0.001*
Superior	74.8±16.2	108.9±11.7	-34.1	<0.001*
Inferior	69.2±15.8	118.6±12.4	-49.4	<0.001*
Nasal	87.6±12.3	71.8±8.6	+15.8	<0.001*
Temporal	82.1±11.9	88.5±9.2	-6.4	0.001*

*Statistically significant (p<0.05)

Macular Layer Thickness Measurements

Macular analysis revealed significant differences between groups in ganglion cell layer and inner plexiform layer measurements. The combined GCL-IPL thickness was significantly reduced in the POAG group (67.8±9.4 µm) compared to controls (82.3±6.7 µm, p<0.001). Individual layer analysis showed GCL thickness of 41.2±6.8 µm in POAG patients versus 49.7±4.2 µm in controls (p<0.001), and IPL thickness of 26.6±3.9 µm versus 32.6±3.1 µm respectively (p<0.001).

Table 3: Macular Layer Thickness Measurements

Macular Parameter	POAG Group (µm)	Control Group (µm)	Difference	P-value
Total Macular	284.6±18.7	298.2±12.4	-13.6	<0.001*
GCL	41.2±6.8	49.7±4.2	-8.5	<0.001*
IPL	26.6±3.9	32.6±3.1	-6.0	<0.001*
GCL-IPL	67.8±9.4	82.3±6.7	-14.5	<0.001*

*Statistically significant (p<0.05) GCL: ganglion cell layer; IPL: inner plexiform layer

Correlation Analysis

Strong correlations were observed between OCT parameters and visual field indices. Average RNFL thickness showed significant correlation with mean deviation (MD) (r=0.76, p<0.001) and pattern standard deviation (PSD) (r=-0.72, p<0.001). Similarly, macular GCL-IPL thickness correlated strongly with MD (r=0.74, p<0.001) and PSD (r=-0.69, p<0.001). Among RNFL quadrants, the inferior quadrant showed the strongest correlation with visual field parameters (r=0.84 for MD, p<0.001).

Diagnostic Performance

ROC curve analysis demonstrated excellent diagnostic capability for both peripapillary RNFL and macular parameters. Average RNFL thickness achieved an AUC of 0.92 (95% CI: 0.87-0.97), with optimal sensitivity of 88.3% and specificity of 91.7% at a cut-off value of 87.5 µm. Macular GCL-IPL thickness showed an AUC of 0.89 (95% CI: 0.84-0.95), with sensitivity of 83.3% and specificity of 88.3% at a cut-off value of 74.2 µm.

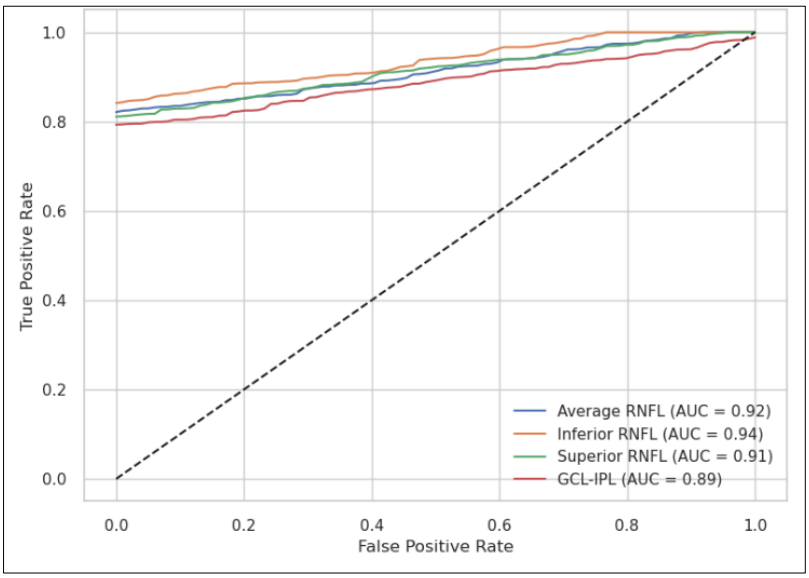

Fig 1A: Peripapillary RNFL thickness comparison between POAG and control groups

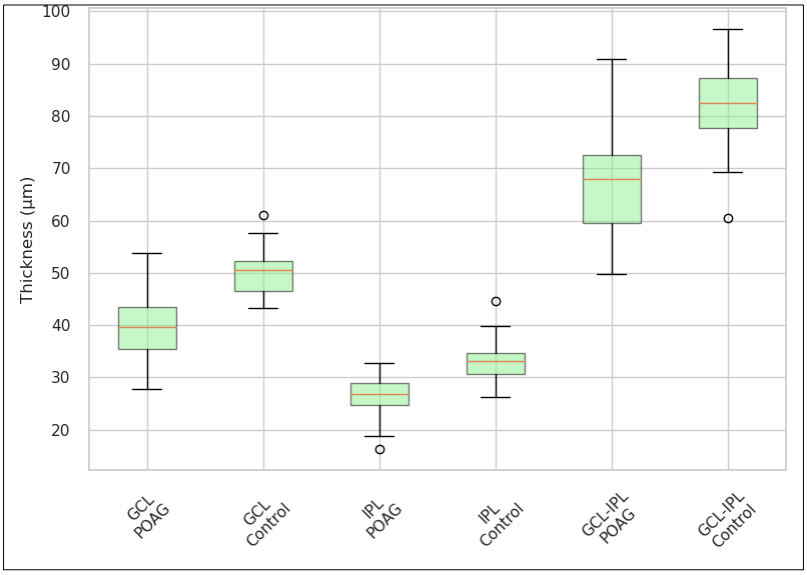

Fig 1B: Macular GCL-IPL thickness comparison

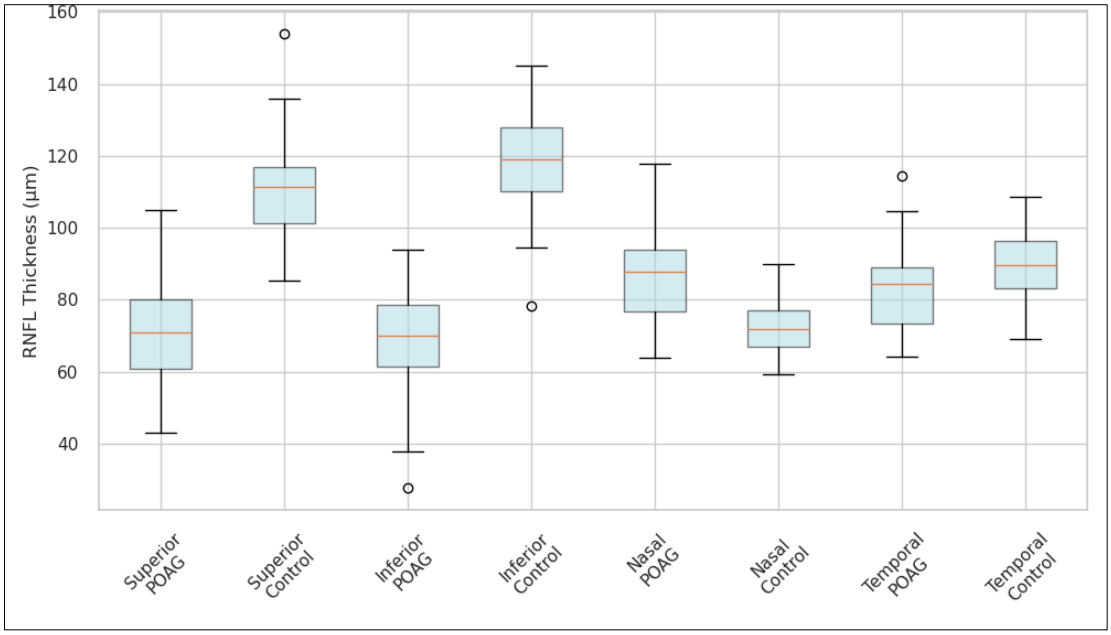

Fig 2A: ROC curves for diagnostic performance

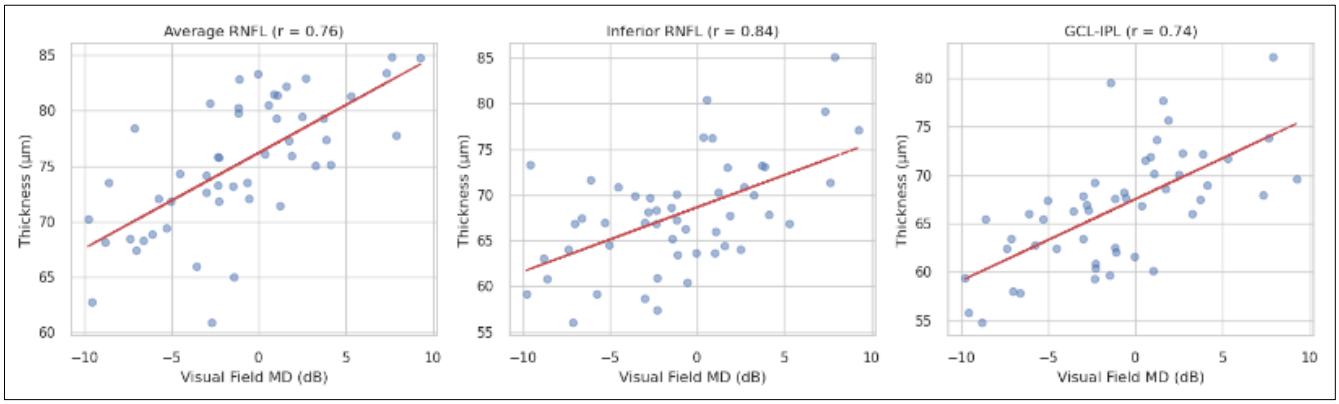

Fig 2B: Correlation between OCT parameters and visual field MD

Discussion

The present study demonstrates the significant value of SD-OCT in evaluating structural changes in primary open-angle glaucoma through quantitative assessment of both peripapillary RNFL and macular layer thickness. Our findings confirm substantial thinning of retinal structures in POAG patients compared to healthy controls, with excellent diagnostic performance and strong structure-function correlations [17].

The pattern of RNFL thinning observed in our study, with preferential involvement of the inferior and superior quadrants, aligns with the characteristic "double arcuate" pattern of glaucomatous damage described in the literature [18]. This pattern reflects the anatomical organization of retinal ganglion cell axons as they course toward the optic nerve head, with fibers from the superior and inferior macula being most vulnerable to glaucomatous damage. The preservation of nasal RNFL thickness, and in some cases apparent thickening, may be explained by the papillomacular bundle location and the different susceptibility of various nerve fiber populations to glaucomatous damage [19].

Our macular analysis results provide compelling evidence for the complementary role of GCL-IPL assessment in glaucoma evaluation. The significant reduction in macular GCL-IPL thickness observed in POAG patients (67.8±9.4 µm vs. 82.3±6.7 µm in controls) supports previous research suggesting that macular analysis can detect glaucomatous damage that may not be apparent with peripapillary RNFL analysis alone [20]. The macular region contains approximately 50% of all retinal ganglion cells, making it a critical area for detecting early glaucomatous changes. The advantage of macular analysis includes reduced measurement variability due to the absence of large blood vessels and more uniform tissue thickness compared to the peripapillary region [21].

The strong correlations observed between OCT parameters and visual field indices (r=0.72-0.84) underscore the clinical relevance of structural measurements in glaucoma management. These correlations are particularly important for monitoring disease progression, as structural changes often precede detectable functional deficits on standard automated perimetry [22]. The inferior RNFL quadrant showed the strongest correlation with visual field parameters, consistent with its known vulnerability in glaucoma and its correspondence to the superior visual field, where early defects commonly occur.

The diagnostic performance of SD-OCT parameters in our study, with AUC values of 0.92 for average RNFL thickness and 0.89 for macular GCL-IPL thickness, demonstrates excellent ability to distinguish between glaucomatous and healthy eyes. These results are consistent with meta-analyses reporting similar diagnostic accuracies for SD-OCT in glaucoma detection [23]. The high sensitivity and specificity values obtained suggest that SD-OCT can serve as a reliable adjunct to clinical examination and visual field testing in glaucoma diagnosis and monitoring.

Several limitations of our study should be acknowledged. The cross-sectional design limits our ability to assess disease progression over time, which is crucial for understanding the temporal relationship between structural and functional changes in glaucoma. Additionally, our study population consisted primarily of moderate to advanced glaucoma cases, which may have enhanced the observed differences between groups. Future longitudinal studies including patients with earlier stages of glaucoma would provide valuable insights into the sequence of structural changes and their relationship to disease progression.

The clinical implications of our findings are significant for glaucoma management. SD-OCT provides objective, quantitative measurements that can aid in early diagnosis, particularly in cases where visual field testing may be unreliable or unavailable. The technology's ability to detect structural changes before functional deficits become apparent makes it invaluable for identifying high-risk patients and initiating early treatment to prevent vision loss.

Furthermore, the excellent reproducibility of SD-OCT measurements makes it ideal for monitoring disease progression and treatment response. The quantitative nature of OCT data allows for precise tracking of changes over time, enabling clinicians to make informed decisions about treatment modifications. This is particularly important given the progressive nature of glaucoma and the need for lifelong monitoring and management.

Conclusion

This study confirms the significant value of spectral domain optical coherence tomography in evaluating structural changes associated with primary open-angle glaucoma. Both peripapillary retinal nerve fiber layer and macular layer thickness measurements demonstrate substantial differences between glaucomatous and healthy eyes, with excellent diagnostic performance and strong correlations with functional visual field parameters. The characteristic pattern of RNFL thinning, particularly in the inferior and superior quadrants, along with significant macular ganglion cell layer

and inner plexiform layer thinning, provides objective evidence of glaucomatous damage that complements traditional diagnostic methods.

SD-OCT technology offers several advantages including high resolution imaging, quantitative measurements, excellent reproducibility, and the ability to detect structural changes that may precede functional visual field defects. These findings support the integration of SD-OCT as a standard component of comprehensive glaucoma evaluation, enhancing our ability to diagnose the disease early, monitor progression accurately, and optimize patient management strategies. The strong structure-function relationships observed in this study further validate the clinical relevance of OCT measurements in glaucoma care.

Future research should focus on longitudinal studies to better understand the temporal progression of structural changes in glaucoma and their relationship to functional decline. Additionally, investigation of newer OCT technologies and analysis techniques may further enhance our ability to detect and monitor glaucomatous damage, ultimately improving patient outcomes through earlier detection and more precise monitoring of this sight-threatening disease.

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