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CORRELATION OF VISUAL FIELD CHANGES WITH OPTICAL COHERENCE TOMOGRAPHY IN PRIMARY OPEN ANGLE GLAUCOMA

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ABSTRACT

PURPOSE: To detect morphological changes in Optic Nerve Head (ONH), macula and Retinal nerve fibre layer (RNFL) using spectral domain optical coherence tomography (SDOCT) and to correlate them with functional loss (Visual field changes) using 24-2 and 10-2 standard automated perimetry in Primary open angle glaucoma patients.

RESULTS: Mean value of 90D cup to disc ratio (CDR) of study subjects was 0.64 ± 0.13 with median (25th-75th percentile) of 0.7(0.6-0.7). Mean value of average RNFL thickness(microns), superior quadrant thickness (micron), inferior quadrant thickness (micron), nasal quadrant thickness (micron) and temporal quadrant thickness (micron) of study subjects was 62.35 ± 14.43, 77.96 ± 14.29, 81.41 ± 22.84, 51.33 ± 21.14 and 50.71 ± 17.71 with median(25th-75th percentile) of 63(52-75), 78(66.25-89), 81.5(64.25-93.75), 54(46-63) and 50.5(39-57.75) respectively. Mean value of average macular thickness (micron), macular GCL-IPL thickness -Superior quadrant (micron) and macular GCL-IPL thickness -Inferior quadrant (micron) of study subjects was 65.6 ± 11.7, 76.49 ± 11.63 and 76.76 ± 16.86 with median (25th-75th percentile) of 64(56-75), 75(67-87.75) and 75.5(65.25-93) respectively.

Mean value of MD and PSD of study subjects was -7.34 ± 4.47 and 6.8 ± 3.11 with median (25th-75th percentile) of -7.65(-11--3.1) and 6.9(3.9-9.1) respectively. 57(41.3%) eyes had early glaucoma, 51(37%) eyes had moderate glaucoma and 30(21.7%) eyes had advanced glaucoma.

CONCLUSION: In present study, ONH parameters (rim area), RNFL parameter (inferior quadrant thickness) and macula parameters (average macular GCLIPL thickness) showed statistically significant correlation with VF MD. Correlation between VF parameters i.e. MD and PSD with OCT parameters shown that there was a relation between Macular GCLIPL thickness ,RNFL thickness and ONH with the changes in the results of VF.

KEYWORDS: Glaucoma, Perimetry, OCT, RNFL, Macular GCLIPL Thickness

INTRODUCTION

Glaucoma is a progressive optic neuropathy that causes atrophy of the optic nerve head (ONH), retinal ganglion cell (RGC) and distinctive visual field losses1. Primary open angle glaucoma (POAG) is perhaps the most common form of glaucoma. Early diagnosis depends on examination of the optic disc, retinal nerve fibre layer (RNFL) and visual fields (VF)1. Advanced glaucoma shows near total cupping of the optic nerve with or without severe visual field (VF) loss within 10 ° of fixation i.e. scotoma encroaching on or splitting fixation.

It is important to obtain a sufficient number of reliable visual field examinations in the early follow up to establish a good baseline and to rule out rapid progression. Standard automated perimetry (SAP) has been preferred method to evaluate the corresponding functional loss in glaucoma.2 Optical Coherence

Tomography (OCT) is a commonly used imaging technology in the evaluation of glaucomatous structural damage7. Optical Coherence Tomography (OCT) is a non-invasive optical technique that uses low coherence interferometry to obtain cross sectional imaging of the optic nerve head and inner retinal layer thickness at the macula3. Inner retinal layer thickness at the macula generally includes Retinal nerve fibre layer (RNFL), ganglion cell layer and the inner plexiform layer thickness (together called as ganglion cell complex, GCC). The use of Optical Coherence Tomography (OCT) for glaucoma diagnosis has become a common clinical practice and provides reliable quantitative data about Retinal nerve fibre layer (RNFL) and Optic Nerve Head (ONH) morphology3. With the advent of spectral domain Optical coherence tomography (SDOCT) another region that has been shown to demonstrate structural changes in glaucoma is macula.4

As the disease is treatable and because the visual impairment caused by primary open angle glaucoma is irreversible, early detection and monitoring of progression is essential. For the proper monitoring of progression of primary open angle glaucoma, rather than approaching anatomical damage simply, it is necessary to focus on the ongoing anatomical and functional relationship and evaluate structural and functional tests together.

In primary open angle glaucoma significant retinal ganglion cell damage can occur before standard tests detect a functional loss of vision. Considerable number of retinal ganglion cells can be lost before any defect in the standard automated perimetry.

With significantly improved scanning speed, image resolution, signal to noise ratio, spectral domain optical coherence tomography not only allow for more information from the biological tissues to be rapidly acquired and visualised at an early stage but also for easier detection of glaucomatous progression.

AIMS AND OBJECTIVE

To detect morphological changes in Optic Nerve Head (ONH), macula and Retinal nerve fibre layer (RNFL) using spectral domain optical coherence tomography (SDOCT) and to correlate them with functional loss (Visual field changes) using 24-2 and 10-2 standard automated perimetry in Primary open angle glaucoma patients.

MATERIALS AND METHODS

The was a prospective cross sectional non interventional study carried out in the outpatient department at tertiary care centre. Approval from institutional ethics committee was taken and all related information was explained in detail to patients. Informed written consent was taken from patients in a language understood by them. Those who were willing to participate were enrolled in the study. All the tests and investigations carried out in single visit. There were no follow up visits.

Sample size was 69 patients with total 138 eyes calculated by prevalence and using the formula $N= t^2 \times P(1-p)/m^2$

INCLUSION CRITERIA

1. Age ≥18 years
2. Best corrected visual acuity of 20/40 or better
3. Refractive error within ±5 diopters (D) sphere and ±3D cylinder.
4. Patient already diagnosed with Primary open angle glaucoma.
5. Advanced Glaucoma
6. VF changes diagnostic for glaucoma (either diffuse depressions of the Visual field or localized defects that conform to nerve fiber bundle patterns)
7. Clear media that do not interfere with OCT scan for Retinal nerve fibre layer (RNFL) assessment for optic disc analysis.
8. Open angle of the anterior chamber (by gonioscopy)

EXCLUSION CRITERIA

1. Any corneal or anterior segment pathology or media opacity that would preclude accurate intraocular pressure measurement or accurate field testing and clear media for OCT
2. Any retinal pathology and peripapillary chorioretinal disease
3. Errors of refraction of more than ±5D sphere and ±3D cylinder
4. Patient unwilling for OCT.
5. Pseudophakic patient in whom POAG was established preoperatively

All patients were subjected to following

1. Detailed history including personal data and any family history of glaucoma
2. Routine ophthalmologic examination including visual acuity with estimation of best corrected visual acuity and anterior segment and fundus examination.
3. Intraocular pressure measurement by Goldman Applanation tonometer
4. Gonioscopy was done using the contact Goldman 3 mirror lens.
5. Optic disc examination- using slit lamp biomicroscopy with noncontact 90D lens
6. Visual Field examination with 24-2 and 10-2 Standard Automated Perimetry
7. Spectral domain optical coherence tomography imaging with cirrus HDOCT
8. Fundus photo
   -central 30 degree
   -Red free for Retinal nerve fibre layer (RNFL)

The visual field examination was performed using Humphrey Field Analyzer, with Swedish interactive threshold algorithm (SITA) standard 24-2 and 10-2 program and mean deviation (MD) and pattern standard deviation (PSD) values on perimetry were recorded.In VF test when fixation losses were < 20 % and false positive and false negative errors were < 20 % ,the test was considered reliable. SDOCT was done for the measurement of ONH analysis, RNFL thickness and macular GCLIPL thickness.

The Visual field examinations and the SDOCT examination was done on the same day in all subjects.

Statistical analysis was done for structure –function associations between optic nerve head (ONH) parameters and perimetry, macula parameters and perimetry, Retinal nerve fibre layer (RNFL) parameters and perimertry.

On perimetry, according to Hodapp Parrish Anderson scale, glaucomatous damage was classified based on VF mean deviation (MD)

1. Glaucoma stage 1 (Early): VF MD< -6 dB
2. Glaucoma stage 2 (moderate): VF MD between -6 dB and -12 dB
3. Glaucoma stage 3 (severe): VF MD > -12 dB

Depending on severity of glaucoma, patients were divided into early, moderate and severe (advanced) groups.

STATISTICAL ANALYSIS

Statistical analysis was done for Spectral domain Optical coherence tomography parameters (optic nerve head, retinal nerve fibre layer, macula) and perimetry parameters (mean deviation, pattern standard deviation) in Primary open angle glaucoma patients and all Spectral domain Optical coherence Tomography parameters were correlated with perimetry parameters statistically.

OBSERVATION AND RESULTS

69 patients of age above 18 years diagnosed with Primary open angle glaucoma were included in the study. All patients were subjected to detailed ophthalmic history with ophthalmologic examination including intraocular pressure, gonioscopy, optic disc examination and visual field examination.

Both eyes of 69 patients-total 138 eyes were examined. Depending on the severity of glaucoma, patients were classified into early, moderate and advanced (severe) stages. (based on Hodapp,Parish and Anderson classification.) According to this classification 57(41.3%) eyes had early glaucoma, 51(37%) eyes had moderate glaucoma and 30(21.7%) eyes had advanced glaucoma.

The age group of patients ranged from 35 to 75 years with a mean of 58.03±10.4 years and a median of 59. 35(50.72%) patients were females and 34(49.28%) patients were males.

In majority [75(54.35%)] of patients, best corrected distant vision was 20/40 followed by 20/30 [44(31.88%)]. Best corrected distant vision was 20/25 in only 19 out of 138 patients (13.77%). In all patients, anterior segment showed no abnormalities.

Mean value of IOP with applanation (mmHg) of study subjects was 23.22 ± 3.6 with median (25th-75th percentile) of 24(20-26). In all 69 patients, gonioscopy showed open angles. Mean value of 90D cup to disc ratio (CDR) of study subjects was 0.64 ± 0.13 with median (25th-75th percentile) of 0.7(0.6-0.7). Mean value of central corneal thickness(µm) of study subjects was 535.9 ± 32.76 with median (25th-75th percentile) of 543(503.75-562).

Mean value of rim area (mm^2), disc area(mm^2), average cup disc ratio, vertical cup disc ratio (C/D) and cup volume data (mm^3) of study subjects was 0.9 ± 0.4, 2.24 ± 0.46, 0.72 ± 0.14, 0.71 ± 0.14 and 0.68 ± 0.31 with median (25th-75th percentile) of 0.8(0.66-1.02), 2.16(1.927-2.6), 0.74(0.652-0.81), 0.74(0.642-0.81) and 0.67(0.431-0.862) respectively. It is shown in table 1.

Mean value of average RNFL thickness(microns), superior quadrant thickness (micron), inferior quadrant thickness (micron), nasal quadrant thickness (micron) and temporal quadrant thickness (micron) of study subjects was 62.35 ± 14.43, 77.96 ± 14.29, 81.41 ± 22.84, 51.33 ± 21.14 and 50.71 ± 17.71 with median(25th-75th percentile) of 63(52-75), 78(66.25-89), 81.5(64.25-93.75), 54(46-63) and 50.5(39-57.75) respectively.

Mean value of average macular thickness (micron), macular GCL-IPL thickness -Superior quadrant (micron) and macular GCL-IPL thickness -Inferior quadrant (micron) of study subjects was 65.6 ± 11.7, 76.49 ± 11.63 and 76.76 ± 16.86 with median (25th-75th percentile) of 64(56-75), 75(67-87.75) and 75.5(65.25-93) respectively.

Mean value of MD and PSD of study subjects was -7.34 ± 4.47 and 6.8 ± 3.11 with median (25th-75th percentile) of -7.65(-11--3.1) and 6.9(3.9-9.1) respectively. It is shown in table 2.57(41.3%) eyes had early glaucoma, 51(37%) eyes had moderate glaucoma and 30(21.7%) eyes had advanced glaucoma.

Mean deviation (MD) on perimetry and ONH, RNFL, GCL-IPL parameters

Early glaucoma:

Significant positive correlation was seen between MD (mean deviation) with average macular thickness (micron) with correlation coefficient of 0.363. There was no/ nonsignificant correlation between MD and other parameters.

Moderate glaucoma:

Significant positive correlation was seen between MD with rim area (mm^2), inferior quadrant thickness (micron) with correlation coefficient of 0.286, 0.307 respectively. No/ nonsignificant correlation was seen between MD and other parameters.

Advanced glaucoma:

There was no/ non-significant correlation between MD and all optic nerve head, retinal nerve fibre and macula parameters.
It is shown in table 13.

Pattern standard deviation (PSD) and ONH, RNFL, GCL-IPL parameters

Early glaucoma:

Significant positive correlation was seen between PSD with temporal quadrant thickness (micron) with correlation coefficient of 0.267. Significant negative correlation was seen between PSD (pattern standard deviation) with rim area (mm^2), nasal quadrant thickness (micron) with correlation coefficient of -0.31, -0.265 respectively. No/ non-significant correlation was seen between PSD and all other parameters.

Moderate glaucoma:
Significant negative correlation was seen between PSD with temporal quadrant thickness (micron) with correlation coefficient of -0.281. No/ non-significant correlation was seen between PSD and other parameters.

Advanced glaucoma:
Significant positive correlation was seen between PSD with temporal quadrant thickness (micron), average macular thickness (micron) with correlation coefficient of 0.415, 0.386 respectively. No/ non-significant correlation was seen between PSD and other parameters except disc area(mm^2) which had a non-significant moderate negative correlation with correlation coefficient of -0.342.
It is shown in table 4 and figure 1 to 14.6.

DISCUSSION
This study was designed with the aim of correlating the ONH parameters and RNFL and macular GCL-IPL thickness with VF defects in POAG patients which helps in diagnosis and monitoring progression of POAG. In the present study OCT measured structural loss at the level of ONH, RNFL, macular GCLIPL while functional loss was measured by VF MD and VF PSD.

In our study, majority 37.68% patients belonged to age group 56-65 years with a mean value of 58.03 ± 10.4 years with median of 59. Study done by **Rao A et al [5]** demonstrated that mean age of the patients was 65 ± 34.3 years ranging between 41 to 99 years. Study done by **Gupta P et al [6]** demonstrated that mean age of the patients was 59.23 ± 9.56 years. In our study, 50.72% patients were females and 49.28% patients were males, showing slight female predominance. Study done by **Hamed MA et al [7]** included 15 (50%) male patients and 15 (50%) female patient showing gender equality. These are comparable to patients in the study by **Takagi et al [8]** Study done by **Gupta P et al [6]** demonstrated that 65% patients were males and 35% patients were females, male predominance.

In our study, mean value of IOP with AT(mmHg) of study subjects was 23.22 ± 3.6 with median of 24. Study done by **Gupta P et al [6]** demonstrated that mean value of IOP with AT(mmHg) of study subjects in early stage was was 19.94 ± 3.81, in moderate stage was 22.69 ± 5.2, in advanced stage was 24.55 ± 9.1 On SD-OCT, mean value of average RNFL thickness(microns) was 62.35 ± 14.43. Study done by **Rao A et al [5]** demonstrated that the average retinal nerve fiber layer (RNFL) thickness in early glaucoma cases was 100 ± 10.7 microns in POAG. Moderate glaucoma cases had an average RNFL thickness ranging from 72-75 microns.

Macular thickness can be affected in POAG due to RGCs damage as RGCs are prominently located in macular region. In our study, mean value of average macular GCIPL thickness (micron) was 65.6 ± 11.7, macular GCL-IPL thickness -Superior quadrant (micron) was 76.49 ± 11.63 and macular GCL-IPL thickness -Inferior quadrant (micron) of study subjects was, 76.76 ± 16.86 with median of 64, 75 and 75.5 respectively.

In our study, mean value of MD (mean deviation) and PSD (pattern standard deviation) of study subjects was -7.34 ± 4.47 and 6.8 ± 3.11 with median of -7.65 and 6.9 respectively.

In early stage of disease, significant positive correlation was seen between mean deviation with average macular GCIPL thickness with correlation coefficient of 0.363. In moderate stage of disease, significant positive correlation was seen between mean deviation with rim area, RNFL inferior quadrant thickness with correlation coefficient of 0.286, 0.307 respectively. No/ non significant correlation was seen between mean deviation with other ONH, RNFL, GCL-IPL parameters in early and moderate stages. In advanced stage of disease no/ non-significant correlation was seen between mean deviation with ONH, RNFL and GCL-IPL parameters. Study done by Choi et al, fou99nd statistical significance of macular GCL-IPL with MD in early and moderate glaucoma. It also showed that average and inferior RNFL thickness had significant correlation with disease severity assessed by MD in early and moderate glaucoma. Our results are comparable with this study. The structural damage in glaucoma occurs primarily in the RGC and these cells are predominantly located in the macula, so there is significant correlation between structural change in the macular GCL-IPL thickness with functional loss in VF in early glaucomatous eyes. Cho et al. Demonstrated a significant correlation between GCL measurements and VF indicating GCL measurements are closely associated with functional loss. In our study significant positive correlation was demonstrated between average macular GCLIPL measurements and VF MD in early glaucoma.

Considering pattern standard deviation (PSD), in early stage of disease, significant positive correlation was seen between pattern standard deviation and RNFL temporal quadrant thickness with correlation coefficient of 0.267. Significant negative correlation was seen between pattern standard deviation with rim area, nasal quadrant thickness with correlation coefficient of -0.31, -0.265 respectively. In moderate stage of disease, significant negative correlation was seen between PSD with temporal quadrant thickness with correlation coefficient of -0.281. In advances stage of disease, significant positive correlation was seen between pattern standard deviation with temporal quadrant thickness, average macular GCLIPL thickness with correlation coefficient of 0.415, 0.386 respectively. No/ non-significant correlation was seen between PSD with other ONH, RNFL and GCL-IPL parameters.

Study done by **Gupta P et al [6]** demonstrated that both peripapillary RNFL and macular GCLIPL thickness showed statistically significant correlation with VF MD. In the early stage of glaucoma, inferior peripapillary RNFL thickness was significantly correlating with VF MD. In the moderate stage, superior peripapillary RNFL thickness followed by superior GCL-IPL thickness was significantly correlating with the MD and in the advanced stage superior macular GCL-IPL was thicker than inferior macular GCL-IPL. Thus, both peripapillary RNFL and macular GCL-IPL thicknesses should be assessed along with VF defects to monitor the severity of the disease.

Study done by **Hamed MA et al [7]** demonstrated that There was also a significant relation between age and retinal thickness. RNFLT is known to decrease with age. This finding was similar to the findings reported by **Alamouti and Funk et al [9]** who also found that both total retinal thickness and the nerve fiber layer thickness significantly decreased with age. Sex was not related to RNFLT in the study which was also shown by **Spry et al [10].**

Contrary to these results, the study by **Harwerth et al [11]** has shown that RNFL thickness may be a more sensitive measurement for early stages and perimetry a better measure for moderate to advanced stages of glaucoma.

CONCLUSION

In present study, ONH parameters (rim area), RNFL parameter (inferior quadrant thickness) and macula parameters (average macular GCLIPL thickness) showed statistically significant correlation with VF MD. Correlation between VF parameters i.e. MD and PSD with OCT parameters shown that there was a relation between Macular GCLIPL thickness ,RNFL thickness and ONH with the changes in the results of VF.

Thus, structural and functional analysis is important for monitoring the severity of the POAG and any advance in the diseases can be prevented. OCT is an important tool which provides objective data regarding RNFL thickness, macular GCLIPL thickness and ONH parameters which could aid in glaucoma diagnosis.

Optic Nerve Head Analysis	**Mean ± SD**	**Median(25th-75th percentile)**	**Range**
Rim area (mm²)	0.9 ± 0.4	0.8(0.66-1.02)	0.3-2.34
Disc area(mm²)	2.24 ± 0.46	2.16(1.927-2.6)	1.47-3.41
Average cup disc ratio	0.72 ± 0.14	0.74(0.652-0.81)	0.19-0.92
Vertical cup disc ratio (C/D)	0.71 ± 0.14	0.74(0.642-0.81)	0.25-0.92
Cup volume data (mm³)	0.68 ± 0.31	0.67(0.431-0.862)	0.01-1.33

Table 1: Descriptive statistics of Optic Nerve Head Analysis of study subjects.

Perimetry	**Mean ± SD**	**Median(25th-75th percentile)**	**Range**
MD (mean deviation)	-7.34 ± 4.47	-7.65(-11--3.1)	-15.6--0.1
PSD (pattern standard deviation)	6.8 ± 3.11	6.9(3.9-9.1)	1.5-12.8

Table 2: Descriptive statistics of perimetry of study subjects.

Variables	Early		Moderate		Advanced	
	r	p value	r	p value	r	p value
Optic Nerve Head Analysis						
Rim area (mm²)	0.025	0.855	0.286	0.042	-0.05	0.791
Disc area(mm²)	0.118	0.382	0.066	0.642	0.128	0.499
Average cup disc ratio	0.050	0.714	0.089	0.536	0.023	0.905
Vertical cup disc ratio (C/D)	0.008	0.952	0.116	0.416	-0.011	0.956
Cup volume data (mm³)	0.178	0.184	0.040	0.779	0.051	0.788
Retinal nerve fibre layer thickness(microns)						
Average RNFL thickness(microns)	-0.043	0.749	0.217	0.126	-0.326	0.079
Superior quadrant thickness (micron)	-0.176	0.191	0.062	0.663	-0.094	0.620
Inferior quadrant thickness (micron)	-0.086	0.524	0.307	0.029	0.102	0.589
Nasal quadrant thickness (micron)	0.047	0.730	-0.146	0.306	0.017	0.931
Temporal quadrant thickness (micron)	-0.198	0.140	-0.187	0.188	-0.031	0.870
Macula parameters						
Average macular GCLIPL thickness (micron)	0.363	0.006	-0.001	0.997	-0.009	0.964
Macular GCL-IPL thickness -Superior quadrant (micron)	0.105	0.435	0.088	0.539	0.224	0.232
Macular GCL-IPL thickness -Inferior quadrant (micron)	-0.096	0.475	0.002	0.990	0.144	0.446

Table 3: Correlation of mean deviation and Optic Nerve Head Analysis, retinal nerve fibre layer thickness(microns) and macula parameters.

Variables	Early		Moderate		Advanced	
	r	p value	r	p value	r	p value
Optic Nerve Head Analysis						
Rim area (mm²)	-0.310	0.019	-0.011	0.940	0.08	0.674
Disc area(mm²)	0.066	0.625	0.233	0.100	-0.342	0.065
Average cup disc ratio	-0.006	0.966	0.016	0.914	0.009	0.962
Vertical cup disc ratio (C/D)	0.108	0.425	0.129	0.365	0.109	0.564
Cup volume data (mm³)	-0.036	0.790	0.058	0.684	-0.143	0.448
Retinal nerve fibre layer thickness(microns)						
Average RNFL thickness(microns)	0.099	0.462	-0.239	0.092	0.154	0.416
Superior quadrant thickness (micron)	0.162	0.229	-0.080	0.574	0.099	0.603
Inferior quadrant thickness (micron)	-0.004	0.978	-0.035	0.808	-0.015	0.936
Nasal quadrant thickness (micron)	-0.265	0.046	-0.198	0.162	-0.123	0.517
Temporal quadrant thickness (micron)	0.267	0.045	-0.281	0.046	0.415	0.023
Macula parameters						
Average macular thickness (micron)	-0.067	0.622	0.040	0.778	0.386	0.036

Macular GCL-IPL thickness -Superior quadrant (micron)	-0.074	0.581	-0.149	0.295	0.049	0.796
Macular GCL-IPL thickness -Inferior quadrant (micron)	-0.099	0.463	0.134	0.348	-0.1	0.597

Table 4:- Correlation of PSD (pattern standard deviation) and Optic Nerve Head Analysis, retinal nerve fibre layer thickness(microns) and macula parameters.

Spearman rank correlation coefficient

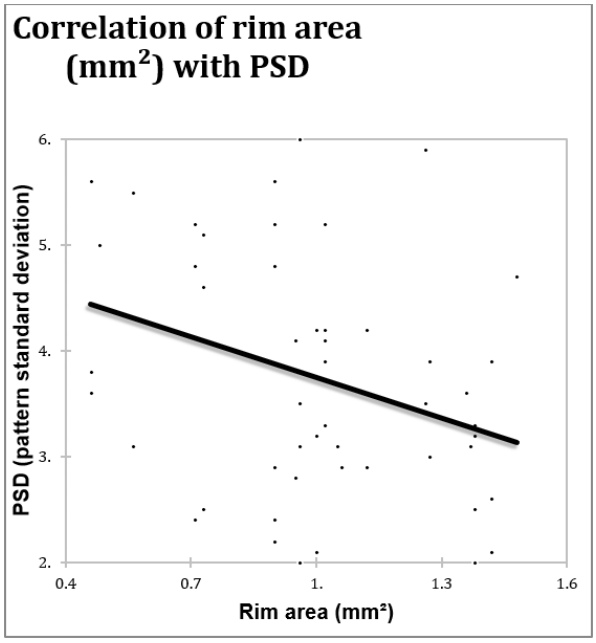

Figure 1: Correlation of rim area (mm²) with PSD (early glaucoma)

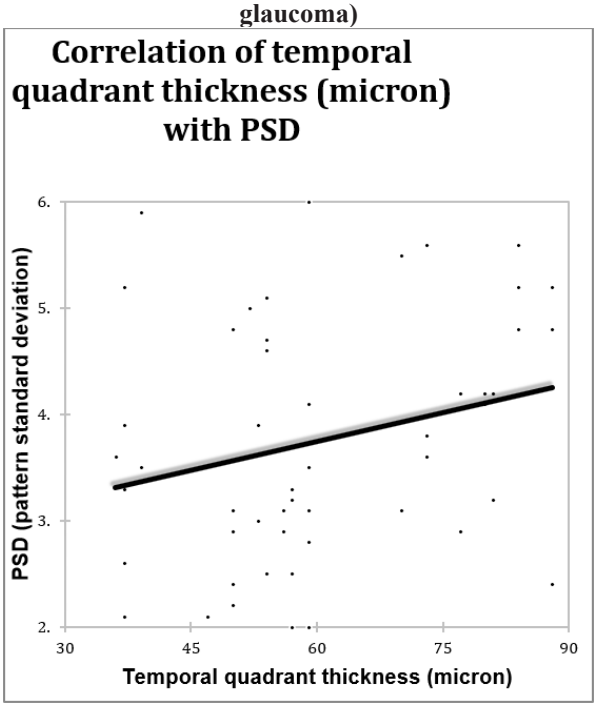

Figure 2: Correlation of temporal quadrant thickness (micron) with PSD (early glaucoma)

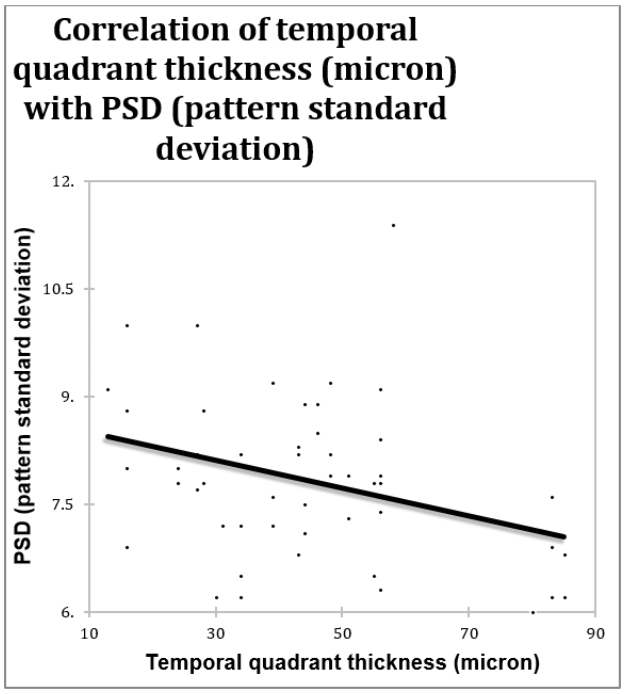

Figure 3: Correlation of temporal quadrant thickness (micron) with PSD (moderate glaucoma)

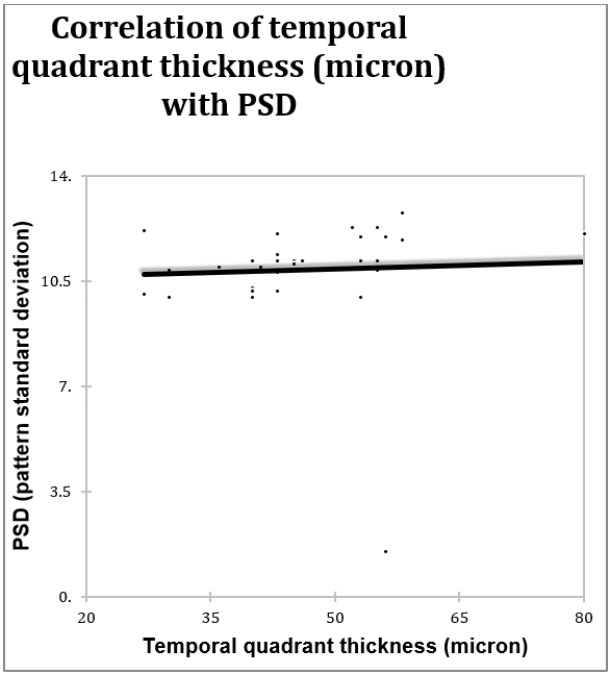

Figure 4: Correlation of temporal quadrant thickness (micron) with PSD (advanced glaucoma)

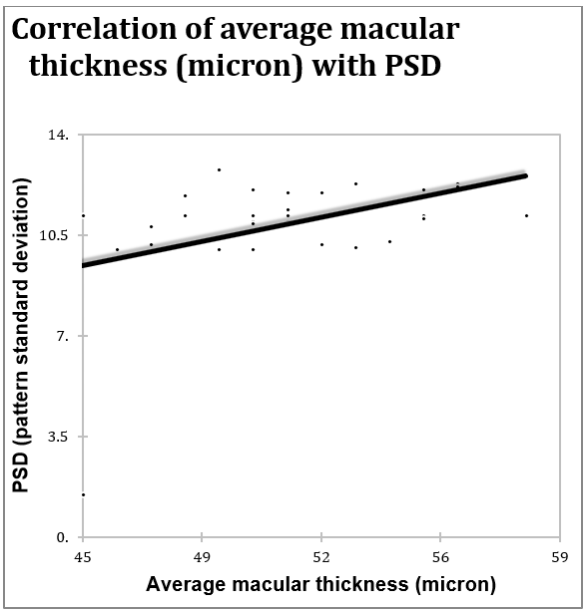

Figure 14.6: Correlation of average macular thickness (micron) with PSD (advanced glaucoma)

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