

## Relationship between peripapillary retinal nerve fiber layer and visual field severity indices in primary open angle glaucoma

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### Abstract:

**Background:** Optical Coherence Tomography (OCT) and visual field (VF) are devices for diagnosis and management of glaucoma. Using both techniques enable us to detect the functional and anatomical changes occur in glaucomatous eyes. Objectives: In this study, we aimed to determine the relationship between optical coherence tomography (OCT) parameters and visual field severity indices computed by standard automated perimetry (SAP) in patients with primary open angle glaucoma and to know the correlation between OCT disc parameter and ganglion cell layer (GCL).

**Methods:** The study included 94 subjects (160 eyes) divided into two groups. **Group 1** included 54 subjects with primary open angle glaucoma (cases) (92 eyes) **Group 2** included 40 healthy non-glaucomatous subjects (controls) (68eyes).OCT disc & macula and VF using standardised automated perimetry were performed for all participants in both groups. Correlations between OCT parameters and VF parameters and between OCT disc parameters and GCL were detected. Area under curve (AUC) was used to detect most important factor to differentiate cases from control. Results: We found strong correlations between MD and each of total , Inferior , Superior p RNFL respectively , PSD is moderately correlated with total ,inferior and superior p RNFL and vertical CDR respectively ,Inferior p RNFL is strongly correlated to inferior GCLcomplex. Regarding the "area under curve (AUC)" : the most important factors to differentiate cases from control are in order: total GCC, followed by inferior GCC, then total p .RNFL.

**Conclusion :** macular scans may be a good alternative to p. RNFL thickness assessment for the detection of glaucoma, we should perform VF test with both macular and p.RNFL scanning in all subjects suspected or known to have glaucoma for better and earlier diagnosis as they improve the sensitivity of glaucoma detection.

**Key words:** OCT, VF ,Glaucoma , macular ganglion cell layer.

### Introduction:

The role of imaging in glaucoma management has significantly increased in recent years, the major development in ophthalmic imaging was the introduction of optical coherence tomography (OCT) in 1991, by Huang et al.<sup>1</sup>

It is a non-invasive cross-sectional imaging technique that allows for high-resolution close to an in-vivo 'optical biopsy' of the retina.

Different scanning modalities:

Peripapillary scan, Optic Nerve Head scan and Macular ganglion cell layers scan.

Visual field test: each point in the VF reflects the visual characteristics of the corresponding point in the retina. It records visual function at each retinal location qualitatively and semi-quantitatively by measuring the weakest perceptible light spot.<sup>2</sup>

Global Indices include:

- Mean Deviation (MD): Derived from the Total Deviation and represents the overall mean departure from the age-corrected norm. A negative value indicates field loss, while a positive value indicates that the field is above average. A P value is provided if the global indices are abnormal. It provides a statistical representation of the population. For example, P <2% means that less than 2% of the population have vision loss worse than measured.<sup>3</sup>
- Pattern Standard Deviation (PSD): Derived from the Pattern Deviation and thus highlights focal loss only. A high PSD, indicating irregular vision, is therefore a more useful indicator of glaucomatous progression, than the MD.<sup>4</sup>

In our study we aimed to determine the relationship between optical coherence tomography (OCT) parameters and visual field severity indices computed by standard automated perimetry (SAP) in patients with primary open angle glaucoma, to know the correlation between OCT disc parameter and ganglion cell layer (GCL) and to know the most important factor to differentiate cases from control.

#### **Subjects and Methods:**

The study included 94 subjects (160 eyes) divided into two groups:

**Group 1** included 54 subjects with primary open angle glaucoma (cases) (92 eyes) with glaucomatous visual field defects and/or evidence of glaucomatous optic neuropathy (GON).

**Group 2** included 40 healthy non-glaucomatous subjects (controls) (68eyes) without visual field damage or other suspicious findings for the disease as a control

All data were collected between March 2016 and march 2017 at Sohag Ophthalmology Investigative Center.

All participants were informed about the tests that were be done to them. Approval from ethical committee of Sohag Faculty of Medicine was obtained.

#### **Group 1(cases):**

**Inclusion criteria :**

Patients (age 18-70 years old ) ,use of anti- glaucomatous medications is permitted.

We take in consideration that all participants had good-quality scans obtained by OCT, good-quality SAP performed within 1 month from OCT imaging.

**Exclusion criteria:**

- 1-Subjects with history of ocular trauma or laser treatment .
- 2.All subjects with diabetes more than 10 years and /or with significant diabetic retinopathy
- 3.Any disease or medication affecting the VF or RNFL

#### **Group 2(controls ):**

All eyes included were having no history of increased IOP, normal SAP result and normal appearance of ONH.

All participants were subjected to:

**1-Full history** taking regarding age, family history ,use of anti-glaucomatous treatment and its duration ,presence of diabetes and its duration.

**2-Comprehensive ophthalmological examination** including best corrected visual acuity (BCVA) , intraocular pressure (IOP)measurement, slit lamp biomicroscopy , gonioscopy, and fundus examination .

**3-Functional and structural evaluation** by standard automated perimetry (SAP) (Humphrey field analyzer 745i) to calculate glaucoma VF severity indices and SD-OCT (Topcon 3D OCT-1 Maestro machine 2000) to detect the average and quadrants peripapillary retinal nerve fiber thickness , optic nerve head and ganglion cells

**Results**

Correlation coefficient between VF severity indices and OCT parameters among glaucoma patients table (1):

There were strong correlations between MD and each of total , Inferior , Superior p RNFL respectively (p <0.001) also there is moderate correlation between MD and each of superior and total GCC, superior m RNFL , total GCL\IPL ,total m RNFL , superior and inferior GCL \IPL, inferior GCC, nasal and temporal p RNFL , inferior m RNFL, vertical and linear CDR, cup area , C\D ratio respectively (p <0.001).

PSD is moderately correlated with total ,inferior and superior p RNFL and vertical CDR respectively (p <0.001) , also there is moderate correlation between PSD and total GCL\IPL ,nasal p RNFL ,total GCC, inferior and superior GCL\IPL ,inferior and superior GCC respectively (p <0.001).

*Correlation between OCT disc parameters and GCL parameters :*

Inferior p RNFL is strongly correlated to inferior GCL++, followed by total GCL++ , then inferior GCL+ respectively (p <0.001).

*ROC Curve analysis of OCT parameters to differentiate cases from controls :*

Regarding the "area under curve (AUC)", table (2): the most important factors to differentiate cases from control are in order: total GCC, followed by inferior GCC, then total p .RNFL and total m. RNFL.

**Tables**

**Table (1).**Correlation between VF severity indices and OCT parameters among glaucoma cases

	Mean deviation		PSD (Pattern SD)	
	r	p	r	P
Total average p.RNFL	0.715	<0.001	-0.504	<0.001
Inferior p.RNFL	0.685	<0.001	-0.536	<0.001
Superior p.RNFL	0.681	<0.001	-0.458	<0.001
Nasal p.RNFL	0.580	<0.001	-0.389	<0.001
Temporal. p.RNFL	0.567	<0.001	-0.343	0.001
Disc area	0.215	0.035	0.207	0.043
Cup area	0.443	<0.001	0.321	0.001
Rim area	0.296	0.003	-0.152	0.139
C/D area ratio	0.421	<0.001	0.283	0.005
Linear CDR	0.451	<0.001	0.321	0.001
Vertical CDR	0.479	<0.001	0.400	<0.001
Cupvolume	0.307	0.002	0.156	0.130
Rim volume	0.283	0.005	-0.149	0.147
Horizontal DD	0.211	0.039	0.147	0.152
Vertical DD	0.114	0.269	0.122	0.235
Superior m.RNFL	0.641	<0.001	-0.226	0.027
Inferior m.RNFL	0.519	<0.001	-0.312	0.002
Total m.RNFL	0.621	<0.001	-0.307	0.002
Superior GCL+	0.598	<0.001	-0.366	<0.001
Inferior GCL+	0.585	<0.001	-0.376	<0.001
Total GCL+	0.624	<0.001	-0.390	<0.001
Superior GCL++	0.664	<0.001	-0.345	0.001
Inferior GCL++	0.593	<0.001	-0.357	<0.001
Total GCL++	0.663	<0.001	-0.378	<0.001

**Table (2)** show AUC to differentiate cases from controls

Test Result Variable(s)	Area	Std. Error	P value	Asymptotic 95% Confidence Interval	
				Lower Bound	Upper Bound
Total average p.RNFL	0.810	0.034	<0.001	0.750	0.870
Inferior p.RNFL	0.701	0.038	0.001	0.665	0.737
Superior p.RNFL	0.735	0.032	<0.001	0.688	0.782
Nasal p.RNFL	0.683	0.038	0.005	0.630	0.736
Temporal. p.RNFL	0.671	0.035	0.008	0.626	0.716

Disc area	0.534	0.046	0.559	0.484	0.584
Cup area	0.630	0.041	0.015	0.590	0.670
Rim area	0.680	0.033	0.006	0.620	0.740
C/D area ratio	0.686	0.036	0.001	0.625	0.747
Linear CDR	0.689	0.036	0.001	0.630	0.748
Vertical CDR	0.669	0.038	0.003	0.670	0.845
Cup volume	0.690	0.036	0.001	0.730	0.750
Rim volume	0.645	0.031	0.018	0.602	0.688
Horizontal DD	0.480	0.046	0.730	0.450	0.510
Vertical DD	0.547	0.045	0.382	0.500	0.594

Superior m.RNFL	0.721	0.041	<0.001	0.689	0.753
Inferior m.RNFL	0.811	0.033	<0.001	0.752	0.870
Total m.RNFL	0.813	0.036	<0.001	0.753	0.873

Superior GCL+	0.748	0.035	<0.001	0.699	0.797
Inferior GCL+	0.793	0.034	<0.001	0.722	0.864
Total GCL+	0.790	0.034	<0.001	0.715	0.865

Superior GCL++	0.788	0.037	<0.001	0.719	0.859
Inferior GCL++	0.864	0.032	<0.001	0.817	0.911
Total GCL++	0.876	0.030	<0.001	0.827	0.925

**Discussion:**

In this study we correlate OCT parameters (ONH, RNFL, GCC) with VF severity indices (MD, PSD). Strong correlation between MD and peripapillary RNFL was identified and moderate correlation between PSD and peripapillary RNFL.

In many studies in the past, a moderate correlation was identified between the peripapillary RNFL thicknesses measured by SD OCT and the glaucoma VF severity (MD, PSD) as in the study of Kang EM ,et al.<sup>5</sup> the absolute values of the correlation coefficients for the average RNFL thickness with MD and PSD were just greater than 0.5 ( they were 0.562 and -0.514 respectively ). This may have been due to the severity of glaucomatous damage as in our study the mean MD was -10.2 d B, while in Kang EM ,et al study the mean MD was 7- d B.

In our study, The largest *r* value were between MD and the average RNFL

thickness (0.715). Among the quadrants, the inferior p RNFL showed the largest *r* value (0.685) followed by superior p RNFL(0.681).

That is agreed with Kang EM ,et al study in which the largest *r* value were between MD and the average RNFL thickness (0.562) and Among the quadrants, the inferior RNFL thickness showed the largest *r* value (0.587).<sup>5</sup> And also this is in agreement with Carolina P.B., et al study. Other previous studies demonstrating that the superior and inferior areas of the optic nerve are most commonly affected in glaucoma.<sup>6,7</sup> But it should be noted that, while sectorial RNFL parameters may increase the chance of detecting localized RNFL damage in glaucoma, these parameters frequently suffer from low reproducibility, as measurements are averaged over only relatively small areas<sup>8,9</sup>

On the other hand, the global average RNFL thickness has generally been

shown to be the most reproducible parameter, which is not surprising considering that its calculation involves averaging measurements over a relatively large area. The improved reproducibility offers large gains in the ability to detect progression over time.<sup>8</sup> Several studies have shown that macular parameters are able to distinguish glaucomatous eyes from those of healthy subjects.<sup>10,11</sup>

In our study, moderate correlation between MD and thickness of ganglion cell layer /inner plexiform, m RNFL and GCC. This agrees with previous studies by Hood et al.<sup>12</sup>

Using regression analysis, the study found that Inferior p RNFL is the most predictable factor for glaucoma (0.966 & p <0.001) with comparable values with inferior ganglion cell complex (0.920 & p <0.001).

That support that p RNFL is slightly more reproducible than macular parameters but results are comparable with agreement with Libosa, et al study.<sup>13</sup> Kim *et al.* study<sup>10</sup> found that RNFL and GCC thickness had a similar diagnostic performance in detecting early, moderate and advanced glaucoma.

Our study found high correlation between inferior p RNFL with inferior GCC, total GCC and total GCL/IPL (0.559, 0.551, 0.541) with p <0.001, this agree with Gadi Wollstein et al. study which found that macular retinal thickness, as measured by OCT, was capable of detecting glaucomatous damage and corresponded with p RNFL thickness; however, p RNFL thickness had higher sensitivity and specificity for the detection of VF abnormalities.

Our study revealed that the total GCC thickness with largest AUC within the macular parameters, performed better than total p. RNFL with the largest AUC within the p. RNFL parameters and also both

performed significantly better than ONH parameter with the largest AUC, C/D area ratio, for differentiating between the glaucomatous and healthy eyes. The total GCC parameter represents m.RNFL + GC/IPL parameters. In agreement with our results; Lisboa et al.,<sup>13</sup> using RTVue OCT, found that both total p.RNFL and GCC averages performed better than the ONH parameter with largest AUC

However in contrast with our results; their study found that the p.RNFL parameter with largest AUC, total p.RNFL thickness, performed significantly better than the macular parameter with largest AUC, GCC average thickness, for differentiating between the preperimetric glaucoma and control groups.

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