

Estimation of the Absolute Defects in the Visual Field using OCT in Glaucoma Patients who Cannot Perform a Reliable Test.

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Research article

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Abstract

Background: To find a method to predict the visual field (VF) of glaucoma patients who cannot perform a reliable test by using RNFL thickness and VF of other glaucoma patients.

Methods: Seventy eight primary open angle and pseudoexfoliation glaucoma follow-up patients were included in the study. Optic disc OCT measurements and VF analysis were obtained in the same day. Garway-Heats maps made, RNFL sectors matched with pattern deviation 24-2 VF sectors and absolute defects were counted. Regression analysis were made. Equations generated between RNFL thickness and absolute defect number. Correlation analysis were performed for the numbers of absolute defects and the findings.

Results: The regression analysis was significantly linear for defect number and RNFL thickness in sectors 3, 4, and 6 (t values were 0.047, 0.04, and 0.001, respectively, $p < 0.05$). The analysis was nonlinear in other sectors (t values were 1.66, 0.37, 0.14, 0.88, and 0.36, respectively, for sectors 1, 2, 5, 7, and 8, $p > 0.05$). The linear and nonlinear equations were generated for these sectors. The correlation between the number of absolute defects of the patient and the number we found by using our formulas in VF Sectors of 1,3,4 and 8 there was a strong correlation ($r=0.68$, $r=0.57$, $r=0.82$ and $r=0.58$ respectively). In VF sectors 3,5,6 and 7 there was a weak correlation ($r= 0.22$, $r= 0.47$, $r=0.32$ and $r=0.48$ respectively).

Conclusion: We think the method that we found is practical to predict the VF of a patient who can not perform it.

Background

Glaucoma is a progressive optic neuropathy that causes a loss of retinal ganglion cells [1]. The diagnosis of glaucoma and the staging of the disease require quantification by ophthalmic examination. [2] Standard automated perimetry is the gold standard for evaluating visual field (VF) sensitivity as a functional test. But the test duration is long in Full Threshold and even more in glaucoma patients [3]. Therefore, there is an inclination to use OCT more in glaucoma diagnosis and follow-up [4]. Although improvements in diagnostic techniques and also studies such as using artificial intelligence in OCT [5], assessment of the visual field is still crucial. Tripping over, bumping into objects driving disabilities related significantly with the loss of binocular visual field in glaucoma and effects the quality of life [6] But the learning effect may take a long time and can sometimes be challenging, especially in elderly people and those with a low education level [7], resulting in overestimation of the VF. Sometimes, a significant test may not be obtained because of the patient's mental state or physical problems. We need a method to assess the VF of these glaucoma patients. As ganglion cell loss is the main pathology in glaucoma, optical coherence tomography (OCT) detects this structural change [8]. Garway-Heath maps correlate structural and functional changes and automated perimetry field regions to the corresponding retinal nerve fiber layer (RNFL) sectors [9]. This model has been validated in previous studies [10, 11]. Thus, the following question is raised: Can we predict the VF of patients with unreliable results by using

OCT? Regression analysis is a powerful statistical method that allows us to examine the relationship between two or more variables [12]. If there is a correspondence between the ganglion cell loss and defects in VF, the number of absolute defects must be correlated with the lost RNFL thickness of the optic nerve head sector. By using RNFL thickness one of the variables and the number of absolute defects in corresponding VF area as the other variable, we may generate a mathematical method for the prediction. In this study we aimed to find this method using the OCT and reliable VF tests of glaucoma patients. We did not meet a study in medical indexes that predicts the absolute defects using OCT.

Methods

We conducted a retrospective review of patients who were being followed up in our glaucoma clinic between January 1, 2011, and November 28, 2016. Our study was approved by the local ethical committee and adhered to the tenets of the Declaration of Helsinki. Seventy-eight glaucoma patients were included in the study.

All participants were 18 years or older. Media opacities that could affect RNFL measurements, including corneal scars, posterior subcapsular cataracts, anterior segment dysgenesis, history of diabetic retinopathy, visual acuity worse than 20/40, and refractive error outside the -6 D to $+6$ D range, comprised the exclusion criteria. Patients with retinal, choroidal, or other optic nerve pathologies, demyelinating diseases and intracranial tumors affecting the VF were also excluded. Our subjects were diagnosed as primary open angle glaucoma or pseudoexfoliation glaucoma. They were all under topical anti glaucomatous treatment. No one of them were treated surgically. Diagnosis criteria for glaucoma were suspicious optic nerve head with borderline hemifield VT result or abnormal hemifield VF test with abnormal OCT with or without elevated intraocular pressure. An abnormal visual field result was defined as having a pattern standard deviation outside the 95% confidence limits or a glaucoma hemifield test (GHT) result outside the reference range on the Swedish interactive threshold algorithm (SITA Standard 24 - 2) of the Humphrey visual field analyzer (Carl Zeiss Meditech, Inc., Dublin, California, USA) [13, 14]. Suspicious disc means that the optic disc with cup/disc asymmetry or bilateral wide cups and thin rims [15].

Optical Coherence Tomography

OCT measurements were performed using Cirrus -HD 5000 OCT (Carl Zeiss Meditech, Dublin, California). The scan rate of the device is 26,000 A scans per second with an axial resolution of 5 μ m. Optic nerve head analysis was performed for all patients. The software outputs discrete RNFL thicknesses for each clock-hour position for the right eyes and the opposite for the left eyes. A signal strength greater than or equal to 6/10 was accepted for the study. The images were obtained by the same technician. RNFL thicknesses criteria was database range at the 1% level (outside normal limits) [16]

VF Analysis

Tests were performed using the Humphrey 750i (Carl Zeiss Meditech, Dublin, California) Swedish Interactive Threshold Algorithm 24 - 2 test. The tests were grouped into early, moderate, and severe glaucoma defects as described by the Hodapp-Parish-Anderson classification. All tests were performed by the same technician.

Garway-Heath maps were created with OCT sectors and the VF pattern deviation map for each patient. Yanagisawa and colleagues [17] named the 12 OCT sectors as S, ST, TS, T, TI, IT, I, IN, NI, N, NS, and SN in the clockwise direction for the left eye. They matched these sectors in the VF and showed them the colored squares. By using this method, we gave numbers for each OCT sectors from 1 to 12 and matched them in the VF (Fig. 1).

We applied the same in the counterclockwise direction for the right eyes.

Statistical Analysis

First, we wanted to find any correlation between sector RNFL thickness and the number of absolute defects in the matched VF region. Thus, we used correlation analysis. To generate an equation for the defect amount for every OCT sector, we first used linear regression analysis. Correlation analysis was applied for the number of absolute defects we found by using our formulas and the number of the defects of the same patients' corresponding RNFL sectors' matched VF location.

Correlation and linear regression analysis were performed using SPSS version 16 software (IBM, Armonk, NY, USA). If the t value calculated by the software was significant, we generated the regression equation by using the parameters calculated by the software. The linear regression equation is shown as

$$y = a + bx$$

If was not significant we used exponential function method to generate non-linear equation described by Marquart [11]

The non- linear exponential equation is shown as

$$y = ae^{bx}$$

where y represents the number of absolute defects and x is the value of the RNFL at the sector, e is equal 2,71, a and b are constants.

Results

The mean age of the patients was 62.41 ± 12.57 years. Forty-five patients were male, and 33 were female. We showed the mean RNFL thicknesses in four quadrants. The mean thickness of the superior quadrant was $66,62 \pm 15,61$ microns, the mean thickness temporal quadrant was $48,43 \pm 13,34$, inferior quadrant was $64,31 \pm 11,46$, and nasal quadrant was $51,32 \pm 13,32$ microns. Most of our patients were in moderate

Loading [MathJax]/jax/output/CommonHTML/fonts/TeX/fontdata.js number of patients in different stages grouped by

using their VFs. This may be the reason of low level of RNFL thicknesses. In mild defect group the patients were using topically prostaglandin analogues or brinzolamide alone, in moderate defect group 25 patients were using prostaglandin analogues and betablocker + carbonyl anhydrase inhibitors combination both and the others were using one of them alone. In advanced group patients were using two or three medicine combinations. The maximum average RNFL thickness was measured as 83µm. The relation between defect number and RNFL thickness was found to be significantly linear in sectors 3, 4, and 6 but was nonlinear in other sectors. The generated equations are shown in Table 2. We evaluated the correlation between the number of absolute defects of the patient and the number we found by using our formulas. In VF Sectors of 1,3,4 and 8 there was a strong correlation ($r = 0.68$, $r = 0.57$, $r = 0.82$ and $r = 0.58$ respectively). In VF sectors 3,5,6 and 7 there was a weak correlation ($r = 0.22$, $r = 0.47$, $r = 0.32$ and $r = 0.48$ respectively).

Table 1
Visual defects classified by using Hodap-Parish-Anderson staging criteria and the mean MD values of them.

	Mild Defect	Moderate Defect	Advanced Defect
Number of Patient	21	37	20
Mean MD (dB)	-4,3 ± 1,15	-8,2 ± 2,24	-14,65 ± 3,12

Table 2
Regression analysis results, linear and nonlinear equations that gives absolute VF defect number of each 8 RNFL sectors.

Sector	t value	p value	Significance	Equation
Sector1	-1,66	0,5	$p > 0,05$	$y = 0,43e^{0.044x}$
Sector2	0,372	0,7	$p > 0,05$	$y = 0,55e^{0.022x}$
Sector3	2,048	0,047	$p < 0,05$	$y = 0,0058x - 1,34$
Sector4	-4,064	0,04	$p < 0,05$	$y = -0,144x + 6,1$
Sector5	-0,2	0,15	$p > 0,05$	$y = 12,3e^{-0.11x}$
Sector6	-3,93	0,0014	$p < 0,05$	$y = -0,0945x + 9,17$
Sector7	0,088	0,37	$p > 0,05$	$y = 3,12e^{-0,039x}$
Sector8	-0,36	0,07	$p < 0,05$	$y = 22,64e^{-0,053x}$

Discussion

Glaucoma affects many people worldwide, and the VF test remains the most common tool for detecting a presence of any disease, VF sensitivity decreases

with age, as does RNFL thickness [18, 19, 20, 21]. Therefore, we used an age-corrected pattern deviation map for the study.

As we said before that we didn't meet a study about estimating the VF absolute defects. In the study of Suda et al, they wanted to evaluate the functional and structural changes and functional changes of glaucoma subjects. They found non-linear relation between structure and function and told that OCT could be used practically for progression follow-up [22]. They used sensitivity values of visual field test points and evaluated the change of them. Similarly, Wu and colleagues were studied on correlation between automated perimetry results and spectralis OCT and found that there was a good correlation. They were also used sensitivity changes [23]. But they were used Kanamori map. The researcher we told above, Suda, was also used Nakanishi and Garway-Heats maps and was stated that, the nasal inferior sector of the Garway-Heath map was correlated most strongly with the temporal superior sector of the RNFL while the strongest correlation was in the superior sector of visual field came from combination with the superior sector of VF and the temporal inferior sector of RNFL in Nakanishi map. We were used only Garway-Heats maps.

If a question arises that what is the threshold under which the RNFL thickness measurement is determined pathologic? Wollstein and associates used broken stick statistical analysis to determine a tipping point of RNFL thickness of 75.3 μm in 72 healthy and 40 glaucomatous eyes using Cirrus HD-OCT [24]. The mean RNFL thickness tipping point was 89 μm . In Aydogan's study, it was 90 μm [25]. The maximum average RNFL thickness that was measured in our study was below all of these levels. In addition, in our study, the mean RNFL measurements in the four quadrants were also less than that found by the other researchers. One of the weaknesses of our study is that some areas of the RNFL may have a higher interindividual variability, but inferior temporal and superior temporal sectors have lower variations. In glaucoma, based on the ISNT rule, the inferior and superior nerve fiber layers are more susceptible to damage, and defects can be seen most often at these parts of the optic nerve [26]. In OCT measurements in the nasal quadrants (including sectors 9, 10, 11, and 12), test-retest reproducibility found the lowest measurements using the time domain and spectral OCT [27]. In addition, Wollstein et al could not detect a tipping point for the nasal quadrants [24]. In our study, we did not find a statistically significant number of defects in these sectors, except in two patients, who had advanced glaucoma VF defects. Therefore, we used the measurements of only the first 8 sectors. Figures 3 and 4 show the estimated VF of two patients by using the RNFL thicknesses and the real VFs.

Conclusion

As a result, we think that our study results may be used a practical method to predict the shape of the VF of an open angle glaucoma who cannot perform a reliable test.

Abbreviations

VF

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Visual Field

OCT

Optical Coherence Tomography

RNFL

Retinal Nerve Fiber Layer

D

Diopter

GHT

Glaucoma Hemifield Test

SITA

Swedish Interactive Threshold Algorithm

S, ST, TS, T, TI, IT, I, IN, NI, N, NS, SN

Superior, Superior Temporal, Temporal Superior,

Declarations

Ethics Approval and Consent to Participate

This study was approved by the Ethical Committee of Istanbul Medipol University. (05.05.2020/361). Each patient or his/her legal representative signed the informed consent under the tenets of the Helsinki Declaration.

Consent for publication

Not applicable.

Availability of Data and Material

Not applicable

Competing interest

The author declares no conflict of interest

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Contribution

Author commented on previous versions of the manuscript and approved the final manuscript.

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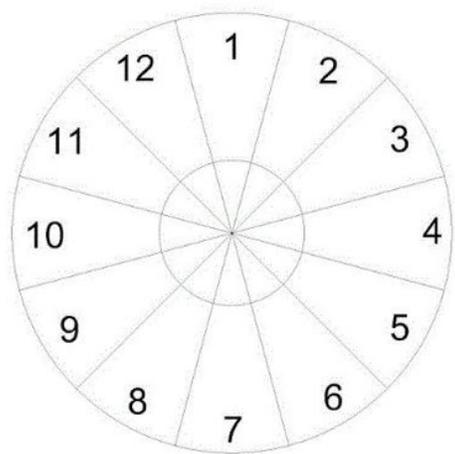
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Figures



		8	8	7	7			
	8	7	7	7	7	7		
8	8	1	6	6	6	6	7	
9		5	5	6	6	6	6	7
10		4	4	3	6	6	1	1
11	1	2	2	2	2	1	1	
	12	1	1	1	1	1		
		12	1	1	1			

Figure 1

Garway-Heath OCT-Visual field map we used for the study. Twelve sectors of RNFL in OCT are represented by the same numbers in visual field sectors.

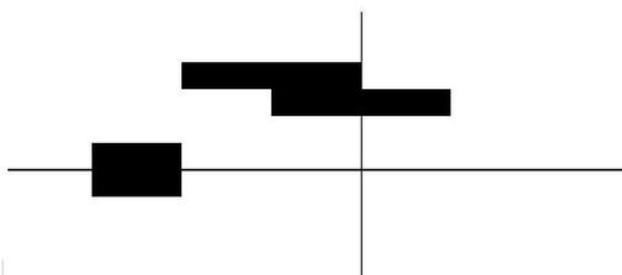
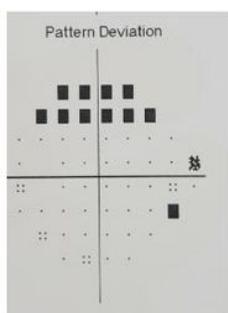


Figure 2

VF of a glaucoma patient and the estimated one that we found by using our method.

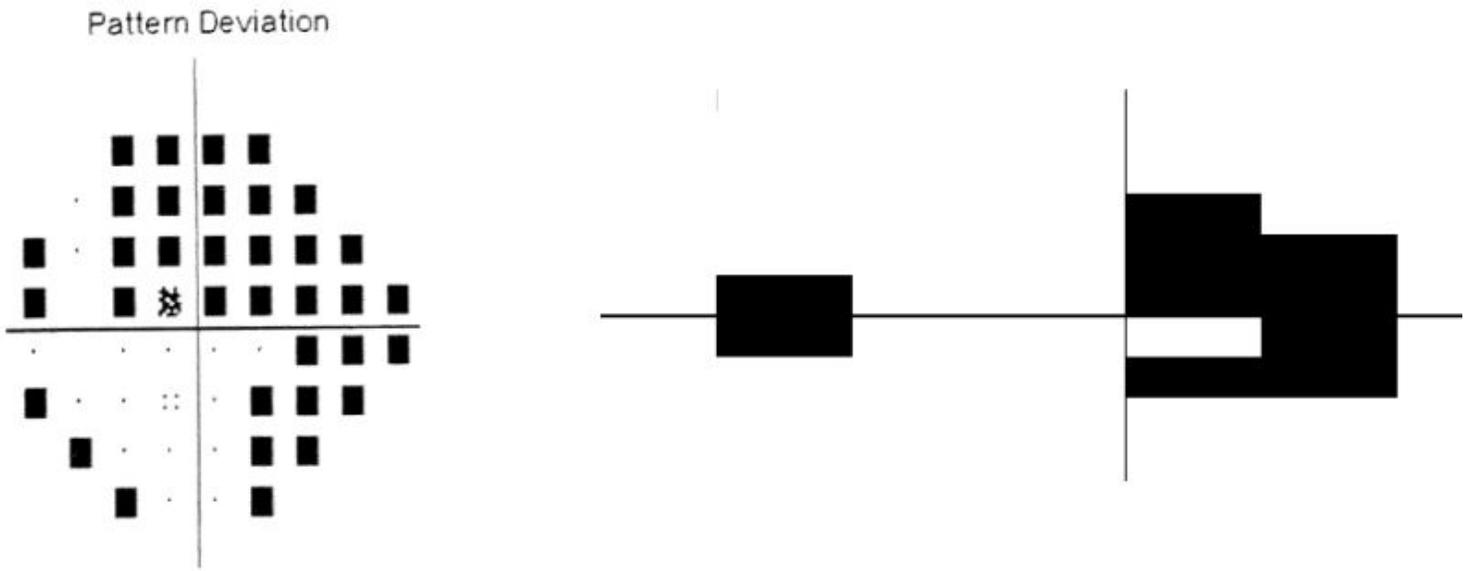


Figure 3

VF of another patient and the estimated one that we found by using our method.