ORIGINAL ARTICLE

Evaluation of the relationship between absolute defects number of visual fields with the retinal nerve fiber layer thicknesses

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ABSTRACT

Purpose: To find a relation between absolute defect number and retinal nerve fiber layer thicknesses.

Materials and 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 on the same day. Garway-Heats maps were made, RNFL sectors matched with pattern deviation 24-2 VF sectors, and absolute defects were counted. Regression analyses were made. Equations were generated between RNFL thickness and absolute defect number. Correlation analyses were performed for the number 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 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).

Conclusions: We think by using our equations it may be possible to predict the absolute defects of VF of a patient who cannot perform it. But It's needed to study defects of probability indexes between 5% and1%.

Keywords: Glaucoma, visual field tests, optic disc, tomography, optical coherence.

INTRODUCTION

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. However, the test duration is long in Full Threshold and even more in glaucoma patients.[3] Therefore, there is an inclination to use optical coherence tomography (OCT) more in glaucoma diagnosis and follow-up.[4] Although improvements in diagnostic techniques and studies such as using artificial intelligence[5], assessment of the visual field is still crucial. Tripping over and bumping into objects, driving disabilities are related significantly to the loss of the binocular visual field in glaucoma and affects 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 an 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, (OCT) detects this structural change.[8] Garway-Heaths maps correlate structural and functional changes and automated perimetry field regions to the corresponding

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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] In the VF printout, the absolute defects in the pattern deviation plot show the deteriorated visual function according to the loss of the retinal nerve fiber layer. If there is a correspondence between the ganglion cell loss and the defects in VF, the number of absolute defects may be correlated with the lost RNFL thicknesses of the optic nerve head sector. By using RNFL thickness as one of the variables and the number of absolute defects in the corresponding VF area as the other variable, we may generate a mathematical method for the prediction of the VF. In this study, we wanted to determine whether it is possible to predict absolute defects using these mathematical formulas.

MATERIALS AND 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 40 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. The patients who have angle recession, who had not been found with high IOP at the time of diagnosis and during the follow-up, heavily pigmented angles with iris defects, glaucoma associated with uveitic diseases, and infectious causes were all excluded.

They were all under topical anti-glaucomatous treatment. No one of them was treated surgically. All patients had abnormal hemifield VF test with abnormal OCT. 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] In OCT, RNFL thickness at the 5% level compared to the normative database (yellow coloring on the RNFL deviation map) and RNFL thickness at the 1% level (red coloring on RNFL deviation map) were accepted as abnormal.

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 µm. 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 were database range at the 1% level (outside normal limits).

VF Analysis

Tests were performed using the Humphrey 750i (Carl Zeiss Meditech, Dublin, California) Swedish Interactive Threshold Algorithm 24-2 test. All tests were performed by the same technician.

Garway-Heaths maps were created with OCT sectors and the VF pattern deviation map for each patient. We gave numbers for each OCT sector from 1 to 12 and matched them in the VF (Figure 1).

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

Glaucoma severity of the patients was classified using MD values in Hodapp-Parish-Anderson criteria.

Statistical Analysis

Correlation analysis was performed to find correlations between RNFL thickness and pattern deviation map absolute defect number. Correlation scatter plots were

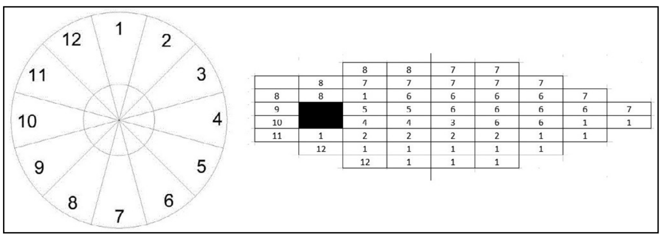


Figure 1: *The Garway-Heats map of the left eye used in our study. RNFL sectors map on the left side and matched points on the visual field pattern deviation map on the right.*

also drawn. Linear regression equations were generated for linear correlations, and non-linear equations were generated for non-linear correlations. Correlation and linear regression analysis were performed using SPSS version 16 software (IBM, Armonk, NY, USA). The linear regression equation is shown as

$$y = a + bx$$

The exponential function method was used to generate the non-linear equation.

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 to 2,71, a and b are constants.

We also used the Jansonius trajectory map of retinal nerve fiber layers to localize the defects generated from OCT matched in the visual field in degrees.[15]

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, temporal, inferior, and nasal quadrants were 66.62 ±15.61, 48.43±13.34, 64.31±11.46 and 51.32±13.32 microns respectively. Most of our patients were in moderate and advanced stages of glaucoma (Table 1). In the mild defect group, the patients were using topically prostaglandin analogs or brinzolamide alone, in the moderate defect group 25 patients were using prostaglandin analogs and beta-blocker + carbonyl anhydrase inhibitors combination, and the others were using one of them alone. In the 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 1,3, 4, 6and 8 but was nonlinear in other sectors. The generated equations are shown in Table 2.

The scatter plots between RNFL thicknesses and absolute defects of pattern deviation maps were shown in Graph1.

Fifty-five of our retinal nerve fiber layer thickness matched defects were found and 21 of them were between -60 and -80 degrees, 14 of them between -80 and -100 degrees, 4 of the sector was between -100 and -120, between -120 and -140 degrees and (-140) -(-150) there was one each of them. Five between 60-80 degrees, 7 between 80-100, and 2 between 100-120 degrees.

DISCUSSION

Glaucoma affects many people worldwide, and the VF test remains the most common tool for detecting functional visual loss in those with the disease. In the absence of any

Table 1: *Glaucoma severity classification by using Hodapp- Parish- Anderson criteria.*

	Early defect	Moderate defect	Severe defect
Number of patients	21	37	20
Mean MD (dB)	-4,3± 1,15	-8,2±2,24	-14,65±3,12

Table 2: *Correlations between retinal nerve fiber layer thickness in sectors and the number of visual field defects. Generated linear and non- lienear equations.*

Sector	r coefficients	t values	p values	Probability*	Equations
Sector1	-0,340	-2,108	0,042	p<0,05	$y = 0{,}123+11{,}29$
Sector2	-0,094	-0,63	0,53	p>0,05	$y = 0{,}55e^{0.022x}$
Sector3	0,315	2,048	0,047	p<0,05	$y = 0{,}0058x - 1{,}34$
Sector4	-0,82	-4,064	0,04	p<0,05	$y = -0{,}144x + 6{,}1$
Sector5	-0,294	-0,2	0,15	p>0,05	$y = 12{,}3e^{-0.11x}$
Sector6	-0,472	-3,93	0,0014	p<0,05	$y = -0{,}0945x + 9{,}17$
Sector7	0,124	0,088	0,37	p>0,05	$y = 3{,}12e^{-0.039x}$
Sector8	-0,359	-0,36	0,07	P<0,05	$y = -0{,}072x + 5{,}5$

* p<0,05

disease, VF sensitivity decreases with age, as does RNFL thickness.[16-19] Therefore, we used an age-corrected pattern deviation map for the study. We could not see any study about defect number correlation. So, we think that this may be the first study about the subject.

In the study of Suda et al., they wanted to evaluate structural and functional changes in glaucoma subjects[20] and used sensitivity values of visual field test points and evaluated the change of them. We were used pattern deviation plots for our study and the numbers of defects in matched VF sector instead of sensitivities. It is not affected by media opacities and will be more reliable. Wu and colleagues studied on correlation between automated perimetry results and spectralis OCT and found that there was a good correlation.[21] They were also used sensitivity changes. But they 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-Heaths 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 also found the same correlation in our study, and we used only Garway-Heats maps. Yanagisawa and colleagues 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.[22] They matched these sectors in the VF and showed them the colored squares. In our study we used numbers instead of colors.

The tipping point of RNFL thickness was found at 89.3 µm in a study, using Cirrus HD-OCT.[23] In Aydogan et al.'s study, it was 90µm.[24] The maximum average RNFL thickness that was measured in our study was below all 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.

Casado et al. mapped RNFL into sectors and named as temporal and nasal superior, inferior etc. similar the method that we used. They also found temporal superior RNFL sectors thinner, again, similar with us. They matched only the shape of visual field.[25]

Nakanishi et al. combined 24-2 and 10-2 VF tests and made a cluster of test points. They analyzed the sensitivity thresholds. Their correlation coefficient was changing in different angles, but strong correlations were also found in inferior VF regions (between 30-100 degrees) similar as our study.[26]

On the other side, Kanamori et al. found inferior RNFL sectors given broader VF cluster defects and having higher correlation oppositely our study that superior RNFL sectors having higher correlation of defect numbers. He was also used 16 RNFL sectors instead of 12.[27]

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.[28] 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.[29] In addition, Wollstein et al could not detect a tipping point for the nasal quadrants.[23] 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 2 and 3 show the estimated VF of two patients by using the RNFL thicknesses and the real VFs.

The number of defects in some areas was not correlated with the equations we found because we have seen that the RNFL thickness and the number of absolute defects in the visual fields may not correlate, may vary among individuals. For an instance, in equal RNFL thicknesses, some patients had 2 absolute defects while the others had 5 absolute defects. Also, on the contrary, similar defect numbers were also present despite different thicknesses. Suda et al, as we told above, were also found non-linear relation between structure and function.[20]

As a result, we think that absolute defect numbers that are formulated from RNFL thicknesses may give an approximate VF shape in patients having open angle glaucoma.

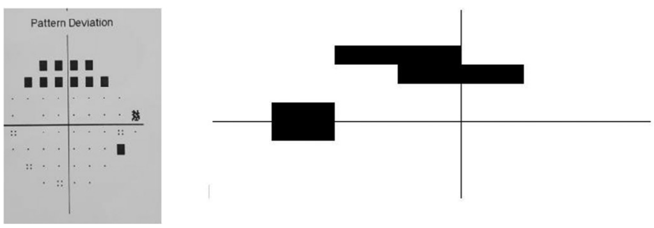
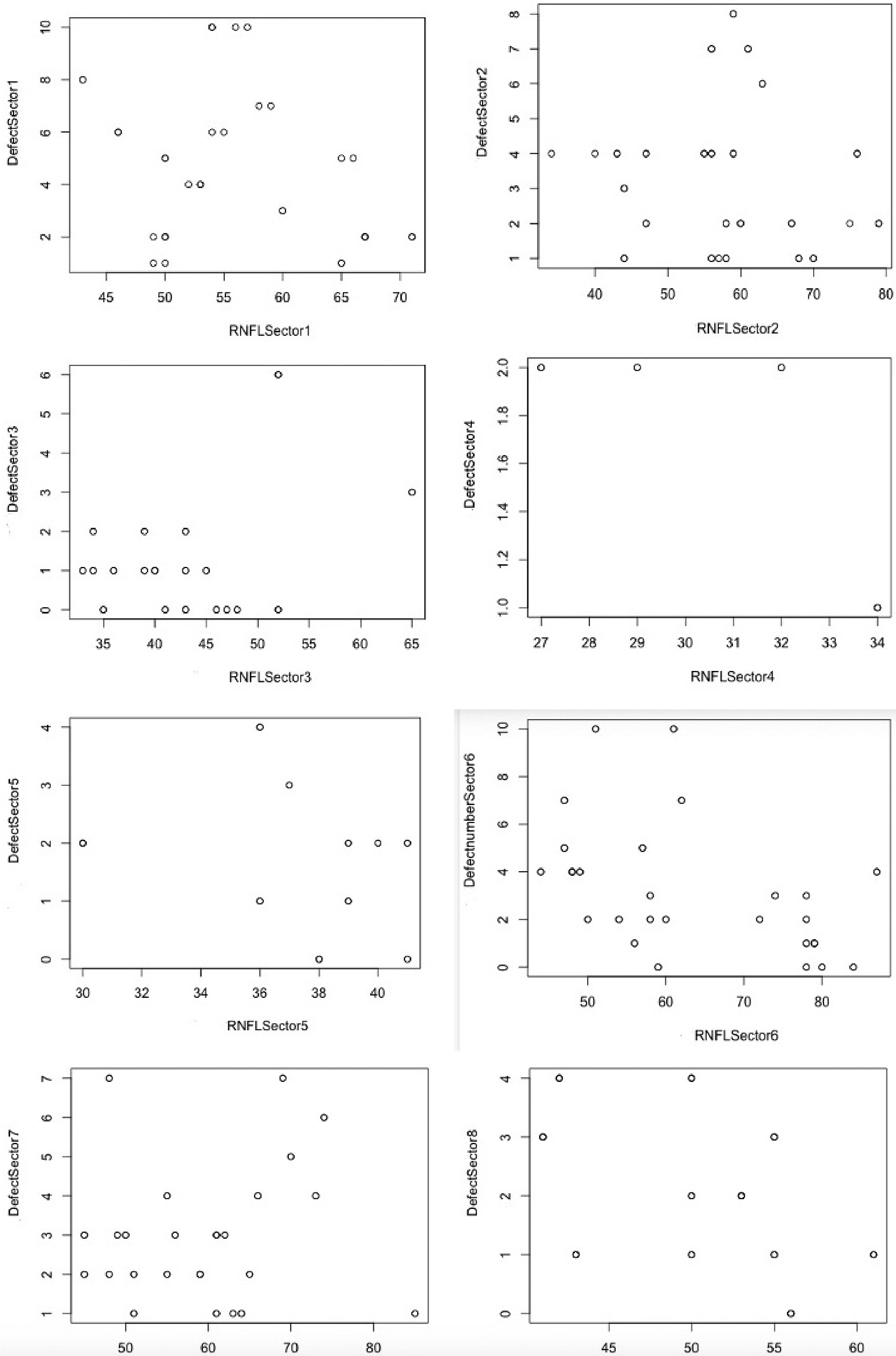


Figure 2: *An example of the visual field of a patient found by using our formula and the actual of it.*



Graph 1: *Scatter plot graph of actual and calculated absolute defects in 8 sectors.*

REFERENCES

1. Quigley HA, Broman AT. The number of people with glaucoma worldwide in 2010 and 2020. Br J Ophthalmol 2006;90:262-7. https://doi.org/10.1136/bjo.2005.081224
2. Medeiros FA, Zangwill LM, Bowd C, et al. Evaluation of retinal nerve fiber layer, optic nerve head, and macular thickness measurements for glaucoma detection using optical coherence tomography. Am J Ophthalmol 2005;139:44-55. https://doi.org/10.1016/j.ajo.2004.08.069
3. Wu Z, Medeiros FA. Recent developments in visual field testing for glaucoma. Curr Opin Ophthalmol 2018;29:141-6. https://doi.org/10.1097/ICU.0000000000000461
4. Zhang X, Dastiridou A, Francis BA, et al. Comparison of Glaucoma Progression Detection by Optical Coherence Tomography and Visual Field. Am J Ophthalmol 2017;184:63-74. https://doi.org/10.1016/j.ajo.2017.09.020
5. Maetschke S, Antony B, Ishikawa H, et al. A feature agnostic approach for glaucoma detection in OCT volumes. PLoS One 2019;14:e0219126. https://doi.org/10.1371/journal.pone.0219126
6. Nelson P, Aspinall P, Papasouliotis O, et al. Quality of life in glaucoma and its relationship with visual function. J Glaucoma 2003;12:139-50. https://doi.org/10.1097/00061198-200304000-00009
7. Aydin A, Kocak I, Aykan U, et al. The influence of the learning effect on automated perimetry in a Turkish population. J Fr Ophtalmol 2015;38:628-32. https://doi.org/10.1016/j.jfo.2015.01.013
8. Greenfield DS. Optic nerve and retinal nerve fiber layer analyzers in glaucoma. Curr Opin Ophthalmol 2002;13:68-76. https://doi.org/10.1097/00055735-200204000-00003
9. Garway-Heath DF, Poinoosawmy D, Fitzke FW, et al. Mapping the visual field to the optic disc in normal tension glaucoma eyes. Ophthalmology 2000;107:1809-15. https://doi.org/10.1016/s0161-6420(00)00284-0
10. Nilforushan N, Nassiri N, Moghimi S, et al. Structure-function relationships between spectral-domain OCT and standard achromatic perimetry. Invest Ophthalmol Vis Sci 2012;53:2740-8. https://doi.org/10.1167/iovs.11-8320
11. Takagishi M, Hirooka K, Baba T, et al. Comparison of retinal nerve fiber layer thickness measurements using time domain and spectral domain optical coherence tomography, and visual field sensitivity. J Glaucoma 2011;20:383-7. https://doi.org/10.1097/IJG.0b013e3181efb371
12. Freedman DA. Statistical Models: Theory and Practice. Cambridge, UK: Cambridge University Press; 2009: 41-72. https://doi.org/10.1017/CBO9780511815867
13. Vianna JR, Butty Z, Torres LA, et al. Outer retinal layer thickness in patients with glaucoma with horizontal hemifield visual field defects. Br J Ophthalmol 2019;103:1217-22. https://doi.org/10.1136/bjophthalmol-2018-312753
14. European Glaucoma Society Terminology and Guidelines for Glaucoma, 4th Edition - Chapter 2: Classification and terminology Supported by the EGS Foundation. Br J Ophthalmol 2017;101:73-127. https://doi.org/10.1136/bjophthalmol-2016-EGSguideline.002
15. Jansonius NM, Nevalainen J, Selig B, et al. A mathematical description of nerve fiber bundle trajectories and their variability in the human retina. Vision Res 2009;49:2157-63. https://doi.org/10.1016/j.visres.2009.04.029
16. Nagai-Kusuhara A, Nakamura M, Fujioka M, et al. Association of retinal nerve fibre layer thickness measured by confocal scanning laser ophthalmoscopy and optical coherence tomography with disc size and axial length. Br J Ophthalmol 2008;92:186-90. https://doi.org/10.1136/bjo.2007.127480
17. Alasil T, Wang K, Keane PA, et al. Analysis of normal retinal nerve fiber layer thickness by age, sex, and race using spectral domain optical coherence tomography. J Glaucoma 2013;22:532-41. https://doi.org/10.1097/IJG.0b013e318255bb4a
18. Bendschneider D, Tornow RP, Horn FK, et al. Retinal nerve fiber layer thickness in normals measured by spectral domain OCT. J Glaucoma 2010;19:475-82. https://doi.org/10.1097/IJG.0b013e3181c4b0c7
19. Budenz DL, Anderson DR, Varma R, et al. Determinants of normal retinal nerve fiber layer thickness measured by Stratus OCT. Ophthalmology 2007;114:1046-52. https://doi.org/10.1016/j.ophtha.2006.08.046
20. Suda K, Akagi T, Nakanishi H, et al. Evaluation of Structure-Function Relationships in Longitudinal Changes of Glaucoma using the Spectralis OCT Follow-Up Mode. Sci Rep 2018;8:17158. https://doi.org/10.1038/s41598-018-35419-y
21. Wu H, de Boer JF, Chen L, et al. Correlation of localized glaucomatous visual field defects and spectral domain optical coherence tomography retinal nerve fiber layer thinning using a modified structure-function map for OCT. Eye (Lond) 2015;29:525-33. https://doi.org/10.1038/eye.2014.317
22. Yanagisawa M, Murata H, Matsuura M, et al. Goldmann V Standard Automated Perimetry Underestimates Central Visual Sensitivity in Glaucomatous Eyes with Increased Axial Length. Transl Vis Sci Technol 2017;6:13. https://doi.org/10.1167/tvst.6.5.13
23. Wollstein G, Kagemann L, Bilonick RA, et al. Retinal nerve fibre layer and visual function loss in glaucoma: the tipping point. Br J Ophthalmol 2012;96:47-52. https://doi.org/10.1136/bjo.2010.196907

24. Aydogan T, Akçay BİS, Kardeş E, et al. Evaluation of spectral domain optical coherence tomography parameters in ocular hypertension, preperimetric, and early glaucoma. Indian J Ophthalmol 2017;65:1143-50. https://doi.org/10.4103/ijo.IJO_157_17

25. Casado A, Cerveró A, López-de-Eguileta A, et al. Topographic correlation and asymmetry analysis of ganglion cell layer thinning and the retinal nerve fiber layer with localized visual field defects. PLoS One 2019;14:e0222347. https://doi.org/10.1371/journal.pone.0222347

26. Nakanishi H, Akagi T, Suda K, et al. Clustering of Combined 24-2 and 10-2 Visual Field Grids and Their Relationship With Circumpapillary Retinal Nerve Fiber Layer Thickness. Invest Ophthalmol Vis Sci 2016;57:3203-10. https://doi.org/10.1167/iovs.15-18798

27. Kanamori A, Naka M, Nagai-Kusuhara A, et al. Regional relationship between retinal nerve fiber layer thickness and corresponding visual field sensitivity in glaucomatous eyes. Arch Ophthalmol 2008;126:1500-6. https://doi.org/10.1001/archopht.126.11.1500

28. Budenz DL, Fredette MJ, Feuer WJ, et al. Reproducibility of peripapillary retinal nerve fiber thickness measurements with stratus OCT in glaucomatous eyes. Ophthalmology 2008;115:661-6. https://doi.org/10.1016/j.ophtha.2007.05.035

29. Garway-Heath DF, Hitchings RA. Quantitative evaluation of the optic nerve head in early glaucoma. Br J Ophthalmol 1998;82:352-61. https://doi.org/10.1136/bjo.82.4.352