ORIGINAL ARTICLE

Reliability of retinal nerve fiber layer color codes of optical coherence tomography in early diagnosis of glaucoma

Nilgun Solmaz[1], Melih Ustaoglu[2], Feyza Onder[3]

ABSTRACT

Purpose: To investigate the reliability of retinal nerve fiber layer (RNFL) color codes of spectral-domain optical coherence tomography (OCT) in early diagnosis of glaucoma using two different devices: the Copernicus and Cirrus.

Materials and Methods: Inter-device concordance was investigated using the intra-class correlation coefficient (ICC) for average and four quadrants peripapillary RNFL thicknesses, and the mixed-design two-way analysis of variance for color-coded graphical formats. The performance of RNFL thicknesses in discriminating early glaucoma from suspected glaucoma was assessed using the area under the receiver operating characteristic (AUROC) curve analysis.

Results: Thirty eyes with suspected glaucoma (Group I) and 30 with early glaucoma (Group II) were enrolled in the study. All RNFL measurements obtained by the Cirrus OCT were thicker than those obtained by the Copernicus OCT ($p < 0.001$). On the 95% confidence interval, the ICC assessed a "moderate to excellent" inter-device concordance for the average and inferior RNFL thicknesses in both groups. Except for the temporal quadrant, the color code concordance ranged from 46.7% to 70% in Group I and from 30% to 40% in Group II. The Cirrus OCT displayed more optimal color codes compare to the Copernicus. The values of AUROC for RNFL thickness ranged from 0.586 to 0.682 ($p < 0.05$, for only the average RNFL) for the Cirrus and from 0.703 to 0.769 ($p<0.05$, for all) for the Copernicus.

Conclusion: The Cirrus and Copernicus OCT yielded different peripapillary RNFL thickness measurements, and differences also existed in their color code interpretations and diagnostic powers.

Keywords: Glaucoma, Optical Coherence Tomography (OCT), retinal nerve fiber layer (RNFL), Color code.

INTRODUCTION

Glaucoma is a multifactorial, progressive, degenerative type of optic neuropathy.[1] It is characterized by the death of retinal ganglion cells and their axons.[2-5] The current gold standards for glaucoma diagnosis are the clinical assessment of the peripapillary retinal nerve fiber layer (RNFL) and optic disc for structural changes and the achromatic perimetry to monitor functional changes.[6] Visual field (VF) testing and clinical assessment of the optic disc are subjective diagnostic methods; also, at least 30% ganglion cell loss is required for the detection of VF defects.[4,5] Detecting structural damage in the RNFL before detecting VF loss is critical in the early diagnosis and management of glaucoma.

Optical coherence tomography (OCT) provides non-invasive cross-sectional imaging of the retina and the optic nerve, and it enables the evaluation and quantification of the neural structures. With the introduction of spectral-domain OCT (SD-OCT), the diagnostic value of OCT in glaucoma cases has increased. It has become more popular in the diagnosis of glaucoma, monitoring of the condition, and quantification of structural damage.[7-11] SD-OCTs allow for the evaluation of the optic nerve head, thickness of the macular ganglion cell layer, and the peripapillary RNFL thickness to facilitate the diagnosis and management of glaucoma. However, peripapillary RNFL analysis remains the most commonly used scanning protocol in the management of glaucoma.[10,11]

1- MD, University of Health Sciences, Haseki Training and Research Hospital, Department of Ophthalmology, Istanbul, Türkiye

2. MD, University of Health Sciences, Bursa Higher Specialization Training and Research Hospital, Department of Ophthalmology, Bursa, Türkiye

3. Prof., MD, University of Health Sciences, Haseki Training and Research Hospital, Department of Ophthalmology, Istanbul, Türkiye

Received: 23.07.2022
Accepted: 20.07.2023
TJ-CEO 2024; 1: 5-13
DOİ: 10.37844/TJ-CEO.2024.1.2

Correspondence Address:
Nilgun Solmaz
Haseki Training and Research Hospital, Sultangazi, Istanbul, Türkiye
Phone: +90 212 453 2000
E-mail: nilgunsolmaz@hotmail.com

There are numerous SD-OCT devices available, and each device has its own diagnostic software and normative database. Previous studies have shown that RNFL thickness measurements differ among SD-OCT devices and cannot be used interchangeably;[12-15] however, the ability of these devices in detecting glaucoma and evaluating its severity is comparable.[10,16-18] OCT devices also provide information on probable RNFL defects using four color codes that are generated after comparison of the RNFL profile with an internal age-matched normative database. Color coding enables clinicians to quickly evaluate whether a particular patient's RNFL thicknesses are within normal limits. Although numerous studies compared the diagnostic abilities of different OCT devices using the values of the area under the receiver operating characteristic (AUROC) curve of RNFL parameters,[10,16-18] only few available studies have evaluated the color code concordance between OCT devices.[19,20] Furthermore, the sensitivity of RNFL parameters in discriminating early glaucoma from suspected glaucoma has not been investigated adequately.

In this study, we aimed to evaluate the reliability of RNFL color codes of OCT devices in early diagnosis of glaucoma by investigating the RNFL thickness and color code concordance between two different SD-OCT devices.

MATERIAL AND METHODS

This was a prospective, cross-sectional study, conducted in a tertiary glaucoma center between October 2016 and March 2017. The study adhered to the tenets of Declaration of Helsinki. It was approved by the Institutional Review Board and informed consent was obtained from all patients.

The inclusion criteria for this study were: follow-up duration of at least 12 months; suspected or early primary open-angle glaucoma; best-corrected visual acuity (BCVA) ≥ 20/40; refractive error within ± 5.00 D spherical equivalent and ± 3.00 D astigmatism; no evidence of a non-glaucomatous optic nerve head, or history or evidence of retinal diseases; no systemic treatments that may be toxic to the retina or optic nerve; and no history of laser therapy or ocular surgery. All subjects underwent a comprehensive ophthalmologic examination including BCVA, slit-lamp biomicroscopy, Goldmann applanation tonometry, gonioscopy, ultrasound pachymetry, dilated fundus examination, VF testing, and retinal nerve fiber analysis via SD-OCT imaging, performed using both the Cirrus HD-OCT 5000 device (Carl Zeiss Meditec, Dublin, CA, USA) and Copernicus SD-OCT device (Optopol Technology S.A., Zawiercie, Poland, Version 4.3 Software). If both eyes of a patient met the inclusion criteria, only one eye was randomly selected and included in this study.

The glaucoma suspects group (Group I) comprised eyes with intraocular pressure (IOP) >21 mmHg, with a healthy optic disc and normal VF results, or eyes with a glaucomatous optic disc appearance and normal VF results.

The early glaucoma group (Group II) comprised eyes with IOP >21 mmHg, open anterior chamber angle and early glaucomatous defect according to Hodapp - Parrish - Anderson criteria.[21] Early glaucomatous defect was determined as the presence of a cluster of 3 or more non-edge points on the pattern standard deviation (PSD) plot, all of those are depressed at a p<5% level and one of those is depressed at a p<1% level or a PSD outside 95% normal limits or a glaucoma hemifield test result outside normal limits, and also the presence of these findings at least two consecutive VF tests.[21]

Visual Field Testing

VF examination was performed using the Swedish Interactive Threshold Algorithm (Humphrey Field Analyzer II 740, 24-2 SITA Standard; Carl Zeiss Meditec). The VF results were considered reliable if the fixation loss was ≤ 20%, and the false-positive and false-negative response rates were ≤ 15%. The VF testing and OCT scans were performed on the same day, and only the patients who had at least two consecutive reliable VF results were enrolled in this study.

Optical Coherence Tomography Measurements

SD-OCT images were obtained using both the Cirrus HD-OCT 5000 and Copernicus SD-OCT devices; all eyes were dilated for the procedure. The OCT images were acquired by the same operator on the same day, and only the images with a signal strength of 6 or higher were included in the study. Cirrus OCT was performed using the optic disc cube 200×200 protocol that generates a cube of data through a 6-mm square grid by acquiring a series of 200 horizontal scan lines, each composed of 200 A-scans. The device measured the peripapillary RNFL thickness from the same cube data along the circumference of a 3.4 mm diameter circle centered at the optic disc. Copernicus OCT was performed using the three-dimensional optic disc program (70 B-scans, 500 A-scans per B-scan) that scans a 5-mm square centered to the optic disc. The RNFL scanning ring diameter was 2.4 mm, and ring thickness was 0.4 mm.

Both OCTs provided an average and four quadrants (superior, inferior, nasal, and temporal) RNFL thickness measurements. The Cirrus OCT created four equal quadrants of 90°, whereas the Copernicus OCT created superior and inferior quadrants of 120°, a nasal quadrant of 70°, and a temporal quadrant of 50°. The RNFL graphic of the Copernicus OCT consisted of ten clock hour sectors, whereas that of the Cirrus OCT device consisted of twelve sectors.

The values of the thinnest 1% of the normative database are marked red and considered "outside normal limits." The values between 1% and 5% are marked yellow and considered borderline/suspect. The values from >5% to 95% represent the wide range for normal values and are marked green. The values >95% of the range are labeled white and indicate the thickest range of the normative database.[22]

Statistical Analysis

Statistical analyses were performed using the Statistical Package for the Social Sciences (SPSS, version 15.0, Inc., Chicago, IL, USA). Differences between the means of the groups were tested using the Student's t-test for independent samples or using nonparametric Mann-Whitney U test if the variables were not normally distributed. The inter-device concordance between the two OCT devices was assessed using the intra-class correlation coefficient (ICC) and the Bland-Altman scatter plot for RNFL thickness measurements, and the 2×2 mixed-design analysis of variance (ANOVA) was used for color-coded graphical formats. ICC estimates and their 95% confidence intervals (CIs) were calculated using single-rating, consistency, and a two-way mixed effects model. Furthermore, receiver operating characteristics (ROC) curve analysis was used to determine the diagnostic performances of RNFL parameters. A P-value less than 0.05 was considered statistically significant.

RESULTS

Sixty eyes of 60 patients, 30 with suspected glaucoma (Group I) and 30 with early glaucoma (Group II), were enrolled in this study. The demographic and clinical characteristics of the subjects are shown in Table 1.

For both groups, all RNFL thickness measurements obtained using the Cirrus OCT were significantly thicker than those obtained using the Copernicus OCT ($p<0.001$, for all) (Table 2). On the 95% confidence interval, the ICC assessed a "moderate to excellent" inter-device concordance for the average and inferior RNFL thicknesses in both groups. The lowest inter-device concordance was recorded in the superior and temporal quadrants in Group I (ICC: 0.626 and 0.527, respectively), and in the nasal and temporal quadrants in Group II (ICC: 0.632 and 0.548, respectively).

The Bland-Altman plots showed a discrepancy in concordance limits between the RNFL thickness measurements obtained using the two devices. Based on the 95% CI ($p<0.001$), the limit of concordance between the devices was 22.0 (-6.6 – 15.4) µm for average RNFL thickness, 40.0 (-11.6 – 28.4) µm for that of the superior, 40.7(-7.8 – 32.9) µm for the inferior, 39.1(-9.7 – 29.4) µm for the nasal, and 36.3 (-5.5 – 30.8) µm for the temporal

Table 1: *Clinical and demographic characteristics of the patients.*

	Group I (Glaucoma Suspect)		Group II (Early Glaucoma)		p
	Min-Max.	Mean±SD	Min-Max.	Mean±SD	
Age, years	38-69	54.5±8.3	37-77	59.5±9.6	0.038
Sex: Male/Female	9 / 21		12/18		0.417
Eye: Right/Left	19 / 11		16/14		0.432
Cup/disk ratio	0.1 – 0.7	0.44±0.16	0.1 – 0.8	0.54±0.21	0.030
CCT (µm)	470 – 673	560.5±40.5	507 – 620	563.4±31.1	0.770
Visual Field MD (dB)	-5.57 – -0.67	-2.11± 0.95	-6.01 – -1.37	-4.32±1.18	<0.001
	(Median: -2.15)		(Median: -4.43)		
Visual Field PSD (dB)	1.26 – 4.96	1.81±0.77	1.47-8.21	3.28±1.39	<0.001
	(Median: 1.60)		(Median:2.94)		

MD: Mean deviation; **PSD**: Pattern standard deviation; **CCT**: Central corneal thickness

Table 2: *The Intraclass Correlation Coefficient of peripapillary RNFL measurements between Cirrus OCT and Copernicus OCT.*

RNFL Thickness Measurements	Cirrus OCT	Copernicus OCT	Difference	p	ICC		p
	Mean±SD	Mean±SD	Mean±SD		Mean	95% CI (Min-Max)	
Group I							
Average	97.4±9.4	94.2±8.3	3.2±4.4	<0.001	0.877	0.758 – 0.940	<0.001
Superior	110.6±13.6	105.1±9.8	5.5±10.3	<0.001	0.626	0.348 – 0.802	<0.001
Inferior	121.9±16.5	109.7±12.5	12.2±8	<0.001	0.813	0.644 – 0.906	<0.001
Nasal	82.2±12.4	73.6±11.0	8.7±7.3	<0.001	0.807	0.633 – 0.903	<0.001
Temporal	72.4±11.0	60.1±7.7	12.3±9.2	<0.001	0.527	0.211 – 0.743	0.001
Group II							
Average	89.6±14.9	84.0±12.1	5.7±6.4	<0.001	0.888	0.779 – 0.945	<0.001
Superior	104.1±18.7	92.8±14.0	11.3±9.4	<0.001	0.837	0.686 – 0.919	<0.001
Inferior	111.2±25.0	98.0±17.6	12.9±11.8	<0.001	0.851	0.711 – 0.926	<0.001
Nasal	76.1±16.2	65.0±11.6	11.1±12.1	<0.001	0.632	0.356 – 0.806	<0.001
Temporal	67.5±11.5	54.5±8.0	12.9±9.4	<0.001	0.548	0.240 – 0.756	0.001

RNFL: Retinal nerve fiber layer; **OCT:** Optical coherence tomography; **ICC:** Intraclass Correlation Coefficient; **CI**: Confidential interval **SD:** Standard deviation

quadrant. The Bland-Altman plot revealed that the bias tended to be greater when the RNFL was thicker, a finding that was more prominent in the inferior quadrant (Figure 1).

The color-coded graphics of RNFL thicknesses, derived from the Copernicus and Cirrus OCT, differed significantly from each other (p <0.05, for all) (Table 3); the difference

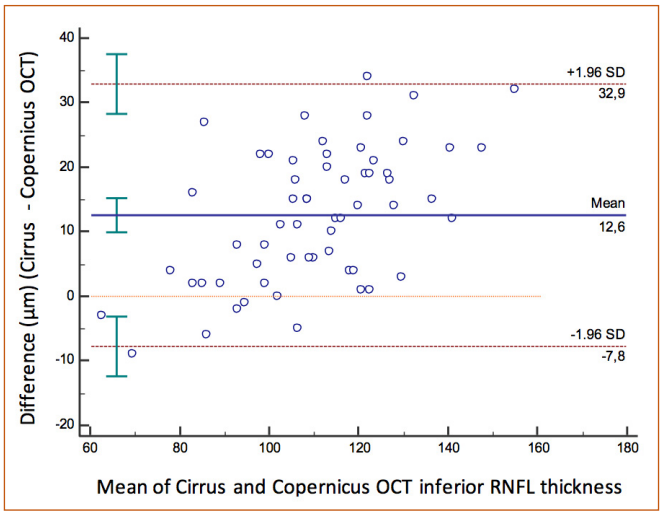

Figure 1: *The Bland-Altman scatter plot revealed that the differences in retinal nerve fiber layer (RNFL) thickness measurements tended to be greater when the RNFL was thick and this discrepancy was more prominent in the inferior quadrant [the slope (R^2 Linear): 0.249].*

was more prominent in Group II (Figure 2). Except for the temporal quadrant that had the highest color code concordance (above 80%) in both groups, the color code concordance between the two OCT devices from 46.7% to 70% in Group I and from 30% to 40% in Group II.

ROC curve analysis demonstrated differences between the diagnostic powers of the devices in discriminating early glaucoma from suspected glaucoma. The AUROC values ranged from 0.586 to 0.682 for the Cirrus OCT and from 0.703 to 0.769 for the Copernicus OCT. All RNFL thickness measurements obtained by the Copernicus, and only the average RNFL thickness obtained by the Cirrus, had fair discrimination powers (p <0.05, for all) (Table 4).

DISCUSSION

In this study, we investigated the inter-device concordance for peripapillary RNFL thickness measurements and color codes and the diagnostic performance of two different SD-OCT devices for the discrimination of early glaucoma from suspected glaucoma. Our results demonstrated that there are notable differences between the RNFL thickness measurements, color code graphics, and diagnostic powers of the Cirrus and Copernicus OCT. The inter-device concordance was good for the average, inferior, and nasal RNFL thicknesses (ICC: 0.877, 0.813, 0.807, respectively) of Group I, and the average, superior, and inferior RNFL

Table 3: *The Color-code agreement between Cirrus and Copernicus OCT. Color-code was considered as white >green>yellow>red.*

		Group I (Glaucoma Suspect)			Group II (Early Glaucoma)		
Color-Code Agreement		N	%	p	N	%	p
Average RNFL	Cirrus = Copernicus	21	70.0	0.003	11	36.7	<0.001
	Cirrus > Copernicus	9	30.0		19	63.3	
	Cirrus < Copernicus	0	0.0		0	0.0	
Superior RNFL	Cirrus = Copernicus	19	63.3	<0.001	9	30.0	<0.001
	Cirrus > Copernicus	10	33.3		20	66.7	
	Cirrus < Copernicus	1	3.3		1	3.3	
Inferior RNFL	Cirrus = Copernicus	16	53.3	<0.001	12	40.0	<0.001
	Cirrus > Copernicus	14	46.7		18	60.0	
	Cirrus < Copernicus	0	0.0		0	0.0	
Nasal RNFL	Cirrus = Copernicus	14	46.7	<0.001	12	40.0	<0.001
	Cirrus > Copernicus	16	53.3		18	60.0	
	Cirrus < Copernicus	0	0.0		0	0.0	
Temporal RNFL	Cirrus = Copernicus	25	83.3	0.025	24	80.0	0.014
	Cirrus > Copernicus	5	16.7		6	20.0	
	Cirrus < Copernicus	0	0.0		0	0.0	

RNFL: Retinal nerve fiber layer; **OCT:** Optical coherence tomography

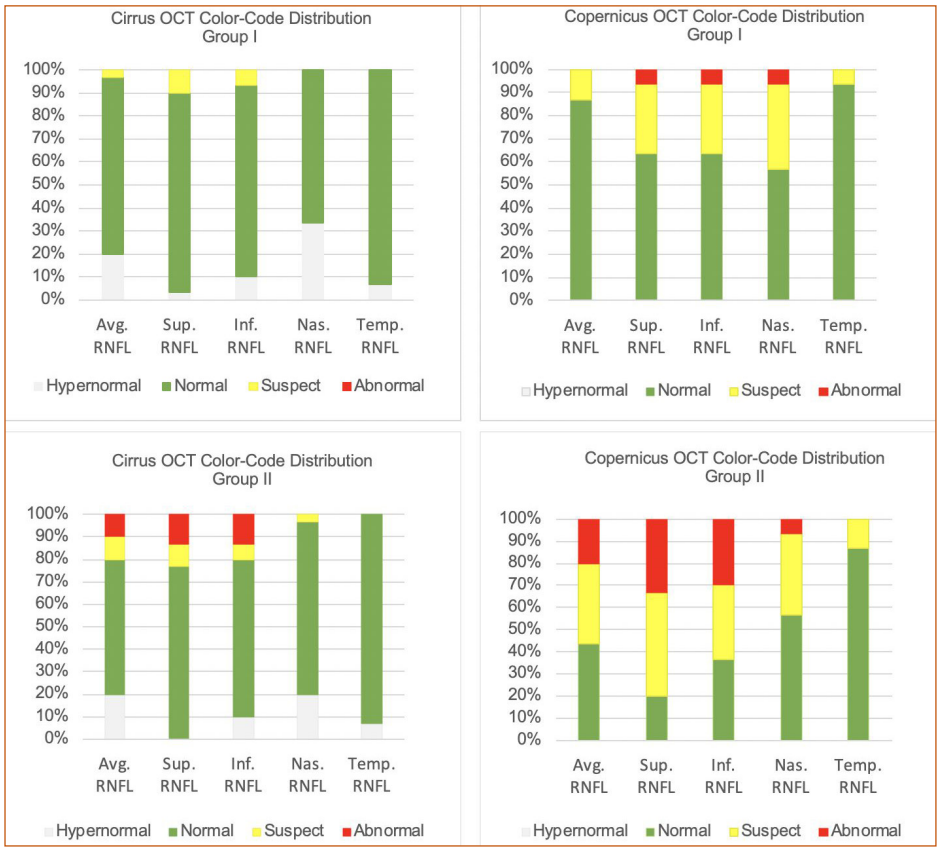

Figure 2: *Distribution of color-codes created by Cirrus and Copernicus optical coherence tomographies in patients with glaucoma suspect (Group I) and early glaucoma (Group II)*

Table 4: *The AUROC values of peripapillary RNFL parameters of Cirrus and Copernicus OCTs for discriminating early glaucoma from the glaucoma suspect.*

	Glaucoma Suspect vs Early Glaucoma	
	AUROC (95% CI)	p
Cirrus OCT RNFL Thicknesses		
Average	0.682 (0.544 - 0.821)	0.015
Superior	0.586 (0.439 - 0.732)	0.255
Inferior	0.624 (0.476 - 0.773)	0.076
Nasal	0.641 (0.498 - 0.784)	0.060
Temporal	0.616 (0.472 - 0.759)	0.124
Copernicus OCT RNFL Thicknesses		
Average	0.769 (0.646 - 0.893)	<0.001
Superior	0.769 (0.644 - 0.894)	<0.001
Inferior	0.703 (0.570 - 0.837)	0.007
Nasal	0.715 (0.582 - 0.848)	0.004
Temporal	0.735 (0.606 - 0.864)	0.002

AUROC: Area under receiver operating characteristic; **RNFL:** Retinal nerve fiber layer; **OCT:** Optical coherence tomography

thicknesses (ICC: 0.888, 0.837, 0.851, respectively) of Group II. Kim et al.[19] investigated the RNFL thickness and color code concordance between Stratus time domain-OCT and Cirrus HD-OCT, and they reported that for glaucomatous eyes, the inter-device concordance was excellent for average RNFL thickness and acceptable for each quadrant, except the nasal. They also demonstrated that when the RNFL was thin, Stratus OCT tended to produce thinner RNFL thickness than those measured by Cirrus OCT and thicker RNFL thickness than those measured by the Cirrus OCT when the RNFL was thick. This inconsistency between Cirrus and Stratus OCT has been reported in previous studies as well.[14,15] In the present study, we also observed partially similar discrepancies in the average and quadrant RNFL thickness measurements (except for the nasal quadrant RNFL thickness). The Bland-Altman scatter plot revealed that the bias of RNFL thickness measurements between the Cirrus and Copernicus OCT tended to be greater when the RNFL was thick in all eyes (Figure 1).

The differences in RNFL thickness are explained based on the differences in the scan paths and retinal layer segmentation algorithms of the devices. All OCT devices identify the vitreoretinal interface as the inner retinal border. Nevertheless, the identification of the outer retinal border significantly differs among devices. The spectral OCT systems typically image the outer retinal layers as three hyperreflective bands. The bands may correspond to the external limiting membrane, the junction of the outer and inner segments of the photoreceptor layer, and the retinal pigment epithelium. The Cirrus OCT uses the outermost hyperreflective band as the outer border of the retina, whereas the Copernicus OCT identifies the second inner reflective band as the outer border of the retina.[8,23,24] However, we could not find any data to explain how this difference affects the RNFL thickness measurement, and why segmentation algorithms do not work in the same way, regardless of the thickness of the RNFL.

Kim et al.[19] reported that the concordance of RNFL color code also ranged from fair to good (K:0.288–0.887) using Cohen's Kappa test, except for the nasal quadrant, 1 to 4, and the 9 o'clock sectors in all glaucoma groups and normal eyes. However, the color code concordance for the four colors was not evaluated in their study; they classified the color codes in only two groups (white and green colors were normal, and yellow and red colors were abnormal). We believe that this method does not reflect the actual concordance, as each color code (red, yellow, green, and white) has a different significance regarding the severity of glaucoma, particularly in cases of glaucoma suspect and early glaucoma. Therefore, we investigated the concordance for the four color codes using a 2×2 mixed-design ANOVA and found that the color code concordance was lower than that reported by Kim et al.[19] For average RNFL thickness, the color code concordance was 70% in Group I and 36.7% in Group II. The Cirrus OCT yielded more optimal color code findings for the average and quadrant RNFL thicknesses than the Copernicus; this discrepancy was more prominent in Group II. The frequency of the more optimal color code interpretation of the Cirrus for average and quadrant RNFL thicknesses (except the temporal) ranged from 60% to 70% in Group II and from 30% to 53% in Group I.

In another study, Rebolleda et al.[20] found a fair color code discordance and a substantial discrepancy between RNFL thickness measurements obtained using the Stratus, Cirrus, and Spectralis OCT in patients with relapsing-remitting multiple sclerosis with and without optic neuritis (ON). The discordance rate was higher for the eyes with ON than

for those without the condition (23.52% vs. 13.2%). They explained that higher color code discordance occurs in advanced glaucoma, and that the ON may be responsible for the higher frequency of abnormal codes. Green color codes represent a wide range of RNFL thicknesses (from the fifth to the 95th percentiles), whereas abnormal color codes represent narrower range (less than a fifth percentile). As a result of this, red and yellow color codes are more likely to disaccord between two devices than green color code.[19,20] We also find this interpretation plausible.

In the present study, the AUROC values of RNFL thicknesses, measured with the Cirrus OCT, were lower than those measured with the Copernicus. Previous studies have demonstrated that disease severity has a significant effect on the diagnostic performance of OCT devices.[18,25-27] Silverman et al.[28] investigated the diagnostic accuracy of Cirrus and Spectralis OCT for eyes with suspected glaucoma and reported that according to the normative database for progressor eyes that developed VF damage, the sensitivity of the average RNFL thickness outside normal limits was 23.5% for the Cirrus and 32.4% for the Spectralis; the sensitivity increased to about 50% for both devices, if at least one RNFL sector was outside normal limits. Unfortunately, we could not evaluate sector RNFL thicknesses and color codes because of proportional differences. Furthermore, the Copernicus OCT is not commonly used, and to the best of our knowledge, no other study, except for our previous study, has investigated its discriminatory power or sensitivity for glaucoma diagnosis. In our previous study, we found that the RNFL parameters, measured with the Copernicus, had favorable AUROC values in the discrimination of early glaucoma from ocular hypertension. However, the sample size of that study was small, and color code sensitivity was not investigated in that study.[29]

We believe that the rate of the inconsistency of RNFL measurements in the current study may not be enough to explain the low color code concordance. This may highlight a normative database discrepancy in addition to the software and hardware differences between the Cirrus and Copernicus OCT.

The normative database for the Cirrus OCT was developed from the data of 284 healthy individuals of different ethnicities; except for Caucasians, only a small number of subjects were included from other ethnicities.[30] Previous studies had reported that RNFL thickness was influenced by age, ethnicity, axial length, refractive power and optic disc size.[30-32] The normative data of the Cirrus OCT are stratified by age, but adjustments for race and refractive power are not available.[30] It has been reported that Asians have a greater RNFL thickness than that in the Cirrus normative database and this caused a poor color code concordance between the original and adjusted database in Korean and Vietnamese populations.[33,34] In another study, Peres et al.35 showed that the RNFL measurements of the Caucasians were significantly thinner than those of the Chinese population, and after applying the ethnicity-specific normative database, the RNFL abnormal color-code color code rate decreased significantly in the Caucasian population, but there was no significant change in the Chinese. They hypothesized that the RNFL measurements of the Caucasian were thinner than the RTVue built-in normative database that includes 18.35% Caucasian subjects, while other ethnicities such as Chinese, Hispanic and African-Americans comprise the rest. Similarly, myopic normative data adjustment has improved the diagnostic sensitivity of color codes as well.[36,37]

In the present study, the Cirrus OCT frequently displayed white color code (hyper normal), especially for the average and nasal quadrant measures, whereas the Copernicus did not display any white color code. Since there was no control group in the study, we could not evaluate the color code rates in the healthy subjects. Bulam et al.[38] reported that the RNFL thickness of the Turkish population in the average, superior, inferior, nasal and temporal quadrants were 95.01, 117.93, 123.80, 71.80 and 66.56 µm., respectively. Gür Güngör et al.[32] also reported similar measurements (94.35, 117.90, 123.76, 67.79 and 68.66 mm., respectively), except the nasal and temporal quadrants. In the two study, all RNFL thicknesses, except the nasal quadrant, are significantly thicker than those of the European descent in the Cirrus database (90.1, 113.0, 115.9, 70.1 and 61.2 µm., respectively).[30] We think that the frequent white color coding of Cirrus OCT may be due to the fact that the European descent makes up 43% of the normative data. However, we do not know exactly the normal range of the population-level variations stratified by age, and how Cirrus proprietary algorithm gives color probability codes. On the other hand, although the company proclaimed that the Copernicus has a normative database of more than 3000 patients, no detailed information has been disclosed yet.[39] We do not know how the RNFL database of the Copernicus is stratified according to age, ethnicity, and refractive power either. We believe that the lack of standardization of the normative databases can limit the value of the color code graphics in the early diagnosis of glaucoma. Serial scans are more useful than a single scan

in making diagnosis or treatment decisions, particularly for patients with suspected glaucoma or early glaucoma.

OCT normative databases must accurately represent the populations to which they are applied. Otherwise, they may lead to incorrect assessments.

Study Limitations

Our study has some limitations. First, the sample sizes of both groups were small. Second, there was no control group that comprised non-glaucomatous eyes. As a result, the inter-device concordance for the normal eyes of the Turkish population could not be tested. In addition, we could not investigate sector defects, which occur before quadrant changes in patients suspected of having glaucoma and patients with early-stage glaucoma, because of the sectional partitioning difference between the Cirrus and Copernicus OCT. New prospective studies with larger sample sizes and control groups that comprise the non-glaucomatous eye may be required to better investigate the differences of RNFL thickness measurements and their color codes among OCT devices.

CONCLUSION

The peripapillary RNFL thicknesses obtained via two different OCT devices used in the present study differed from each other. The OCT devices not only yielded various RNFL thickness measurements, but differences existed in their color code interpretations. We suggest that the software and normative database differences between devices as well as individual features of patients are considered when evaluating OCT scans, particularly in the diagnosis of early glaucoma.

REFERENCES

1. Casson RJ, Chidlow G, Wood JP, et al. Definition of glaucoma: clinical and experimental concepts. Clin Exp Ophthalmol 2012;40:341-9. https://doi.org/10.1111/j.1442-9071.2012.02773.x
2. Quigley HA, Dunkelberger GR, Green WR. Retinal ganglion cell atrophy correlated with automated perimetry in human eyes with glaucoma. Am J Ophthalmol 1989;107:453-64. https://doi.org/10.1016/0002-9394(89)90488-1
3. Quigley HA, Katz J, Derick RJ, et al. An evaluation of optic disc and nerve fiber layer examinations in monitoring progression of early glaucoma damage. Ophthalmology 1992;99:19-28. https://doi.org/10.1016/s0161-6420(92)32018-4
4. Sommer A, Katz J, Quigley HA, et al. Clinically detectable nerve fiber atrophy precedes the onset of glaucomatous field loss. Arch Ophthalmol 1991;109:77-83. https://doi.org/10.1001/archopht.1991.01080010079037
5. Kerrigan-Baumrind LA, Quigley HA, Pease ME, et al. Number of ganglion cells in glaucoma eyes compared with threshold visual field tests in the same persons. Invest Ophthalmol Vis Sci 2000;41:741-8.
6. Medeiros FA, Zangwill LM, Bowd C, et al. Use of progressive glaucomatous optic disk change as the reference standard for evaluation of diagnostic tests in glaucoma. Am J Ophthalmol 2005;139:1010-8. https://doi.org/10.1016/j.ajo.2005.01.003
7. Dharwadkar S, Nayak B. Optical coherence tomography in glaucoma-I. J Clin Ophthalmol Res 2017;5:51-63. https://doi.org/10.4103/2320-3897.195312
8. Schuman JS. Spectral domain optical coherence tomography for glaucoma (an AOS thesis). Trans Am Ophthalmol Soc 2008;106:426-58.
9. Dong ZM, Wollstein G, Schuman JS. Clinical Utility of Optical Coherence Tomography in Glaucoma. Invest Ophthalmol Vis Sci 2016;57:556-67. https://doi.org/10.1167/iovs.16-19933
10. Kansal V, Armstrong JJ, Pintwala R, et al. Optical coherence tomography for glaucoma diagnosis: An evidence based meta-analysis. PLoS One 2018;13:e0190621. https://doi.org/10.1371/journal.pone.0190621
11. Bussel II, Wollstein G, Schuman JS. OCT for glaucoma diagnosis, screening and detection of glaucoma progression. Br J Ophthalmol 2014;98 Suppl 2:ii15-19. https://doi.org/10.1136/bjophthalmol-2013-304326
12. Seibold LK, Mandava N, Kahook MY. Comparison of retinal nerve fiber layer thickness in normal eyes using time-domain and spectral-domain optical coherence tomography. Am J Ophthalmol 2010;150:807-14. https://doi.org/10.1016/j.ajo.2010.06.024
13. Leite MT, Rao HL, Weinreb RN, et al. Agreement among spectral-domain optical coherence tomography instruments for assessing retinal nerve fiber layer thickness. Am J Ophthalmol 2011;151:85-92.e1. https://doi.org/10.1016/j.ajo.2010.06.041
14. Lee ES, Kang SY, Choi EH, et al. Comparisons of nerve fiber layer thickness measurements between Stratus, Cirrus, and RTVue OCTs in healthy and glaucomatous eyes. Optom Vis Sci 2011;88:751-8. https://doi.org/10.1097/OPX.0b013e318215cc40
15. Knight OJ, Chang RT, Feuer WJ, et al. Comparison of retinal nerve fiber layer measurements using time domain and spectral domain optical coherent tomography. Ophthalmology 2009;116:1271-7. https://doi.org/10.1016/j.ophtha.2008.12.032
16. Akashi A, Kanamori A, Nakamura M, et al. Comparative assessment for the ability of Cirrus, RTVue, and 3D-OCT to diagnose glaucoma. Invest Ophthalmol Vis Sci 2013;54:4478-84. https://doi.org/10.1167/iovs.12-11268
17. Leite MT, Rao HL, Zangwill LM, et al. Comparison of the diagnostic accuracies of the Spectralis, Cirrus, and RTVue optical coherence tomography devices in glaucoma. Ophthalmology 2011;118:1334-9. https://doi.org/10.1016/j.ophtha.2010.11.029

18. Chen TC, Hoguet A, Junk AK, et al. Spectral-Domain OCT: Helping the Clinician Diagnose Glaucoma: A Report by the American Academy of Ophthalmology. Ophthalmology 2018;125:1817-27. https://doi.org/10.1016/j.ophtha.2018.05.008
19. Kim CY, Jung JW, Lee SY, et al. Agreement of retinal nerve fiber layer color codes between Stratus and Cirrus OCT according to glaucoma severity. Invest Ophthalmol Vis Sci 2012;53:3193-3200. https://doi.org/10.1167/iovs.12-9440
20. Rebolleda G, González-López JJ, Muñoz-Negrete FJ, et al. Color-code agreement among stratus, cirrus, and spectralis optical coherence tomography in relapsing-remitting multiple sclerosis with and without prior optic neuritis. Am J Ophthalmol 2013;155:890-897. https://doi.org/10.1016/j.ajo.2012.11.025
21. Hodapp E, Parrish RK, Anderson DR. Clinical decisions in glaucoma. Mosby Incorporated; 1993.
22. Budenz DL, Anderson DR, Varma R, et al. Determinants of normal retinal nerve fiber layer thickness measured by Stratus OCT. Ophthalmology 2007;114:1046-1052. https://doi.org/10.1016/j.ophtha.2006.08.046
23. Giani A, Cigada M, Choudhry N, et al. Reproducibility of retinal thickness measurements on normal and pathologic eyes by different optical coherence tomography instruments. Am J Ophthalmol 2010;150:815-824. https://doi.org/10.1016/j.ajo.2010.06.025
24. Wolf-Schnurrbusch UE, Ceklic L, Brinkmann CK, et al. Macular thickness measurements in healthy eyes using six different optical coherence tomography instruments. Invest Ophthalmol Vis Sci 2009;50:3432-3437. https://doi.org/10.1167/iovs.08-2970
25. Leite MT, Zangwill LM, Weinreb RN, et al. Effect of disease severity on the performance of Cirrus spectral-domain OCT for glaucoma diagnosis. Invest Ophthalmol Vis Sci 2010;51:4104-4109. https://doi.org/10.1167/iovs.09-4716
26. Bengtsson B, Andersson S, Heijl A. Performance of time-domain and spectral-domain Optical Coherence Tomography for glaucoma screening. Acta Ophthalmol 2012;90:310-315. https://doi.org/10.1111/j.1755-3768.2010.01977.x
27. Ustaoglu M, Solmaz N, Onder F. Discriminating performance of macular ganglion cell-inner plexiform layer thicknesses at different stages of glaucoma. Int J Ophthalmol 2019;12:464-471. https://doi.org/10.18240/ijo.2019.03.18
28. Silverman AL, Hammel N, Khachatryan N, et al. Diagnostic Accuracy of the Spectralis and Cirrus Reference Databases in Differentiating between Healthy and Early Glaucoma Eyes. Ophthalmology 2016;123:408-414. https://doi.org/10.1016/j.ophtha.2015.09.047
29. Solmaz N, Yaya O, Onder F. Optic nerve head and retinal nerve fiber layer analysis in ocular hypertension and early-stage glucoma using spectral-domain optical coherence tomography Copernicus. Turk J Ophthalmol 2014;44:35-41. https://doi.org/10.4274/tjo.71677
30. Knight OJ, Girkin CA, Budenz DL, Durbin MK, Feuer WJ; Cirrus OCT Normative Database Study Group. Effect of race, age, and axial length on optic nerve head parameters and retinal nerve fiber layer thickness measured by Cirrus HD-OCT. Arch Ophthalmol 2012;130:312-8. https://doi.org/10.1001/archopthalmol.2011.1576
31. Kang SH, Hong SW, Im SK, et al. Effect of myopia on the thickness of the retinal nerve fiber layer measured by Cirrus HD optical coherence tomography. Invest Ophthalmol Vis Sci 2010;51:4075-83. https://doi.org/10.1167/iovs.09-4737
32. Gür Güngör S, Akman A, Küçüködük A,et al. Retinal Nerve Fiber Layer Thicknesses in Three Different Optic Nerve Head Size Groups Measured by Cirrus Spectral Domain Optical Coherence Tomography. Turk J Ophthalmol 2016;46:58-61. https://doi.org/10.4274/tjo.29567
33. Hong S, Kim SM, Park K, et al. Adjusted color probability codes for peripapillary retinal nerve fiber layer thickness in healthy Koreans. BMC Ophthalmol 2014;14:38. https://doi.org/10.1186/1471-2415-14-38
34. Perez CI, Chansangpetch S, Thai A, et al. Normative Database and Color-code Agreement of Peripapillary Retinal Nerve Fiber Layer and Macular Ganglion Cell-inner Plexiform Layer Thickness in a Vietnamese Population. J Glaucoma 2018;27:665-73. https://doi.org/10.1097/IJG.0000000000001001
35. Perez CI, Chansangpetch S, Mora M, et al. Ethnicity-Specific Database Improves the Diagnostic Ability of Peripapillary Retinal Nerve Fiber Layer Thickness to Detect Glaucoma. Am J Ophthalmol 2021;221:311-22. https://doi.org/10.1016/j.ajo.2020.07.043
36. Seol BR, Kim DM, Park KH, et al. Assessment of Optical Coherence Tomography Color Probability Codes in Myopic Glaucoma Eyes After Applying a Myopic Normative Database. Am J Ophthalmol 2017;183:147-55. https://doi.org/10.1016/j.ajo.2017.09.010
37. Biswas S, Lin C, Leung CK. Evaluation of a Myopic Normative Database for Analysis of Retinal Nerve Fiber Layer Thickness. JAMA Ophthalmol 2016;134:1032-9. https://doi.org/10.1001/jamaophthalmol.2016.2343
38. Bulam B, Gür Güngör S, Akman A. Optic Nerve Head Parameters in Healthy Turkish Population Using Spectral Domain Optical Coherence Tomography. Glo-Kat 2014;9:181-4.
39. Kiernan DF, Hariprasad SM. Normative Databases in SD-OCT: A Status Report. A comprehensive look at the evolution of OCT software design and database development. Retinal Physician 2010 April. Available at: https://retinalphysician.com/issues/2010/april/normative-databases-in-sd-oct-a-status-report/