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Article

New Normative Database of Inner Macular Layer Thickness Measured by Spectralis OCT Used as Reference Standard for Glaucoma Detection

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Purpose: This study examines the capacity to detect glaucoma of inner macular layer thickness measured by spectral-domain optical coherence tomography (SD-OCT) using a new normative database as the reference standard.

Methods: Participants ($N = 148$) were recruited from Leuven (Belgium) and Zaragoza (Spain): 74 patients with early/moderate glaucoma and 74 age-matched healthy controls. One eye was randomly selected for a macular scan using the Spectralis SD-OCT. The variables measured with the instrument's segmentation software were: macular nerve fiber layer (mRNFL), ganglion cell layer (GCL), and inner plexiform layer (IPL) volume and thickness along with circumpapillary RNFL thickness (cpRNFL). The new normative database of macular variables was used to define the cutoff of normality as the fifth percentile by age group. Sensitivity, specificity, and area under the receiver operating characteristic curve (AUROC) of each macular measurement and of cpRNFL were used to distinguish between patients and controls.

Results: Overall sensitivity and specificity to detect early-moderate glaucoma were 42.2% and 88.9% for mRNFL, 42.4% and 95.6% for GCL, 42.2% and 94.5% for IPL, and 53% and 94.6% for RNFL, respectively. The best macular variable to discriminate between the two groups of subjects was outer temporal GCL thickness as indicated by an AUROC of 0.903. This variable performed similarly to mean cpRNFL thickness (AUROC = 0.845; $P = 0.29$).

Conclusions: Using our normative database as reference, the diagnostic power of inner macular layer thickness proved comparable to that of peripapillary RNFL thickness.

Translational Relevance: Spectralis SD-OCT, cpRNFL thickness, and individual macular inner layer thicknesses show comparable diagnostic capacity for glaucoma and RNFL, GCL, and IPL thickness may be useful as an alternative diagnostic test when the measure of cpRNFL shows artifacts.

Introduction

Damage to the macula is common during the early stages of glaucoma.[1] However, this damage may be missed by both routine optical coherence tomography (OCT) and visual field (VF). Routine VF tests use test points spaced 6° apart. In the 24-2 VF test, for example, only four of the test points fall in the region of the macula,[1] which has the greatest density of ganglion cells. In patients with central VF loss, it has been shown that the thickness of the ganglion cell-inner plexiform complex is a better variable to detect

glaucoma than peripapillary retinal nerve fiber layer (RNFL) thickness.[2] Detecting macular thickness changes is important since have been recently reported that over 50% of eyes with mild to moderate glaucoma had defects within the central ±3° of the visual field.[3]

The latest software of the spectral-domain (SD) OCT instrument Spectralis allows for the automatic segmentation of the retinal layers but lacks a normative database for the thickness of each layer. Currently, a normative database of the thickness of each macular layer using Spectralis SD-OCT is not included in the device, and it would be useful to know if the inner macular layer thickness is within normal limits in glaucoma suspects or when peripapillary RNFL is not helpful due peripapillary abnormalities.

In prior work, we generated a normative database for macular inner retinal layer thickness consisting of the volumes and thicknesses of the macular RNFL (mRNFL), ganglion cell layer (GCL), and inner plexiform layer (IPL).[4] For this study 300 healthy volunteers were recruited between the relatives and employees of Hospital Clínico San Carlos (Madrid, Spain) to develop the normative database. Every eye included in the study had a visual acuity equal or greater than 20/40, a sphere between ±5 diopters (D) and a cylinder between ±3 D, and no other ocular abnormalities. Macular OCT scans were performed on all patients with Spectralis OCT, the volume and the thickness of mRNFL, GCL, and IPL were analyzed with the Spectralis OCT segmentation software. The mean, 1st, 5th, and 95th percentile and the confidence interval of 95th and 99th were calculated for each variable to develop the normative database.

The present study was designed to determine the diagnostic capacity of inner retinal layer thickness to detect glaucoma using this database generated as recommended by Realini et al.[5] to define the cutoff of normality. This diagnostic capacity was then compared with that of the thickness of the circumpapillary RNFL (cpRNFL).

Materials and Methods

Subjects

For this multicenter, observational, cross-sectional study, 148 eyes of patients with incipient to moderate glaucoma and control subjects were examined. All participants signed an informed consent form after listening to a detailed explanation of the tests and their purpose. The study protocol adhered to the tenets of the Declaration of Helsinki and received institutional review board approval from the Hospital Clínico San Carlos, Madrid (Spain), Hospital Miguel Servet, Zaragoza (Spain), and UZ Leuven, Leuven (Belgium).

All subjects underwent a complete ophthalmic examination including biomicroscopy, measurement of intraocular pressure (IOP), refraction, and a fundus exam. Medical records were also examined.

Inclusion criteria were: a visual acuity equal or greater than 20/40, a sphere between ±5 D, and a cylinder between ±3 D. Participants recently undergoing eye surgery (<1 year), with macular or retinal abnormalities and/or a medical history of neurological disease, diabetes, or any uncontrolled disease were excluded. Additional exclusion criteria for control subjects were a medical history of IOP >21 mm Hg or glaucoma.

Only Caucasian individuals were selected for this study. For the patient group, 74 patients with primary open-angle glaucoma were recruited among the outpatients of the Glaucoma Clinic UZ Leuven and Hospital Miguel Servet, Zaragoza. Glaucoma diagnosis was performed by a glaucoma expert according to the criteria: glaucomatous optic neuropathy, IOP >21 mm Hg, and a visual field defect indicated by an Octopus perimetry (Haag-Streit, Mason, OH) test result of mean deviation (MD) from 3 to 9 dB. Patients with secondary glaucoma were excluded.

All patients underwent VF testing at least twice before their inclusion in the study. To define a VF defect as glaucomatous at least one of the following had to be detected in consecutive tests: having a cluster of three or more nonedge points showing a $P < 0.05$ and at least one point with a $P < 0.01$ in the pattern deviation probability plot, or pattern standard deviation of less than 5%. Reliability criteria were fixation losses of 20% or less, false-positive results of 15% or less, and false-negative results of 33% or less.

For the control group, we recruited 74 healthy subjects visiting the Glaucoma Clinic UZ Leuven and Hospital Miguel Servet, Zaragoza for a routine eye test. These participants were selected following the recommendations of Realini et al.[4]

In each participant, one eye was randomly selected for the final analysis provided both eyes met the inclusion criteria. An online statistical computing web programming was used to generate the randomization schedule.

Optical Coherence Tomography

The Spectralis OCT (software version 6.0c; Heidelberg Engineering, Heidelberg, Germany) was used by an experienced operator to scan the macular and peripapillary regions on the same day as the rest of the tests without pupil dilation in a dark room. The automatic eye tracking technology of the Spectralis OCT maintains fixation on the retina, and only well-centered images with a signal strength of >20 db were accepted.

CpRNFL thickness measurements were made in the participants from Zaragoza (24 glaucoma patients and 24 controls) by conducting circular scans at a scanning angle of 12°, assuming a standard corneal curvature of 7.7 mm; thus, projecting a 3.5-mm diameter circle on the retina. This full RNFL circle scan contained 768 A-scans along a peripapillary circle of 360°. The Spectralis software divides this circle into 6 regions: temporal, superotemporal, superonasal, nasal, inferonasal, and inferotemporal. Overall, RNFL thickness is provided as a number in the center.

For the macular measurements in all participants, the scan was conducted on a 20° × 20° cube with 49 raster lines separated by 120 µm, each containing 1046 pixels. Macular and inner retinal layer thicknesses were measured on 1-, 3-, and 6-mm rings as indicated in the macular map reported in the Early Treatment Diabetic Retinopathy Study (ETDRS). The 1-mm ring was defined as central thickness and the 3- and 6-mm rings as inner and outer rings each divided into the quadrants superior, nasal, inferior, and temporal. The numerical values for each of the nine subfields and macular volume were recorded and the device's segmentation software was then used to obtain individual retinal layer thickness measurements for the mRNFL, GCL, and IPL.

Statistical Analysis

Descriptive statistics are provided as mean ± standard deviation. Mean macular RNFL, GCL, IPL, and peripapillary RNFL thicknesses were compared between control subjects and glaucoma patients using the Student's *t*-test for independent samples (applying Bonferroni correction).

The diagnostic capacity of each variable to differentiate between healthy and glaucoma eyes was determined by calculating the sensitivity, specificity, positive predictive value, negative predictive value, positive and negative likelihood ratio, and diagnostic odds ratio. The cutoff used was the fifth percentile in the normality database for each of four established age group (18–33, 34–50, 51–68, and 69–87 years).

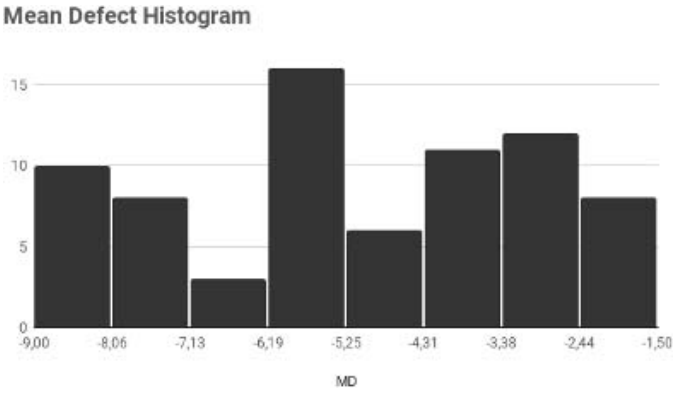

Figure 1. Histogram of perimetry mean defect for glaucoma patients.

We also calculated areas under receiver operating characteristic curves (AUROC) for two specific purposes: to assess the diagnostic power of each variable and compare the discrimination capacities of the macular and peripapillary variables. Finally, the differences between the macular variable AUROC and peripapillary variable AUROC were examined using the method of DeLong et al.[6] All statistical tests were performed using the software package SPSS 15 edition (SPSS, Inc., Chicago, IL). Significance was set at $P < 0.05$.

Results

The study participants (67 men, 81 women, all Caucasian) were recruited from the UZ Leuven Hospital ($n = 100$) and Hospital Miguel Servet, Zaragoza ($n = 48$). In these subjects, data for analysis were obtained for 78 right eyes and 70 left eyes. Glaucoma patients and control subjects were of similar mean age, 62.53 ± 8.80 years and 61.95 ± 9.58 years, respectively ($P = 0.7$). The mean MD for the glaucoma patients was −7.40 ± 6.91 dB (Fig. 1).

Mean thickness data for mRNFL, GCL, IPL ($n = 148$), and cpRNFL ($n = 48$) are provided in Table 1. When retinal layer thicknesses were compared between patients and controls, the major differences detected expressed as mean thickness reductions in glaucoma patients versus controls were: mRNFL outer inferior quadrant 13.99 µm; GCL, inner temporal quadrant 12.69 µm, outer temporal quadrant 9.84 µm, and inner inferior quadrant 10.91 µm; and IPL, inner temporal quadrant 7.58 µm. For cpRNFL, the greatest mean thickness reduction of

Table 1. Retinal Layer Thicknesses and Volumes Measured in Glaucoma Patients and Controls

Parameter	Control	Glaucoma (MD > −9 dB)	*P*
Macular RNFL			
Volume, mm^3	0.93 ± 0.11	0.74 ± 0.14	<0.001
Central, μm	13.03 ± 2.55	11.59 ± 3.00	<0.001
Inner nasal, μm	21.00 ± 2.40	20.23 ± 2.88	0.08
Outer nasal, μm	49.34 ± 7.92	39.18 ± 9.63	<0.001
Inner superior, μm	24.53 ± 3.36	21.82 ± 3.39	<0.001
Outer superior, μm	37.80 ± 6.73	29.80 ± 7.60	<0.001
Inner temporal, μm	17.30 ± 1.37	17.89 ± 1.88	0.03
Outer temporal, μm	19.34 ± 1.96	18.07 ± 2.04	<0.001
Inner inferior, μm	25.08 ± 3.72	21.46 ± 3.62	<0.001
Outer inferior, μm	40.76 ± 7.26	26.77 ± 9.18	<0.001
GCL			
Volume, mm^3	1.07 ± 0.10	0.86 ± 0.14	<0.001
Central, μm	16.95 ± 5.74	14.04 ± 4.61	<0.001
Inner nasal, μm	50.12 ± 6.77	42.66 ± 9.55	<0.001
Outer nasal, μm	37.26 ± 3.72	32.20 ± 5.53	<0.001
Inner superior, μm	51.36 ± 5.89	42.57 ± 9.95	<0.001
Outer superior, μm	34.32 ± 3.52	28.88 ± 4.69	<0.001
Inner temporal, μm	46.22 ± 6.12	33.53 ± 8.89	<0.001
Outer temporal, μm	35.53 ± 4.76	25.69 ± 5.68	<0.001
Inner inferior, μm	50.99 ± 5.69	40.08 ± 10.09	<0.001
Outer inferior, μm	32.91 ± 3.50	26.27 ± 5.39	<0.001
IPL			
Volume, mm^3	0.98 ± 0.07	0.77 ± 0.09	<0.001
Central, μm	22.30 ± 4.49	20.34 ± 3.93	0.01
Inner nasal, μm	42.34 ± 3.79	37.50 ± 5.54	<0.001
Outer nasal, μm	28.96 ± 2.91	25.69 ± 3.95	<0.001
Inner superior, μm	41.04 ± 3.76	35.82 ± 6.04	<0.001
Outer superior, μm	28.04 ± 2.66	24.39 ± 3.44	<0.001
Inner temporal, μm	41.39 ± 4.04	33.81 ± 5.56	<0.001
Outer temporal, μm	32.31 ± 3.36	26.91 ± 3.94	<0.001
Inner inferior, μm	40.73 ± 3.87	34.32 ± 6.02	<0.001
Outer inferior, μm	27.03 ± 3.04	22.68 ± 3.37	<0.001
cpRNFL			
Global, μm	95.71 ± 14.89	70.67 ± 17.95	<0.001
Temporal, μm	69.71 ± 15.28	59.29 ± 12.23	0.01
Superior temporal, μm	133.46 ± 19.61	96.83 ± 28.55	<0.001
Inferior temporal, μm	136.88 ± 22.90	89.38 ± 36.71	<0.001
Nasal, μm	73.71 ± 18.83	53.50 ± 18.9	<0.001
Superior nasal, μm	99.75 ± 24.50	77.04 ± 27.36	<0.001
Inferior nasal, μm	104.54 ± 24.84	76.54 ± 27.45	<0.001

47.5 μm was observed in the inferior temporal quadrant.

The AUROC, sensitivity, specificity, positive and negative predictive values, positive and negative likelihood ratios, and the diagnostic odds ratios calculated for each variable are shown in Table 2. To calculate all these indicators except AUROC, we used the fifth percentile obtained in the normative database.

According to the cutoffs defined, the variables showing the best sensitivity (S) and specificity (Sp) to

Table 2. Glaucoma Diagnostic Capacity of Inner Macular Layers and Circumpapillary RNFL Using as Reference the New Normative Database

Parameter	AUROC	Sensitivity %	Specificity %	VPP %	VPN %	LR+	LR−	OR
Macular RNFL, $n = 148$								
Volume	0.862	63.5	93.2	90.4	71.9	9.4	0.39	24.02
Central	0.638	23	94.6	81	55.1	4.25	0.81	5.22
Inner nasal	0.598	28.4	89.2	72.4	55.5	2.63	0.8	3.27
Outer nasal	0.795	44.6	91.9	84.6	62.4	5.5	0.6	9.12
Inner superior	0.695	40.5	94.6	88.20	61.4	7.5	0.63	11.93
Outer superior	0.796	43.2	93.2	86.5	62.2	6.4	0.61	10.51
Inner temporal	0.408	24.3	74.3	48.6	49.5	0.95	1.02	0.93
Outer temporal	0.685	44.6	81.1	70.2	59.4	2.36	0.68	3.45
Inner inferior	0.759	41.9	87.8	77.5	60.2	3.44	0.66	5.21
Outer inferior	0.880	68.9	89.2	86.4	74.2	6.38	0.35	18.29
GCL, $n = 148$								
Volume	0.889	50	98.6	97.4	66.4	37	0.51	73
Central	0.657	24.3	93.2	78.3	55.2	3.6	0.81	4.44
Inner nasal	0.761	28.4	94.6	84	56.9	5.25	0.76	6.93
Outer nasal	0.775	23	98.6	94.4	56.2	17	0.78	21.77
Inner superior	0.779	32.4	97.3	92.3	59	12	0.69	17.28
Outer superior	0.817	37.8	98.6	96.6	61.3	28	0.63	44.43
Inner temporal	0.869	67.6	93.2	90.9	74.2	10	0.35	28.75
Outer temporal	0.903	71.6	87.5	85.5	75	5.73	0.32	17.67
Inner inferior	0.830	41.9	95.9	91.2	62.3	10.33	0.61	17.06
Outer inferior	0.843	47.3	98.6	97.2	65.2	35	0.53	65.51
IPL, $n = 148$								
Volume	0.844	51.4	94.6	90.5	66	9.5	0.51	18.47
Central	0.623	14.9	94.6	73.3	52.6	2.75	0.9	3.06
Inner nasal	0.761	40.5	97.3	93.8	62.1	15	0.61	24.55
Outer nasal	0.734	33.8	95.9	89.3	59.2	8.33	0.69	12.07
Inner superior	0.757	39.2	91.9	82.9	60.2	4.83	0.66	7.3
Outer superior	0.790	55.4	90.5	85.4	67	5.86	0.49	11.89
Inner temporal	0.848	52.7	97.3	95.1	67.3	19.5	0.49	40.11
Outer temporal	0.856	25.7	97.3	90.5	56.7	9.5	0.76	12.44
Inner inferior	0.801	54.1	95.9	93	67.6	13.33	0.48	27.84
Outer inferior	0.816	54.1	90.5	85.1	66.3	5.71	0.51	11.26
Peripapillary RNFL, $n = 48$								
Overall	0.845	70.8	95.7	94.4	76.7	17	0.3	55.86
Temporal	0.731	66.7	95.8	94.1	74.2	16	0.35	46
Superior temporal	0.853	62.5	95.8	93.8	71.9	15	0.39	38.33
Inferior temporal	0.856	70.8	87.5	85	75	5.67	0.33	17
Nasal	0.806	41.7	95.8	90.9	62.2	10	0.61	16.43
Superior nasal	0.755	50	91.7	85.7	64.7	6	0.55	11
Inferior nasal	0.810	33.3	100	100	60	0	0.67	0

VPP, positive predictive value; VPN, negative predictive value; LR+, positive likelihood ratio; LR−, negative likelihood ratio; OR: diagnostic odds ratio.

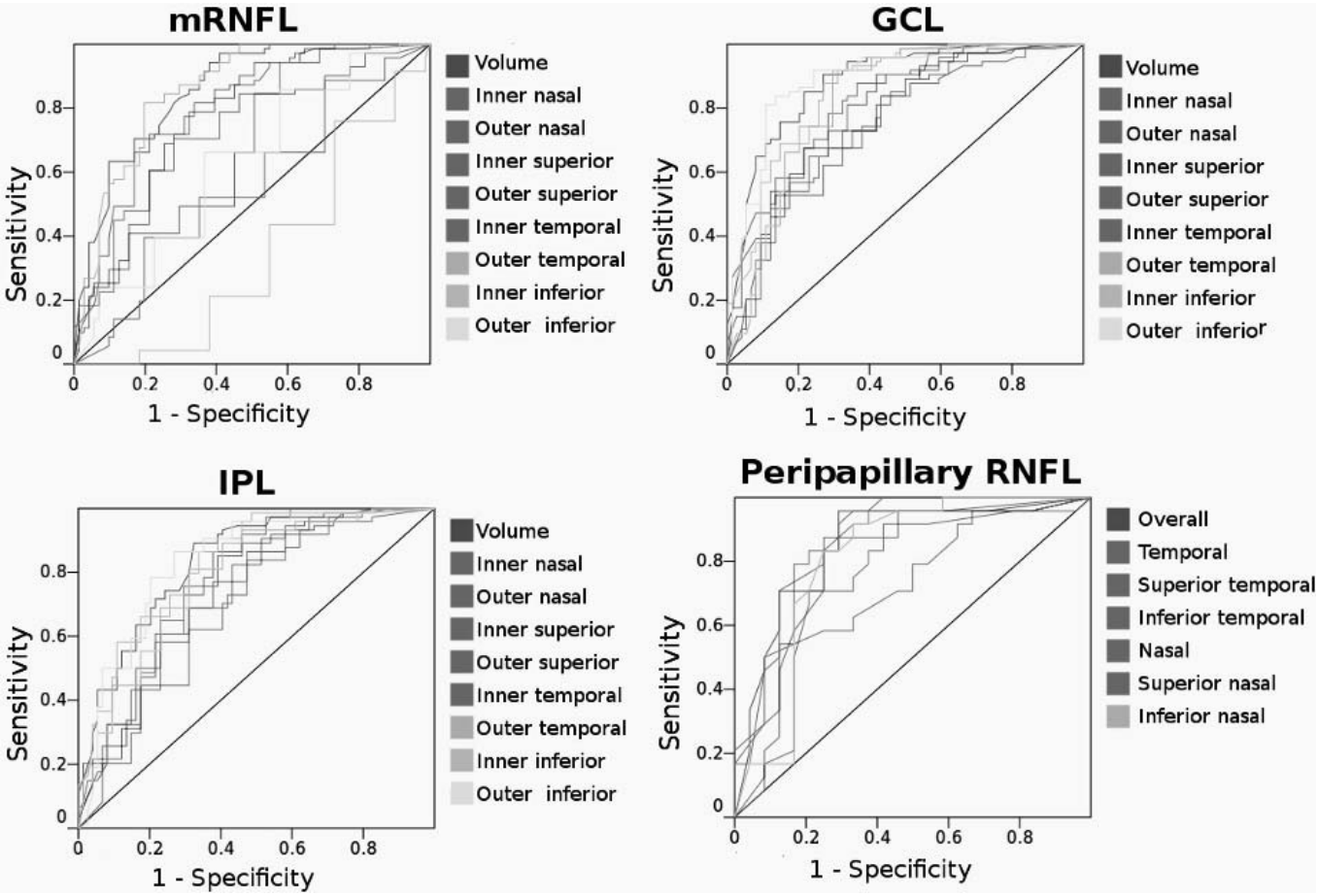

Figure 2. ROC curve plots for mRNFL, GCL, IPL, and peripapillary RNFL.

distinguish between glaucomatous and normal eyes were mRNFL volume (S = 63.5%; Sp = 93.2%), inner temporal GCL thickness (S = 67.5%; Sp = 93.2%), inner inferior IPL thickness (S = 54.1%; Sp = 95.9%), and overall cpRNFL thickness (S = 70.8%; Sp = 95.7%).

According to the AUROC recorded for each layer examined, the outer inferior mRNFL zone (AUROC = 0.880) showed the best diagnostic capacity, while worse results were obtained for the inner nasal and inner temporal mRNFL quadrants with AUROC close to 0.5. For the GCL, the best AUROC was obtained for the outer temporal quadrant (0.930) and all remaining zones except the central one showed AUROC over 0.7. For the IPL, the best AUROC was that recorded for the outer temporal quadrant (0.856) though again every subfield but the central one returned an AUROC greater than 0.7. The ROC curve plots for each layer are represented in Figure 2.

No significant differences were found between the two best AUROC observed for the macular retinal inner layers and the AUROC recorded for mean overall cpRNFL thickness. The results of this analysis are shown in Table 3.

Discussion

Recent efforts have been made to develop new imaging techniques that will help detect glaucoma in its early stages. One of these techniques, SD-OCT, has served to identify new structural parameters to measure RNFL thickness in the peripapillary area, as well as retinal thickness and retinal inner layer thicknesses in the region of the macula.[7]

In our study, significantly reduced thicknesses were observed in glaucoma patients compared with healthy controls in most inner retinal layer zones of the macular area (mRNFL, GCL, and IPL). It is important to study this differences to understand how glaucoma affects the macula and it may be helpful diagnosing glaucoma in an earlier stage.

In the inner temporal zone our mRNFL thickness measurements indicated a thickness increase of 0.59

Table 3. Comparing Areas Under the ROC Curves Among the Best Discriminatory Parameters

Comparison Between		Difference Between AUROC	*P*
Overall cpRNFL thickness	Outer superior mRNFL thickness	0.0842	0.258
	mRNFL volume	0.0399	0.580
	Outer temporal GLC thickness	0.0747	0.287
	GCL volume	0.0304	0.656
	Inner temporal IPL thickness	0.0920	0.266
	Outer temporal IPL thickness	0.0208	0.777

μm for glaucoma patients versus controls. This increase, despite being statistically significant ($P = 0.03$), is not clinically relevant. The most pronounced mRNFL thickness reduction detected was that noted for the outer inferior quadrant (mean reduction 13.99 μm). Other authors such as Hood et al.[1] have also reported greatest RNFL thickness reductions in glaucomatous eyes in the arcuate regions, with greatest thinning produced in the outer inferior zone.

Consistent with the present findings, in the study by Hood et al.[1] greater thinning of the GCL-IPL complex was detected in the temporal quadrants of the macula. Also in line with our measurements, Tan et al.[8] noted greatest ganglion cell complex thickness reductions in preperimetric glaucoma patients versus controls in the temporal quadrants. Similarly, a recent study has shown GCL and IPL thinning when these layers were measured individually by Spectralis OCT in patients with glaucoma compared with healthy individuals.[9]

When comparing the glaucoma diagnostic capacity of the retinal inner layers, the mRNFL measurement that showed the best AUROC was the outer inferior quadrant. Inner nasal and inner temporal mRNFL thicknesses offered the worse diagnostic power indicated by AUROC close to 0.5. Consequently, we can state that this inner region is barely able to discriminate between healthy subjects and glaucoma patients. In a similar study comparing glaucoma suspect patients and controls, the best AUROC for mRNFL thickness were obtained for the quadrants inner temporal (AUROC = 0.742) and outer temporal (AUROC = 0.660).[9] These findings are in agreement with the present results and are also in line with histologic observations of the death of the ganglion cell body when the axon degenerates.[10]

Among our GCL thickness measurements, those that showed the best AUROC were the measurements taken in the outer temporal and remaining subfields except the central zone that showed AUROC over 0.7. For IPL thickness, the highest AUROC was obtained for the outer temporal and, again, areas under the curve for every zone but the central were greater than 0.7. These results are similar to those obtained in the study by Chien et al.,[9] in which best AUROC were obtained in the outer temporal quadrant, both for GCL and IPL thickness (0.942 and 0.890, respectively). The best AUROC obtained by Chien et al.[8] is slightly higher than the one obtained in our study. This small difference could be attributed to the glaucoma patients in the Chien et al.[8] study showing a greater mean visual field defect than our glaucoma patients (MD = −7.40 ± 6.91 dB vs. −5.01 ± 2.06 dB). This difference is important because it could indicate that the diagnostic power of the test improves with glaucoma severity, as occurs with most diagnostic tests.

The GCL and IPL thinning found here in patients with glaucoma is consistent with the thickness reductions recently reported by Lee et al.,[11] who observed greater AUROC for Spectralis-OCT IPL plus GCL thickness in the outer temporal and outer inferior quadrants.

The sensitivity and specificity of the cutoffs defined by the new database of retinal layer thicknesses by macular zone are similar to those reported by others. In the Cochrane library review, the sensitivities and specificities of several GCC and GCL-IPL parameters reported in 35 studies measured with the instruments Topcon 3D OCT, RTVue OCT, and Cirrus HD OCT were in the same range as observed for cpRNFL thickness measurements.[12]

In our study, except for measurements in the IPL nasal quadrants, inner layers thickness in the outer zones showed a better diagnostic capacity than thickness measurements made in the inner quadrants of the macula. This is attributable to a greater susceptibility to glaucomatous damage of the outer arcuate fibers followed by the superior arcuate fibers, which encompass the outer areas of the ETDRS subfields. In contrast, the papillomacular bundle, which contains fibers from the central ETDRS zones, remains unaffected until advanced stages of glauco-

ma. This vulnerability of the inferior arcuate fibers can be explained by their introduction in the optic nerve through the inferior quadrant of the optic disc, which is the first affected structure in this progressive optic neuropathy. In contrast, the superior arcuate fibers insert in the optic nerve through the temporal zone. Thus, this region is unaffected until more advanced stages of glaucoma.[1]

No significant differences were found here between the best AUROC obtained for the macular parameters and the AUROC obtained for overall cpRNFL thickness. This finding is in agreement with the findings of the Cochrane library review,[12] in which no differences emerged among the diagnostic capacities of retinal inner layer thickness, optic nerve head parameters and cpRNFL thickness. However, it should be stressed that no Spectralis SD-OCT measurements were included in the Cochrane review. Martínez de la Casa et al.[13] reported a significant difference when comparing AUROC for macular RNFL thickness measured in the outer temporal quadrant and the cpRNFL variable showing the best diagnostic capacity, temporal cpRNFL thickness (difference between both AUROC = 0.147, P = 0.042). In contrast, in a recent study published by Pazos et al.,[14] though macular variables showed a high diagnostic power, the diagnostic capacity of both macular and peripapillary parameters was comparable. This differences in the results may be due to the difference on the glaucoma stage of the patients, because the patients included by Martinez de la Casa et al. were glaucoma suspects, and ours and Pazos et al. patients had established glaucoma.

In a recent review,[15] the diagnostic capacities of macular and peripapillary measurements made by RTVue, Topcon 3D, and Cirrus OCT reported in 34 studies (n = 2164 participants) were compared. The conclusion of this review was that using the methods available today, cpRNFL thickness measurements are better than macular thickness measurements to detect glaucoma though the differences detected using these OCT techniques were small.

Our study has several limitations. As it is a case-control study, it could overestimate the diagnostic capacity of the tests used. Also, the age group of the subjects was taken into account when establishing the cutoff point for glaucoma, whereas sex was not considered. Several studies have shown thickness differences between males and females in the majority of quadrants[16–18] possibly leading to the incorrect classification of subjects with normal, borderline, or abnormal retinal layer thickness measurements. Another limitation of our study was that only Caucasian patients were included, such that results might not be the same for patients of other ethnicities.[19–21] Only patients with moderate refractive errors were include in this study, so ours results may not be applicable to patients with high refractive errors. This measurements where done with three different Spectralis OCT devices but small changes may be found when using another device. Further, as it was a cross-sectional study, neither patients nor controls were followed after the Spectralis OCT measurements. Therefore, some control subjects may have developed glaucoma in the months following their inclusion in the study. Finally, the sample size used to compare the diagnostic capacities of retinal inner layer thicknesses and peripapillary RNFL thickness was small (n = 48), so discrete differences could have been undetected.

Currently, Spectralis SD-OCT does not provide any data about the normality or abnormality of the macular layer thickness, and it only shows a thickness distribution map of every layer. To the authors knowledge, this is the first study to analyze the diagnostic capacity of the inner macular layer thickness using a normative database, and including the normality values in the device would made the results interpretation easier.

In summary, as measured by Spectralis SD-OCT, cpRNFL thickness and individual macular inner layer thicknesses show comparable diagnostic capacity for glaucoma. Notwithstanding, it has been suggested that macular OCT might perform better in patients with central VF defects than in patients with peripheral defects.[2] There is, therefore, a need for further studies on this topic in which the pattern of the VF defect is also considered.

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