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The Relationship between Visual Field and Retinal Nerve Fiber Layer Measurements in Patients with Multiple Sclerosis

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Abstract

Purpose—To investigate the relationship between visual function, measured by standard automated perimetry (SAP), and retinal nerve fiber layer (RNFL) thickness, measured by optical coherence tomography (OCT), in patients with multiple sclerosis (MS).

Methods—SAP and RNFL thickness were measured in patients with MS in 28 eyes with the last optic neuritis (ON) ≥ 6 months prior (ON group) and 33 eyes without ON history (non-ON group). Abnormal overall or quadrant RNFL thickness was defined by measured values below 5% of the norm. A whole visual field or a sector of the field was classified as abnormal by using cluster criteria on total-deviation plots. Agreement between SAP and OCT results in classifying eyes/sectors was presented as a percentage of observed agreement, along with the *ACI* statistic, which corrects for chance agreement. Regression analyses were performed relating several SAP parameters and RNFL thickness in the ON group.

Results—ON eyes showed more loss of visual sensitivity (MD, $P = 0.02$) and more loss of RNFL thickness ($P < 0.0001$) than did non-ON eyes. SAP and OCT agreed in 86% ($ACI = 0.78$) of eyes and 69% ($ACI = 0.38$) of sectors in the ON group and 61% ($ACI = 0.33$) of eyes and 66% ($ACI = 0.48$) of sectors in the non-ON group. Overall RNFL thickness was related to MD (dB) by a simple exponential function ($R^2 = 0.48$), supporting a linear relationship between these measures when both are expressed on linear scales. Absolute Pearson correlation coefficients for overall RNFL thickness and several SAP parameters ranged from 0.51 to 0.69.

Conclusions—Good agreement between SAP and OCT was found in ON eyes but not in non-ON eyes or in individual sectors in either group. The findings in this study provide further support for the utility of combining structural and functional testing in clinical research on patients with MS, as well as in future neuroprotection trials for which the anterior visual pathways in patients with MS and optic neuritis may be used as a model.

Multiple sclerosis (MS) is an inflammatory demyelinating disease of the central nervous system that often involves the optic nerve. More than 50% of patients with MS have optic neuritis (ON) at some time during the disease. After recovery from an acute ON attack, subjective visual complaints, and abnormal visual functions frequently remain even in the presence of apparently normal visual acuities.^{1–4}

The current understanding of the pathogenesis of MS suggests that persistent visual disability after recovery of ON is attributed to axonal damage in the optic nerve.^{5,6} In fact, retinal ganglion cell (RGC) axonal loss in ON was reported decades ago, based on careful fundoscopic examination,^{7,8} and demonstrated by direct axonal counting in postmortem tissue.⁹ Recent developments in optical imaging devices have allowed noninvasive quantitative measurements of RGC axons (i.e., the retinal nerve fiber layer [RNFL]) in patients with ON and MS.^{10–13} In particular, optical coherence tomography (OCT), which provides cross-sectional measurements of RNFL thickness that are close to anatomic resolution,¹⁴ has been used in several recent studies of patients with ON/MS.^{15–19} OCT has revealed significant thinning of the RNFL, within 3 to 6 months after an acute episode of ON, in as many as three quarters of patients tested.^{15,20} The RGC axonal damage revealed by OCT appeared to be more prevalent and extensive than the residual functional deficits reported in patients with ON.^{21,22} This finding raises the question of whether structural tests such as OCT are more advantageous than functional tests such as standard automated perimetry (SAP), in measuring optic nerve damage in ON/MS.²³ A good understanding of the structural and functional relationship of RGCs is not only fundamental in the study of the underlying visual mechanisms, but is also important for selecting an appropriate strategy to monitor disease progression and evaluate the efficacy of treatments in the clinic.

Structural and functional relationships have been extensively studied in glaucoma and, despite the ongoing controversies and debates, in general, a concordance between SAP and RGCs/RNFL was demonstrated when appropriate scales were applied for comparison.^{24–27} In optic neuritis, a detailed comparison between visual sensitivity loss and RNFL loss in ON is clearly needed as well. In this study, a topographic comparison was made between SAP and OCT RNFL thickness measurements in eyes of patients with MS, with and without a history of optic neuritis. Regression analyses were performed on data from ON eyes between RNFL thickness and several SAP parameters in logarithmic or linear scales. To allow sufficient time for retrograde degeneration in the RNFL, only eyes with at least a 6-month recovery time from the last episode of ON were studied.^{15,18,28,29}

Methods

Subjects

Thirty-six patients with MS (9 men, 27 women) were enrolled in the study. Thirty-four had relapsing–remitting (RR) MS and two had secondary progressive MS. The duration of the disease ranged from newly diagnosed to 21 years with a median of 5 years. The age range was 21 to 56 years with a mean of 39 ± 9 SD years.

All patients went through comprehensive neuro-ophthalmic examinations, and all related medical records were carefully reviewed. The diagnosis of ON was based on clinical criteria.³⁰ The patients had no concomitant ocular diseases or systemic conditions that could affect the visual system.

Procedures adhered to the tenets of Declaration of Helsinki, and the protocol was approved by the University of Houston committee for the protection of human subjects. All patients gave informed consent to participate in the study.

Optical Coherence Tomography

The Stratus OCT 3000 system (Carl Zeiss Meditec, Inc., Dublin, CA) was used to acquire three 3.4-mm diameter circular scans centered on the optic disc (Fast RNFL protocol). The overall RNFL thickness along the circumference and the sector thickness in every quadrant were automatically calculated by the OCT software and compared with a built-in normative database of age-matched control subjects. The overall and sector RNFL thickness of each

eye was assigned a rank of normal ($P > 5\%$) or below normal ($P < 5\%$ or worse). A trained ophthalmic technician performed all OCT testing.

Standard Automated Perimetry

SAP was measured with the SITA (Swedish interactive threshold algorithm) 24-2 (20 patients) or 30-2 (16 patients) protocols using the Humphrey field analyzer 750 (Carl Zeiss Meditec, Inc.) with a Goldman size III (0.43°) stimulus on a 31.5-apostilb background. A test result was considered unreliable if false positives, false negatives, or fixation losses were greater than 33%.

For sector comparison, a visual field (24-2) was divided into four sectors that topographically corresponded to the four quadrants of OCT RNFL (nasal, N; temporal, T; superior, S; inferior, I) as illustrated in Figure 1. This topographic relationship was based on the retinal nerve fibers' entry position at the optic nerve head for each field test point as shown in Figure 4 of Garway-Heath et al.³¹ For 30-2 fields, only the 24-2 matrix was used. A whole field or a sector of the field was considered abnormal when test points on the total-deviation plot satisfied one of the following cluster criteria^{32–35}: an abnormal cluster was defined as at least two adjacent points in a field or a sector depressed by $P < 1\%$, or at least three adjacent points depressed by $P < 5\%$, with one of the three points depressed by $P < 1\%$. For a whole field and for inferior and superior field sectors, a cluster could contain no more than 1 point from the peripheral rim points on 24-2 fields.^{36,37} We used total-deviation plots instead of pattern deviation plots for analysis, because according to the results of the Optic Neuritis Treatment Trial (ONTT), about half of the field abnormality in ON was diffuse in nature,²¹ and, in addition, none of our subjects had abnormal media opacity.

To measure the extent of field defects for a sector or a whole field, both severity score (SS) and percentage of abnormal test points ($P < 5\%$) on total-deviation plots were used. The severity score was modified from that of Danesh-Meyer et al.³⁸ and calculated as the sum of a numerical value of each abnormal point on the total-deviation plot ($P > 5\% = 0$, $P < 5\% = 1$, $P < 1\%$ or $2\% = 2$, $P < 0.5\% = 3$) divided by the number of test points in a sector or a whole field. Other parameters/formats used to represent SAP were MD in decibels, unlogged deviation, visual sensitivity (VS) in decibels, and unlogged VS in 1/Lambert (L). Sector MD (in decibels) was calculated by averaging the deviation values on total-deviation plots for each sector. To calculate unlogged deviation, the deviation at each test point of the total-deviation plot was divided by 10, and then the antilog was taken. The unlogged deviations were averaged for a whole field or a sector. VS for a whole field or a sector was taken as the corresponding average of the raw sensitivity data at each test point. VS (1/L) at each test location was calculated by dividing the raw sensitivity data (in decibels) by 10 then unlogging it. It was then averaged for a whole field or a sector.

Statistical Analysis

The data are reported as the mean $\pm$ SD. The differences between ON and non-ON groups and those of ON eyes with normal acuities versus those with reduced acuities were evaluated with two-sample *t*-tests.

Agreement between SAP and OCT in classifying eyes/sectors was presented as an observed percentage of agreement (P_a , see Table 1 and equation 2) and the probability of agreement after correcting for chance (AC1, see Table 1 and equation 1). It is important to realize that any two tests may classify some subjects into the same category simply by chance. An extreme example of chance agreement is that if two tests each randomly classify a subject as normal or abnormal with no consideration of the subject's characteristics whatsoever, the chance of these two tests agreeing will be 0.50. There are several methods of correcting

chance agreement (simultaneous occurrence of random classification), including the commonly used κ statistic. A problem with the κ statistic is that it varies widely with the prevalence of a trait (in our case, the prevalence of abnormal eyes). For example, it will give very low agreement when the prevalence of a trait is low or high, even though the two tests are in high agreement (i.e., P_a is high). For this reason, we chose the *ACI* statistic, which, in our hands, avoided the strong bias of the κ test.³⁹ However, caution should be exercised for interpretation of the statistics, because even *ACI* still depends somewhat on the prevalence of a trait and tends to yield a slightly elevated value when a trait's prevalence is low (e.g., see non-ON group, sectors in Table 5).

ACI statistics for data shown in Table 1 is defined as

$$ACI = \frac{P_a - P_e}{1 - P_e}, \quad (1)$$

where P_a is the percentage of observed agreement calculated as

$$P_a = \frac{a+d}{n}, \quad (2)$$

and P_e is the probability of agreement expected by chance and is computed as

$$P_e = 2P_+ * (1 - P_+), \quad (3)$$

where

$$P_+ = \frac{(A_+ + B_+)/2}{n}. \quad (4)$$

The relationship between overall RNFL thickness and SAP MD was evaluated with an exponential function based on a linear model proposed for glaucomatous eyes by Hood.²⁷ The model assumes a linear relationship between RNFL thickness and loss of visual sensitivity, when both are on a linear scale. Such a relationship becomes exponential when loss of sensitivity is expressed in decibels. The coefficient of determination (R^2) represents the amount of variation accounted for by the regression function. To assess the correlation between RNFL thickness and various SAP parameters, Pearson's correlation coefficient (r) was used.

Results

Data from 61 eyes of 36 patients with MS (seven eyes with ON <6 months prior and four eyes with unreliable SAP were excluded) are reported. Patients' demographic and clinical information are listed in Table 2A (the ON group, 28 eyes) and Table 2B (the non-ON group, 33 eyes). Eighteen ON eyes had experienced one episode of ON, whereas 10 eyes had had two or more episodes. The time elapsed from the last ON event to the present study ranged from 6 months to 30 years with a median duration of 2 years.

Averaged MD and overall RNFL thickness for ON and non-ON eyes are presented in Table 3. The MD and overall RNFL thickness of ON versus non-ON eyes were significantly different ($P = 0.02$ and < 0.0001 , respectively). In the ON group, eyes with worse visual

acuity (VA) showed more severe loss of sensitivity (MD) and RNFL compared with those with VA better than 20/25 ($P = 0.005$ and 0.009 , respectively).

Qualitative Comparison of SAP and RNFL Thickness

A whole field or a sector of the field was considered to be abnormal when it met the cluster criteria (see the Methods section). An overall or quadrant RNFL thickness was considered to be abnormal when it was below 5% of the OCT built-in norms.

For the ON group (Table 4), SAP showed 82% (23/28) of the eyes and 51% (57/112) of the sectors to be abnormal, whereas OCT RNFL thickness identified 75% (21/28) of the eyes and 55% (62/112) of the quadrants as abnormal. The percentage of agreement of the two tests was 86% ($ACI = 0.78$) among eyes and 69% ($ACI = 0.38$) among sectors (Table 5). We further divided the ON eyes based on their SAP MD being worse or better than -3 dB, a criterion sometimes used for defining an abnormal visual field (Table 5).^{21,40} Of the 12 ON eyes with MD worse than ($<$) -3 dB, all had abnormal overall RNFL thickness (11 of them were <75 μ m) and abnormal field clusters thus showing 100% agreement ($ACI = 1$). Sectoral agreement in these 12 eyes was 81% ($ACI = 0.74$). In contrast, eyes with MD ≥ -3 dB showed poor agreement in general (a relatively high percentage of agreement in the nasal sector was due to a low incidence of abnormality in this sector). Also, among the 16 eyes with MD ≥ -3 dB, 9 eyes were identified as abnormal by OCT, compared with 11 by SAP (8 eyes were abnormal by both tests).

In the non-ON group (Table 6), 48% (16/33) of the eyes and 29% (39/132) of the sectors showed abnormal SAP, whereas 9% (3/33) of the eyes and 15% (20/132) of quadrants had an abnormal RNFL thickness. Agreement between the two tests was 61% ($ACI = 0.33$) for whole eyes and 66% ($ACI = 0.48$) for all sectors (Table 5). In this group, the prevalence of abnormal fields was significantly more than abnormal RNFL, both in eyes (48% vs. 9%, $P < 0.0001$) and inferior sectors (39% vs. 6%, $P < 0.0001$). Very few eyes (9%) and sectors (5%) were classified as abnormal by both tests.

Relationship between the Extent of Field Defects and RNFL Thickness

A scatterplot of MD versus the overall RNFL thickness for all eyes is shown in Figure 2. The two outliers of the non-ON eyes represented the two eyes of one patient (subject 26, Table 2B) with reliable (30-2 threshold, fixation loss 3/21 OD, 1/22 OS; false-positive errors 1% OD, 0% OS; and false-negative errors 6% OD, 0% OS) and severe field loss, but surprisingly normal RNFL in each eye. Of note, objective perimetry performed by recording multifocal visual evoked potentials (mfVEPs) in the course of a related study was completely normal (latency and amplitude) in both eyes of this patient (see the Discussion section).

The relationship between RNFL thickness and MD in ON eyes was evaluated with an exponential function, based on a linear model proposed for glaucomatous eyes by Hood.²⁷ The model assumes a linear relationship between RNFL thickness and loss of visual sensitivity when both are on a linear scale; and such a relationship becomes exponential when loss of sensitivity is expressed in logarithmic unit decibels. As shown in Figure 2, approximately 48% of the variance can be accounted for by the exponential function (solid line, $n = 28$). To ensure no contamination from intrasubject correlation, we performed regression analysis by including only one eye from a patient (the eye with worse MD was selected in patients with bilateral ON) and the result was almost identical (Fig. 2, dashed line, $n = 21$).

To examine which SAP measurements had better linear correlation with RNFL thickness, Pearson correlation coefficients were calculated between several SAP parameters and RNFL

thickness (Table 7). The overall RNFL thickness demonstrated relatively stronger linear correlations with the following whole field parameters: SS ($r = -0.65$, $P < 0.0001$), percentage of abnormal points ($r = -0.66$, $P < 0.0001$), unlogged deviation ($r = 0.69$, $P < 0.0001$), and VS in 1/L ($r = 0.66$, $P < 0.0001$). Figure 3 shows the scatterplots and linear regressions for overall RNFL and these four SAP parameters.

Correlations between sectoral parameters were generally weaker than the whole-eye correlations and varied for sectors and the field parameters used (Table 7). Overall, sector I showed the best correlation followed by sector T, then sector S. Sector N did not show a significant correlation with any SAP parameters. Pearson correlation coefficients for sector I were -0.67 ($P < 0.0001$) for SS, -0.67 ($P < 0.0001$) for percentage of abnormal points and 0.62 ($P < 0.0001$) for VS (1/L). It should be noted that the percent change in RNFL thickness for ON eyes, compared to the OCT norms published by Budenz et al.²⁰ which also showed lower values for sectors T and N than S and I, was not significantly different for the different sectors (Table 7).

Discussion

SAP and OCT showed good agreement (86%, $ACI = 0.78$) in classifying the ON eyes as abnormal or not. In contrast, the two tests did not agree as well in classifying the non-ON eyes or individual sectors of both ON and non-ON groups.

Many factors can contribute to disagreement between tests. An obvious reason for disagreements between SAP and OCT is the uncertainty of either one or both tests in detecting abnormalities near threshold, which is related to the sensitivity and specificity of each test. In other words, the strength of agreement between two tests depends on the severity of the deficits in the data sampled (see Table 5; ON eyes with MD < -3 dB versus those with MD ≥ -3 dB). A weaker agreement in our non-ON group is expected as a result of the mild deficits involved. Similarly, Costello et al.¹⁵ found a significant correlation between MD and RNFL thickness only among ON eyes with more severe damage. Quantitative analysis between SAP and RNFL thickness also showed no correlation in patients with preperimetric glaucoma,^{41,42} or relatively poor correlation when glaucomatous damage was mild.⁴³

Another cause of disagreement is the inherent limitations of each test itself. The two outliers in the non-ON group (subject 26) show one such example. The normal mfVEP findings in this patient, obtained in related, concurrent studies, suggest that the disagreement between RNFL thickness and SAP is most likely due to limitations of subjective perimetry, although defects beyond the primary visual cortex cannot be ruled out completely.⁴⁴ This patient had secondary progressive MS. MS patients, especially those with severe disease, may have cognitive dysfunction or slowed reaction times, which can interfere with decision-making during the subjective field testing. In such cases, objective perimetry such as can be achieved via the mfVEP approach can be useful for measuring functional deficits (Laron M et al. *IOVS* 2007;48:ARVO E-Abstract 3761). Of course, OCT RNFL measurements may also be technically limited by, for example, how well the measurements are centered around the optic disc.

Agreement between SAP and OCT in MS patients is further limited by the fact that the former measures the function of the entire visual pathways, whereas the latter measures the RGC axonal integrity, and MS may involve central visual pathways and mechanisms not leading to retrograde degeneration in RNFL. This may also explain the higher prevalence of field abnormalities, compared with RNFL defects, detected in our non-ON eyes.

One explanation for the weaker agreement observed between sectors than the whole field is related to whether defects are “diffuse” or localized. In contrast to the common belief that the temporal sector of the optic disc is more affected in ON (probably due to the frequently observed temporal “pallor” in ON eyes), our results clearly showed that all sectors of the optic nerve was similarly affected. The average loss of RNFL for different sectors varied from 20% to 30% (Table 7). However, as the temporal RNFL thickness is thin to begin with (see average quadrant RNFL thickness in normal population in Ref. ²⁰), loss of RNFL in this region may lead to easier recognition of pallor than in other sectors, which have thicker baseline RNFL. Similarly, abnormal clusters on visual fields are not localized to one sector. In 22 of the 23 eyes that showed abnormal clusters, the clusters crossed the boundaries of at least two sectors of the field. Compared with glaucoma in which arcuate nerve bundles are more susceptible to damage, defects in ON seemed more diffuse, in the sense that they cover field locations corresponding to two or more quadrants of the OCT RNFL. It is possible that dividing a diffuse defect into sectors may increase the “miss” rate of a defect, especially the mild ones, by one test, and lead to less robust agreement between tests. For this reason, sectoral agreement in ON eyes with more severe defects (MD worse than -3 dB) is fairly good except for the nasal sector (Table 5). Of course, any topographic correlation between structure and function is limited by the lack of an optimal structure-to-function map and the large individual variability in such maps.^{31,45,46}

The quantitative relationship between visual sensitivity and RNFL thickness depends on the scale used for sensitivity measurement.^{42,47,48} When a logarithmic scale is used for visual sensitivity, the overall RNFL thickness in ON eyes is a simple exponential function of the MD in decibels (Fig. 2, $R^2 = 0.48$).²⁷ This exponential relationship has two clinical implications. First, it means that a large amount of RNFL reduction is needed for a small sensitivity loss in decibels. In this study, an RNFL thickness of $75\text{ }\mu\text{m}$ ($\sim 25\text{ }\mu\text{m}$ [25%] reduction of RNFL assuming a normal thickness around $100\text{ }\mu\text{m}$ ²⁰) corresponds to a 3 dB (50%) loss of MD, which is consistent with the postmortem histology findings in glaucoma.^{49,50} Second, when functional loss is worse than -10 dB, it is better to use MD for monitoring disease progression, because the RNFL loss has almost reached a plateau (Fig. 2). It is also interesting to note that the overall RNFL thickness in our sample “bottoms out” around $60\text{ }\mu\text{m}$, higher than those reported in glaucoma.²⁷ Whether this represents data variability or a different disease mechanism involving glial tissues needs further study.

A more straightforward representation of the relationship between structure and function in ON eyes is to express both measurements in linear scales (Fig. 3). The absolute Pearson correlation coefficients between overall RNFL thickness and the whole field’s SS, the percentage of abnormal points, the unlogged deviation, or the linear VS (1/L) range from 0.65 to 0.69. The linear correlation is generally weaker in individual sectors, especially sector N.⁵¹ A poor correlation in sector N may be attributed to only three points being measured, all of them located on the rim of the 24-2 field test.

A limitation of the present study is that we selected only visual fields based on the closest time to the date of OCT test (mostly the same day) instead of those with repeatable visual fields. Since patients with resolved optic neuritis tend to have large long- and short-term variability in SAP,⁴⁰ future study design may involve repeated SAPs or an objective perimetry, such as mfVEP for confirmation of functional defects. Similarly, repeated OCT RNFL thickness measurements should also be beneficial.

Clinically, it will be helpful to establish baseline RNFL thickness and functional measurements in all MS patients at the time of MS diagnosis. Change in RNFL thickness and/or visual function over time is likely the best approach in monitoring the disease progression.

Lastly, despite possible topographical differences and etiologies, it is important to point out that the structural and functional relationship found in optic neuritis is, in general, very similar to that in glaucoma. Cell death, regardless of the causes and mechanisms involved, is essentially responsible for permanent functional loss. This supports the idea that axonal loss is the anatomic substrate for irreversible functional disability in patients with ON/MS.^{5,6}

In conclusion, comparison between abnormalities detected by SAP and RNFL measurements showed good agreement in ON eyes. Regression analyses between several SAP parameters and RNFL thickness support a linear relationship between structural and functional measurements when both are expressed in linear scales. Combining information from structural and functional tests and following individuals longitudinally is probably the best strategy for assessing and monitoring the optic nerve involvement in patients with MS.

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Figure 1.

A map between OCT RNFL quadrants and corresponding sectors on SAP 24-2 based on the study of Garway-Heath et al.³¹ For simplicity, sectors in this study were referenced by the RNFL quadrants (e.g., sector I denotes an inferior RNFL quadrant and the corresponding superior sector of the 24-2 visual field).

Figure 2.

Scatterplots of MD versus overall RNFL thickness for (group 1) all non-ON eyes ($n = 33$), (group 2) all ON eyes ($n = 28$), and (group 3) one ON eye per patient ($n = 21$; only the worse MD eye was included for patients with bilateral ON). *Solid and dashed lines:* regression for groups 2 and 3, based on a linear model: $y = a \cdot 10^{(0.1 \cdot x)} + b$, where x is the MD and y is the RNFL thickness.²⁷ The resulted fitting parameters were very similar for group 2 and group 3. For group 2, $R^2 = 0.48$, $a = 38.91$, $b = 59.56$; for group 3, $R^2 = 0.48$, $a = 39.45$, $b = 58.14$. To illustrate the linear model (*inset*), MD in dB was converted to linear units: $\text{unlogged MD} = 10^{(0.1 \cdot x)}$, and plotted versus overall RFL thickness for all ON eyes ($n = 28$). *Solid line:* linear regression ($R^2 = 0.48$).

Figure 3. Scatterplots and linear regression between overall RNFL thickness and (A) SS of SAP total-deviation plots, (B) percentage of abnormal points ($P < 5\%$) on total-deviation plots, (C) average unlogged deviation, and (D) average visual sensitivity (1/L).

Table 1Distribution of n Subjects by Tests and Their Classification

		Test A		Total
		Yes	No	
Test B	Yes	a	b	$B_+ = a + b$
	No	c	d	$B_- = c + d$
	Total	$A_+ = a + c$	$A_- = b + d$	$n = a + b + c + d$

Table 2

Demographic and Clinical Data

Subject	Age/Sex	MS Type	Eye	Total Number of ON Attacks	Months from Last ON Attack	A. The ON Group		
						V/A	MD (dB)	Overall RNFL (μ m)
1	42/F	RR	R	4	10	20/50+1	-18.28	72.51
2	33/M	RR	R	1	20	20/15	-1.59	72.22
2	33/M	RR	L	1	20	20/20+1	-7.35	52.08
3	32/F	RR	R	1	84	20/20	-2.22	71.54
4	52/F	2nd progressive	R	2	48	20/25	-24.91	67.94
4	52/F	2nd progressive	L	2	48	20/25	-28.54	60.69
5	47/F	RR	R	1	192	20/20-3	-1.89	85.79
5	47/F	RR	L	1	192	20/40-1	-2.44	74.81
6	28/F	RR	R	1	12	20/30	-6.05	73.61
7	55/M	RR	L	2	11	20/15-2	-2.69	78.66
8	38/F	RR	L	1	48	20/30+2	-2.15	76.34
9	38/F	RR	L	1	180	20/25	-8.99	52.94
10	48/F	RR	R	1	360	20/25	-7.79	66.3
11	51/F	RR	L	2	6	20/20-2	-0.77	95.79
12	23/F	RR	R	1	18	20/20-1	-3.00	97.24
13	35/F	RR	R	1	6	20/15	-1.01	101.22
14	39/M	RR	R	2	24	20/40	-20.06	56.28
14	39/M	RR	L	2	24	20/60	-23.95	65.01
15	49/F	RR	R	2	12	20/20-1	-2.47	54.96
16	31/F	RR	R	1	120	20/15	-2.10	80.67
17	44/F	RR	R	Many	132	20/20	-5.17	63.27
17	44/F	RR	L	Many	24	20/20	-2.48	102.5
18	37/F	RR	L	1	36	20/20	-1.87	101.77
19	30/F	RR	R	1	66	20/25-3	-3.54	81.95
19	30/F	RR	L	1	24	20/25-1	-3.73	72.37
20	56/F	RR	L	1	144	20/15	-2.50	78.13

A. The ON Group

Subject	Age/Sex	MS Type	Eye	Total Number of ON Attacks	Months from Last ON Attack	VA	MD (dB)	Overall RNFL (μ m)
21	26/M	RR	R	1	9	20/15	-1.80	92.83
21	26/M	RR	L	1	9	20/15	-2.37	82.01

B. The Non-ON Group

Subject	Age/Sex	MS Type	Eye	VA	MD (dB)	Overall RNFL (μ m)
1	42/F	RR	L	20/20-1	-1.85	85.31
3	32/F	RR	R	20/20	-1.29	79.58
6	28/F	RR	L	20/15	-7.07	86.58
8	38/F	RR	R	20/20	-2.15	113.10
9	38/F	RR	R	20/20	-1.95	74.94
10	48/F	RR	L	20/15	-2.41	109.04
12	23/F	RR	L	20/20	-3.32	114.73
13	35/F	RR	L	20/15	-0.59	101.80
16	31/F	RR	L	20/15	-2.78	78.16
18	37/F	RR	R	20/20	-0.94	104.90
20	56/F	RR	R	20/20+1	-2.41	80.29
22	40/F	RR	L	20/20	0.26	104.41
23	37/M	RR	R	20/20	0.01	107.20
23	37/M	RR	L	20/20	0.15	105.29
24	33/M	RR	L	20/15	-0.12	89.38
25	41/F	RR	L	20/20	-0.95	94.22
26	41/F	2nd progressive	R	20/20+1	-17.8	107.49
26	41/F	2nd progressive	L	20/20+1	-19.74	106.33
27	50/M	RR	R	20/15	0.10	92.08
27	50/M	RR	L	20/20	0.66	88.70
28	26/F	RR	L	20/25-2	-0.60	88.10
29	21/F	RR	L	20/15	-1.50	100.02
30	38/M	RR	L	20/15	-1.05	111.80
31	39/F	RR	R	20/25-2	-4.28	93.58

B. The Non-ON Group

Subject	Age/Sex	MS Type	Eye	VA	MD (dB)	Overall RNFL (μ m)
31	39/F	RR	L	20/25-2	-2.26	98.55
32	41/F	RR	R	20/20	-0.70	84.25
32	41/F	RR	L	20/20	0.88	82.29
33	34/F	RR	L	20/15	-0.20	91.42
34	40/F	RR	R	20/15-2	-3.57	101.86
34	40/F	RR	L	20/15-3	-3.84	117.58
35	47/F	RR	L	20/15	-1.75	92.56
36	46/M	RR	R	20/40-1	-2.51	89.95
36	46/M	RR	L	20/20	-2.35	107.49

Table 3

MD and Overall RNFL Thickness in the Study Groups

	SAP MD (dB)	Overall RNFL Thickness (μm)
ON eyes ($n = 28$)	-6.85 ± 8.15	76.12 ± 14.92
VA >20/25 ($n = 16$)	-2.58 ± 1.60	81.92 ± 16.22
VA 20/25–20/60 ($n = 12$)	-12.54 ± 9.88	68.40 ± 8.58
Non-ON eyes ($n = 33$)	-2.66 ± 4.47	96.45 ± 11.73

Data are the mean $\pm$ SD.

Table 4

Eyes and Sectors in the ON Group Classified as Abnormal by SAP Cluster Criteria or RNFL Thickness

	ON Eyes (<i>n</i> = 28)		ON Sectors (<i>n</i> = 112)	
	Abnormal RNFL	Normal RNFL	Abnormal RNFL	Normal RNFL
Abnormal SAP	20 (71%)	3 (11%)	42 (38%)	15 (13%)
Normal SAP	1 (4%)	4 (14%)	20 (18%)	35 (31%)

Data are the number (and percentage) of eyes or sectors.

Table 5

Observed Agreement between SAP and OCT and the ACI Statistics

	ON Group					
	All Eyes (<i>n</i> = 28)		Eyes with MD < -3 dB (<i>n</i> = 12)		Eyes with MD ≥ -3 dB (<i>n</i> = 16)	
	Agreement (%)	ACI	Agreement (%)	ACI	Agreement (%)	ACI
Eyes	86	0.78	100	1.00	75	0.53
Sector I	71	0.44	83	0.80	63	0.34
Sector T	71	0.43	83	0.77	63	0.34
Sector S	61	0.32	92	0.91	38	-0.25
Sector N	71	0.49	67	0.35	75	0.68
All sectors	69	0.38	81	0.74	59	0.29
					66	0.48
					61	0.33
					67	0.49
					70	0.59
					58	0.21
					70	0.59
					66	0.48

Table 6

Eyes and Sectors in the Non-ON Group Classified as Abnormal by SAP Cluster Criteria or RNFL Thickness

	Non-ON Eyes (<i>n</i> = 33)		Non-ON Sectors (<i>n</i> = 132)	
	Abnormal RNFL	Normal RNFL	Abnormal RNFL	Normal RNFL
Abnormal SAP	3 (9%)	13 (39%)	7 (5%)	32 (24%)
Normal SAP	0 (0%)	17 (52%)	13 (10%)	80 (61%)

Data are the number (and percentage) of eyes or sectors.

Table 7
The ON Group: Pearson's Correlation Coefficients and Probabilities for SAP Parameters and RNFL Thickness

	SS vs. RNFL	% Abn Points vs. RNFL	MD (dB) vs. RNFL	Unlogged Deviation vs. RNFL	VS (dB) vs. RNFL	VS (dB) vs. log RNFL	VS (I/L) vs. RNFL	Average RNFL $\pm$ SD (%norm *)
Whole eyes	-0.65 (0.0001)	-0.66 (0.0001)	0.51 (0.005)	0.69 (0.0001)	0.52 (0.005)	0.52 (0.005)	0.66 (0.0001)	76 $\pm$ 15 (76%)
Sector I	-0.67 (0.0001)	-0.67 (0.0001)	0.47 (0.012)	0.54 (0.003)	0.47 (0.012)	0.45 (0.017)	0.62 (0.0001)	101 $\pm$ 20 (80%)
Sector T	-0.55 (0.002)	-0.53 (0.004)	0.51 (0.005)	0.51 (0.006)	0.53 (0.004)	0.59 (0.001)	0.61 (0.001)	53 $\pm$ 17 (77%)
Sector S	-0.45 (0.017)	-0.46 (0.015)	0.20 (0.315)	0.34 (0.079)	0.31 (0.112)	0.29 (0.142)	0.44 (0.019)	93 $\pm$ 18 (75%)
Sector N	-0.32 (0.100)	-0.28 (0.157)	0.21 (0.281)	0.23 (0.245)	0.22 (0.262)	0.22 (0.258)	0.28 (0.148)	57 $\pm$ 21 (70%)

Last column shows the average RNFL thickness $\pm$ SD (and its percent of normative values). SS, severity score; % Abn points, percentage of abnormal points on total deviation plots; VS; visual sensitivity.

* Based on the normative values of RNFL thickness (μ m) published by Budenz et al.²⁰ 100 $\pm$ 12 for overall RNFL and 126 $\pm$ 18, 69 $\pm$ 13, 124 $\pm$ 18, and 81 $\pm$ 18 for sectors I, T, S, and N, respectively.