A new parameter for assessing the thickness of the retinal nerve fiber layer for glaucoma diagnosis

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ABSTRACT: Purpose. *To investigate a new method for assessing the thickness of the retinal nerve fiber layer thickness (NFLT) for glaucoma diagnosis, using scanning laser polarimetry.*
Material and Methods. *Thirty eyes of thirty patients with ocular hypertension or glaucoma were examined using a scanning laser polarimeter. NFLT was measured in each of four 90-degree quadrants; superior (S), temporal (T), inferior (I) and nasal (N) along 1.5-disc diameters concentric from the disc margin. The new parameters S-N (meaning the thickness of the superior nerve fiber layer over the nasal one) etc. were compared with the conventional parameters (S, S/N, etc.). The correlations between these parameters and the mean threshold of the associated visual field test points were included in the comparison.*
Results. *The total thickness (sum of S, I, N and T), N and T did not correlate to the visual field, but S and I did. The new parameters were well correlated to the visual field, S-N giving the best correlation coefficient (rs=0.782, p<0.0001), and sensitivity and specificity (the area under the receiver operating characteristic curves was 0.91).*
Conclusions. *The nasal NFLT was the smallest part of individual variation and glaucomatous damage. The new parameters, based on the nasal NFLT, were good evaluators of the changes in glaucoma. (Eur J Ophthalmol 1999; 9: 93-8)*

KEY WORDS: Glaucoma, Nerve fiber layer, Scanning laser polarimetry, Ocular hypertension

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INTRODUCTION

Retinal nerve fiber layer assessment serves as an early indicator of glaucomatous damage (1), because axon loss in the retinal nerve fiber layer is the earliest observable sign of damage in glaucoma (2). Changes in the optic disc are reported to occur earlier than visual field changes in patients with glaucomatous damage (1, 2). The C/D ratio is often used clinically to evaluate the optic disc, but it shows large individual differences (3).

Computer image analysis has also been used. In one study employing correction for the magnifying effect of refraction, the rim area, cup volume and other parameters of the optic disc were calculated in patients with glaucoma, and comparisons were made with their visual field defects. The rim area and the peripapillary nerve fiber layer profiles of the optic disc margin showed a better correlation with the magnitude of visual field loss than with the cup/disc ratio, and relative nerve fiber layer surface height at the optic disk margin has been reported to show an even closer correlation with visual field change (4, 5).

However, the disc margin is greatly influenced by

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the size and shape of the optic disc and by blood vessels, so more accurate results may be obtained by measuring the thickness of the retinal nerve fiber layer at sites away from the disc. Scanning laser polarimetry, based on the refraction of laser light pro-

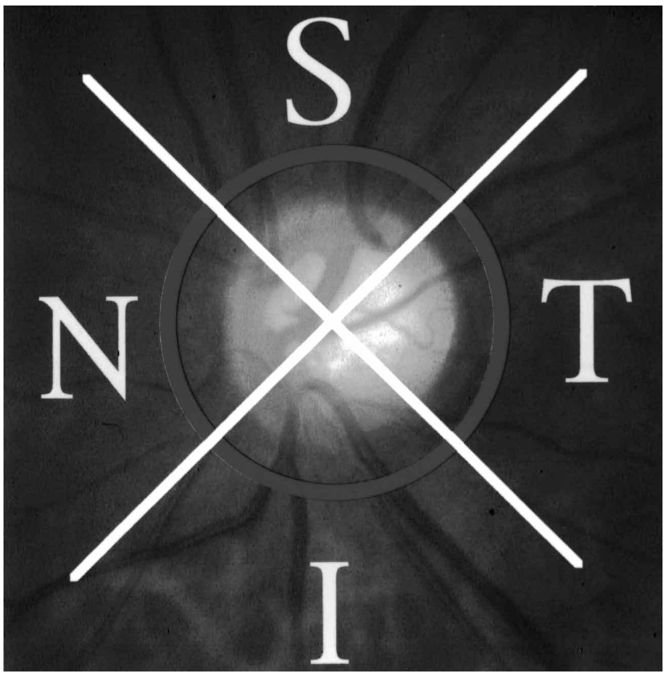

Fig. 1 - *A circle is drawn around the optic disc at 1.5 disc diameters distance. The retinal nerve fiber layer thickness is measured on the circle and divided into four 90-degree quadrants for analysis.*

duced by the nerve fibers, directly measures the thickness of the nerve fiber layer in the retina (6). Widely varying results have been reported and the scanning laser polarimeter is still experimental (7). There appears to be considerable overlap between glaucomatous and healthy eyes with respect to retinal thickness, so the diagnostic value of this assessment remains unclear (8, 9).

The following information has been published so far:

1) There are individual and age-related differences in the thickness of the retinal nerve fiber layer, and glaucoma cannot be evaluated on the basis of local thickness alone (9, 10).

2) In healthy eyes, the superior or inferior arcuate bundle is thick above and below the optic disc, whereas in glaucomatous eyes it is thin and flattened (5, 8).

3) Glaucomatous damage is least likely to be manifested on the nasal side of the retina (11).

4) It is generally accepted that anatomical changes such as those due to myopia are more likely on the temporal side of the retina, and are unlikely to be manifested on the nasal side (12).

5) The nerve fiber thickness decreases with increasing distance from the disc margin (13).

6) Inter-observer differences in scanning laser polarimetry values tend to occur on the temporal side, with artifacts being produced by conus, etc. (7, 8).

We felt that evaluating nerve fiber thickness needed a reliable baseline. With the above findings in mind,

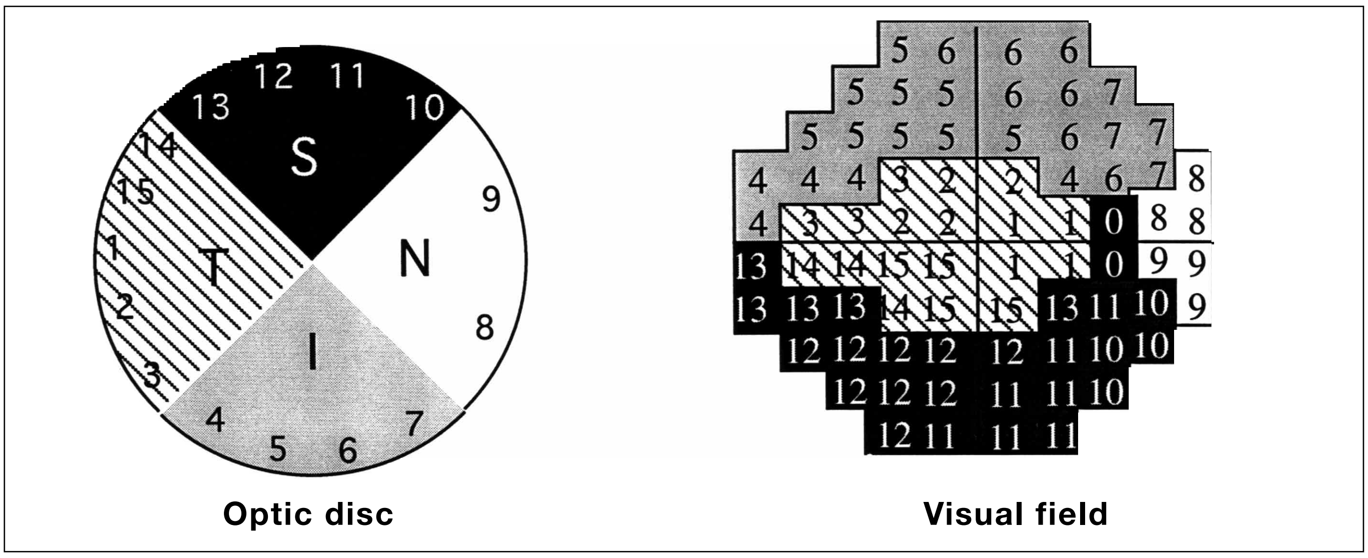

Fig. 2 - *Relationships between optic disc and visual field. The numbers indicate the corresponding areas between nerve fiber and visual field test point.*

therefore, we set out to determine the parameter of nerve fiber layer thickness that correlates best glaucomatous visual field changes.

MATERIAL AND METHODS

At the glaucoma clinic of Yamanashi Medical University Hospital, thirty eyes of thirty patients were enrolled for this study. Four had ocular hypertension (OH), 17 had primary open angle glaucoma (POAG) and 9 normal tension glaucoma (NTG). Mean age was 61.7±13.1 years (range 34-81 years). Eyes with a myopic refractive error exceeding -8.0 diopters were excluded because of their different optic disc morphology. The mean refractive error was -1.1±2.2D (range -5.0 to +3.0D). Patients with a small pupil or medial opacity were excluded.

The retinal nerve fiber layer thickness was measured with a Nerve Fiber Analyzer version 2.1.07alpha (NFAII: Laser Diagnostic Technologies, Inc., San Diego, California) (6, 8, 10). This new scanning laser ophthalmoscope uses the polarization properties of the retinal nerve fiber layer to determine its thickness. Using the NFA, the retinal nerve fiber layer thickness was generally (7-10, 14) measured in each of four 90-degree quadrants: superior (S), temporal (T), inferior (I) and nasal (N) along the 1.5 disc diameters concentric from the disc margin, shown in Figure 1. Two trained operators measured the nerve fiber layer thickness three times for each eye.

For each eye, visual field analysis, was done with the 30-2 program of the Humphrey visual field analyzer (HFA). Each test point of perimetry was numbered in accordance with the location of the nerve fibers around the optic disc as in the previous report (15) (Fig. 2).

Five nerve fiber parameters were calculated for S, I, and T with respect to N and/or the Total, ie the sum

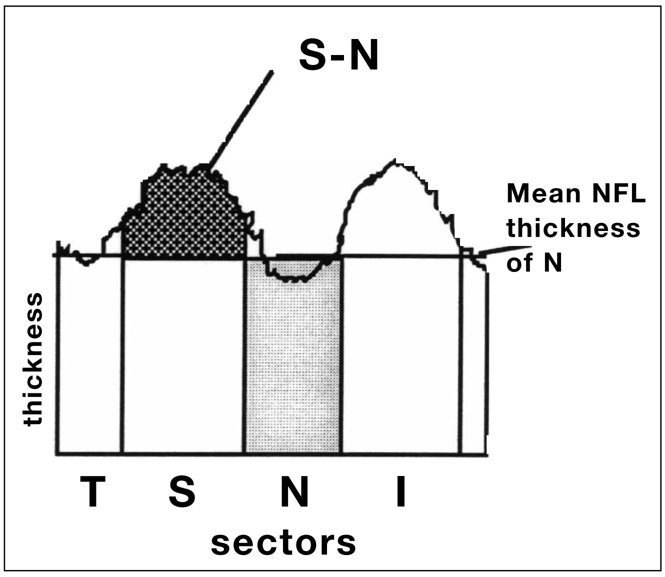

Fig. 3 - *The peripapillary nerve fiber layer profiles. T, S, N and I refer to temporal, superior, nasal and inferior locations. The typical double-hump pattern corresponds to the nerve fiber bundles at the superior and inferior poles of the optic disc.*

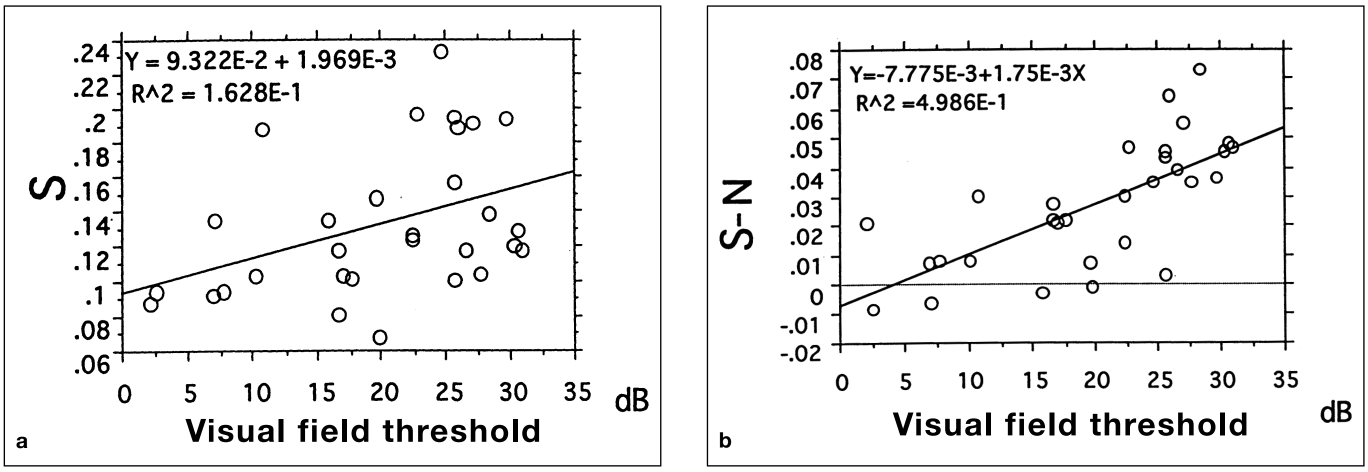

Fig. 4 - a) *Scatter plot showing the distribution of 30 eyes according to the conventional parameter S and mean threshold of the corresponding inferior visual field.*
b) *Scatter plot showing the distribution of 30 eyes according to the new parameter S-N and mean threshold of the corresponding inferior visual field.*

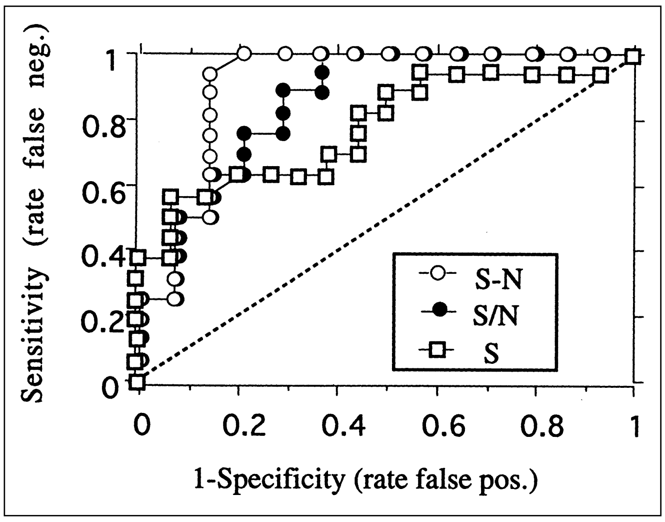

Fig. 5 - *Receiver operating characteristic (ROC) curves for the parameters S (open squares), S/N (filled circles) and S-N (open circles). Area under the ROC curve were respectively 0.75, 0.86 and 0.91.*

of all four: (S+I+T+N). For example, for the S sector, there are five parameters, S/N, S-N, S/Total, (S-N)/N and (S-N)T/Total. S/N indicates the ratio of the superior nerve fiber layer thickness to the nasal fiber layer thickness. S-N means the thickness of the superior nerve fiber layer over the nasal one. S/Total means the ratio of S to the whole thickness (Fig. 3).

The new parameters (S-N, I-N, etc.) were compared with the conventional parameters (S, S/N, etc.). The correlations with the mean threshold of the associated visual fields were included in the comparison.

The sensitivity and specificity of these parameters to glaucomatous damage were investigated. The criterion of glaucomatous damage was 0.5% or less probability of total deviation, with the HFA Statpac. Only patients in whom scanning laser polarimetry and visual field analysis with HFA were measured successfully were selected for this statistical analysis.

TABLE I - CORRELATIONS BETWEEN NFLT PARAMETERS AND VISUAL FIELD THRESHOLD

	Parameters	Spearman correlation coefficient	p-value
Conventional Parameters	total	0.305	0.1007
	S	0.455	0.0143
	N	-0.235	0.2059
	I	0.439	0.0179
	T	-0.162	0.3825
	S/N	0.700	0.0002
	I/N	0.707	0.0001
	T/N	-0.016	0.9303
	S/I	0.129	0.4856
	S/T	0.603	0.0012
	I/T	0.596	0.0013
New Parameters	S/total	0.692	0.0002
	I/total	0.588	0.0016
	T/total	-0.521	0.0050
	S-N	0.782	<0.0001
	I-N	0.714	0.0001
	T-N	0.020	0.9151
	(S-N)/N	0.700	0.0002
	(I-N)/N	0.707	0.0001
	(T-N)/N	-0.016	0.9303
	(S-N)/total	0.706	0.0001
	(I-N)/total	0.682	0.0002
	(T-N)/total	0.054	0.7710

RESULTS

The correlation between each nerve fiber index and the corresponding filed index was evaluated. S and I were both positively correlated with the mean threshold of the corresponding visual field, but the correlation between T and the mean threshold of the corresponding visual field was not significant (Tab. I).

The new parameters (S-N, I-N, etc.) were well correlated with the change of the visual field except for those associated with T (Tab. I). The scattergrams of S and S-N are shown in Figure 4. A better correlation was found in S-N. The correlation between nerve fiber layer thickness and visual field threshold was best with the parameter S-N (Tab. I).

The sensitivities of S, S/N and S-N were compared by the receiver operating characteristic (ROC) curves (Fig. 5). The S-N curves shifted to the upper left of the diagram indicate enhanced sensitivity and specificity.

DISCUSSION

Generally, we cannot diagnose obesity only from body weight, and we need to correct it for height. Similarly, the nerve fiber layer thickness needs some correction for glaucoma diagnosis. In some studies only considering nerve fiber layer thickness, considerable overlap was found between healthy subjects and glaucoma patients (8, 9). Investigators were aware of the need for new methods to evaluate nerve fiber layer thickness.

Corrections based on mean values for the nasal and temporal retinas were made in an attempt to reduce the overlap, and there was some improvement in correlation coefficients between nerve fiber thickness and mean deviation of the half visual field (9). We tried to find another method to correct for the nerve fiber thickness. We found that the new parameter S-N was better than the conventional parameter S or S/N. The new parameters were more sensitive and specific for glaucoma diagnosis, and better correlated with the mean threshold of the corresponding visual field.

The nerve fiber layer thickness of the nasal retina was used to correct for the thickness of other parts of the nerve fiber layer. We have our doubts about the temporal retinal thickness used for the correction. The characteristics of the temporal retina are as follows: 1) The reproducibility of measurements is worse on the temporal side (7). 2) There are frequent changes in shape, such as those due to myopia on the temporal side. 3) Glaucomatous changes are less likely to be manifested on the nasal side, but a number of patients show changes on the temporal side in the early stage of the disease.

Tjon-Fo-Sang reported high sensitivity and specificity for glaucoma diagnosis by laser scanning polarimetry with the conventional parameter S/I, meaning the ratio of the thickness of the superior nerve fiber layer to the inferior fiber layer (16). Better results can be obtained using a correction such as our new parameters.

The present study did not include a comparison with healthy subjects, but OH was compared with various stages of glaucoma. Nevertheless, there was considerably less overlap with the new parameters, and close correlations with the visual fields were confirmed. In the future, we plan a comparison with age-matched healthy subjects.

At present, the reliability of the NFA is judged solely on the basis of the reproducibility of measurements, and there still remain some differences between researchers. Therefore, a device capable of taking pictures automatically is needed so as to reduce artifacts. In the meantime, it is important to consider low-artifact parameters. Changes in the retinal nerve fibers may possibly arise earlier than visual field changes and may be of diagnostic value. Applying our new parameters, we hope that the study of nerve fiber thickness will eventually become clinically useful, and will be used in routine clinical examinations.

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