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CLINICAL EVALUATION OF RETINAL NERVE FIBER LAYER ATROPHY IN GLAUCOMA[*1,*2] -CORRELATION BETWEEN VISUAL FIELD DAMAGE AND THE FUNDUSCOPIC NFA APPEARANCE-

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INDEXING WORDS

nerve fiber layer atrophy; optic disc cupping; glaucoma

SYNOPSIS

The purpose of this report is to clarify the clinical significance of nerve fiber layer atrophy (NFA) in the diagnosis of glaucoma.

The assessment was made only in the arcuate area, named F1 and F2 sectors.

First, 29 eyes with glaucoma were evaluated. Rim/disc ratios were calculated in each the F1 and F2 sectors. The sensitivity corresponding to the F1 and F2 sectors was determined by automatic perimeter (Octopus). Each sector was devided into three subsectors in relation to the distance from the disc margin.

Retinal sensitivity in the proximal subsector was closely correlated with the rim/disc ratio in the corresponding sector and with the enlargement of glaucomatous cupping.

NFA was expressed as a proximal, a distal or a total atrophy pattern. Proximal and distal visual field damage was prone to be

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associated with the proximal and distal NFA type respectively.

Second, we examined photographs of 784 normal eyes and 50 glaucomatous eyes.

The difference in the ratio of appearance of NFA was statistically significant between the 20-30s and 40-60s age groups, and between the C/D ratio < 0.5 and C/D ratio > 0.5 groups.

The appearance of the NFA was also classified into five patterns, according to the width. Almost all the NFAs in the normal eyes showed milder patterns, whereas almost all the NFAs in the glaucoma group showed stronger patterns.

It was suggested that one of the mechanisms that causes NFA in glaucoma was a strong nerve fiber drop out that differed from aging such as local circulatory disturbance.

The findings indicate that the visual field damage in glaucoma can be estimated from the funduscopic appearance of NFA.

INTRODUCTION

Since its clinical significance had been clarified by Hoyt et al.[2] in 1972, the appearance of retinal nerve fiber layer atrophy (NFA) has been widely recognized as one of the essential clinical findings suggesting functional damage: visual field damage, together with optic disc cupping in glaucoma. However, it is also reported that a similar phenomenon is observed in the normal eye.[1,8,9,11] Considering those facts, identification of visual field damage is not always easy if we judge only from the NFA appearance.

To clarify the points differentiating NFA in damaged and normal eyes, and also its clinical significance in the diagnosis of glaucoma, we first assessed its mode of apperance for retinal sensitivity change associated with NFA in glaucoma, and then analytically investigated the point of difference with NFA occuring also in the normal eye, as well as the relation between optic disc cupping and NFA.

SUBJECTS AND METHODS

The assessment was made according to the previous report.[4] The studies were made at sectors named F1 and F2 (Fig. 1) in the

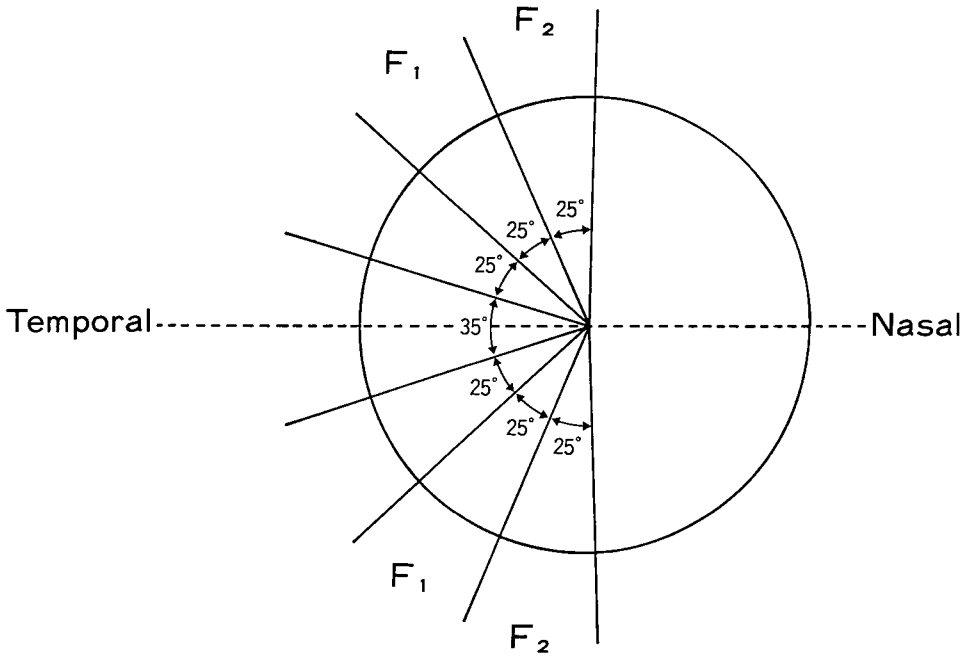

Fig. 1 Method. Optic disc division into 12 sectors.

superior and inferior arcuate area where the NFA appearance ratio is high[6] and nerve fibers course the longest distance, and taking the course of the nerve fiver into consideration, the optic discs were divided into 12 sectors.

A. Analysis of retinal sensitivity with glaucomatous NFA

29 eyes from 21 cases with primary open angle glaucoma in the early to middle stages were employed; 12 males and 9 females aged 22-74, averaging 49.9. A visual field examination within 0-60° was performed with the Octopus automatic perimeter 500E, programs 38 and 42, and a color stereoscopic disc photograph and a red-free fundus photograph using Wratten Filter No. 58. were taken.

1) Quantification of retinal sensitivity

A total of 144 measuring points of program 38 (0-30°) and 42 (30-60°) by Octopus 500E were divided correspondingly into a total

of 4 sectors of the superior and inferior F1 and F2 sectors, as shown in Fig. 2, along the nerve fiber. Further, to estimate the influence exerted by the region of decreased retinal sensitivity on the formation of optic disc cupping, each sector was divided into 3 subsectors along the vertical line passing through the fixation point and a 30° circumference. The subsectors were numbered 1, 2 and 3 in order from the optic disc side.

The mean of the values measured in all of the subsectors was calculated as a percentage of the normal subjects by age (%S).

2) Classification of NFA pattern according to the region

The morbid NFAs were classified into three patterns according to the region where NFA were present. The first pattern was a

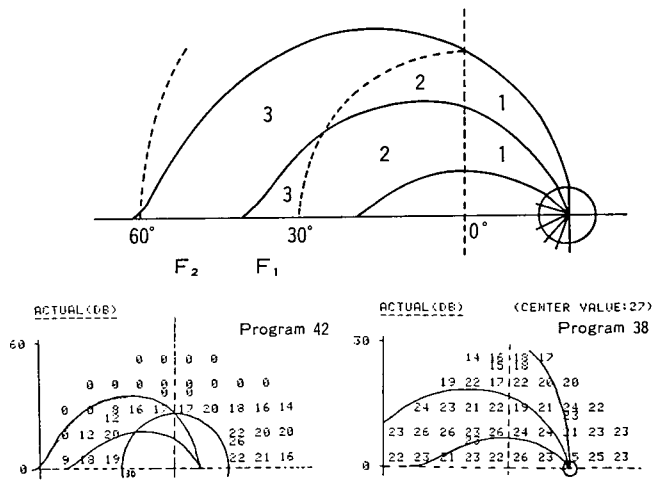

Fig. 2 Method. A total of 144 measuring points of program 38 and program 42 by Octopus 500E were divided corresponding to 4 sectors of the superior and inferior F1 and F2. Further, each sector was divided into 3 subsectors, numbered 1, 2 and 3 in order from the optic disc side.

proximal NFA in which NFA was present adjacent to the optic disc. The second pattern was a distal NFA in which NFA was present distally from the optic disc. And the last pattern was a total NFA in which NFA was observed to be quite evenly distributed in the nerve fascicle.

3) Measurement of rim area

For the estimation of optic disc change, the optic rim areas (Rim A) were measured at F1, F2 optic disc sectors respectively.

The ratios in the optic disc were measured using a digitizer (Taros) on the optic disc photographs magnified to about 10 cm { Rim A = (optic disc area - cupping area) / optic disc area in the each sector }. The cupping margin was determined with a stereoscopic photograph.

The following analyses were made:
1. The correlation between Rim A and %S per subsector.
2. The correlation between the region with decreased retinal sensitivity and the NFA pattern.

B. Comparison of NFA pattern between a galucomatous eye and a normal eye

For the glaucoma group, 50 eyes were selected from among 47 glaucoma patients (aged 22-68, averaging 48.5) in the early to middle stages in which NFAs were observed in color fundus photographs (Canon CF-60Z, field angle 60°).

At the same time 784 eyes from 392 cases were selected from the normal group (aged 20-67, averaging 41.7) which was chosen among regular health check-up patients in 1985, except patients with systemic hypertension and diabetes mellitus. Fundus color photographs were taken of the posterior pole (Canon CR-45NM, field angle 45°).

The following assessments of 1, 2 and 3 were made for F1 and F2 sectors in both groups:

1) Group C and Group S

The groups in which NFAs were present in connection with and separate from the optic disc were defined as the connected group (Group C) and separated group (Group S), respectively.

2) Classification of NFA patterns, according to the width

NFA observed were classified into Wedge, Band, Slit, Rough and Fine patterns in the order of the largest widths (Fig. 3). The standards established for the classification were : NFA in 1/2-1/1 of each sector - Wedge; NFA in 1/3-1/2 - Band; NFA in 1/4-1/3 - Slit; NFA with rough combed defect in 1/8-1/4 - Rough (Fig. 4); and finer NFA without combed-like parallerism - Fine (Fig. 5).

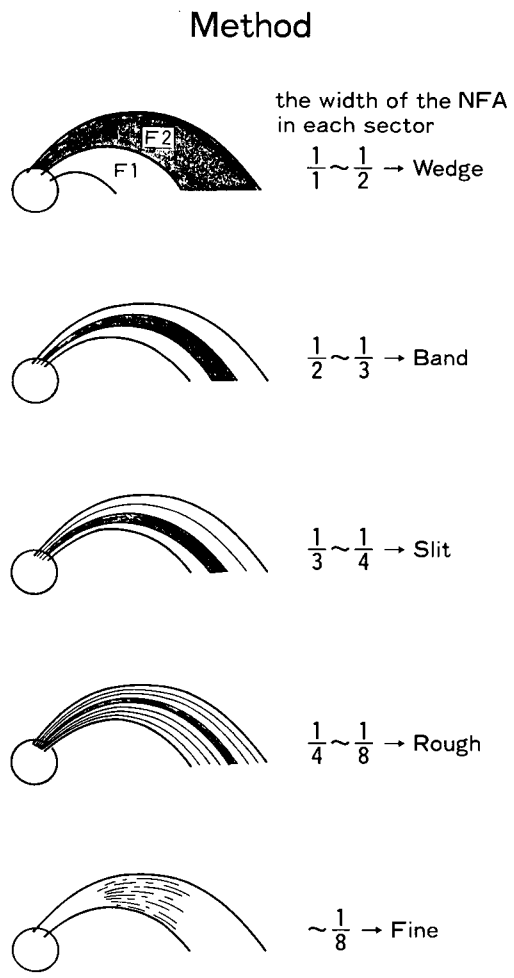

Fig. 3 Classification of NFA pattern, according to the width of each sector.

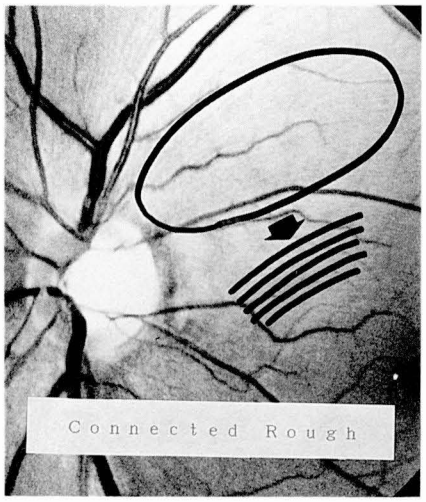

Fig. 4
A connected Rough NFA in the superior F1 area.

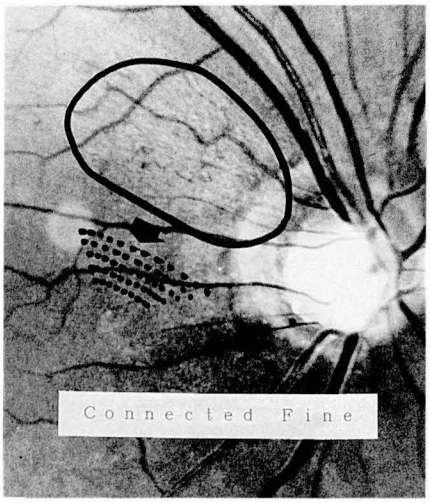

Fig. 5
A connected Fine NFA in the superior F1 sector.

When more than 2 NFAs were observed in the same sector by the classification described in 1 and 2, only Group C was selected if the groups were C and S, and the stronger pattern was adopted.

3) Classification of optic disc cupping

C/D ratios in the vertical direction were classified into 4 stages, i.e., C/D ratio less than 1/3 - cupping 1; in 1/3-1/2 - cupping 2; in 1/2-2/3 - cupping 3; and more than 2/3 - cupping 4.

The following analyses were made:

1. NFA appearance ratio by age group.
2. Characteristic NFA patterns in Group C.
3. Relation between the degree of optic disc cupping and the NFA pattern.

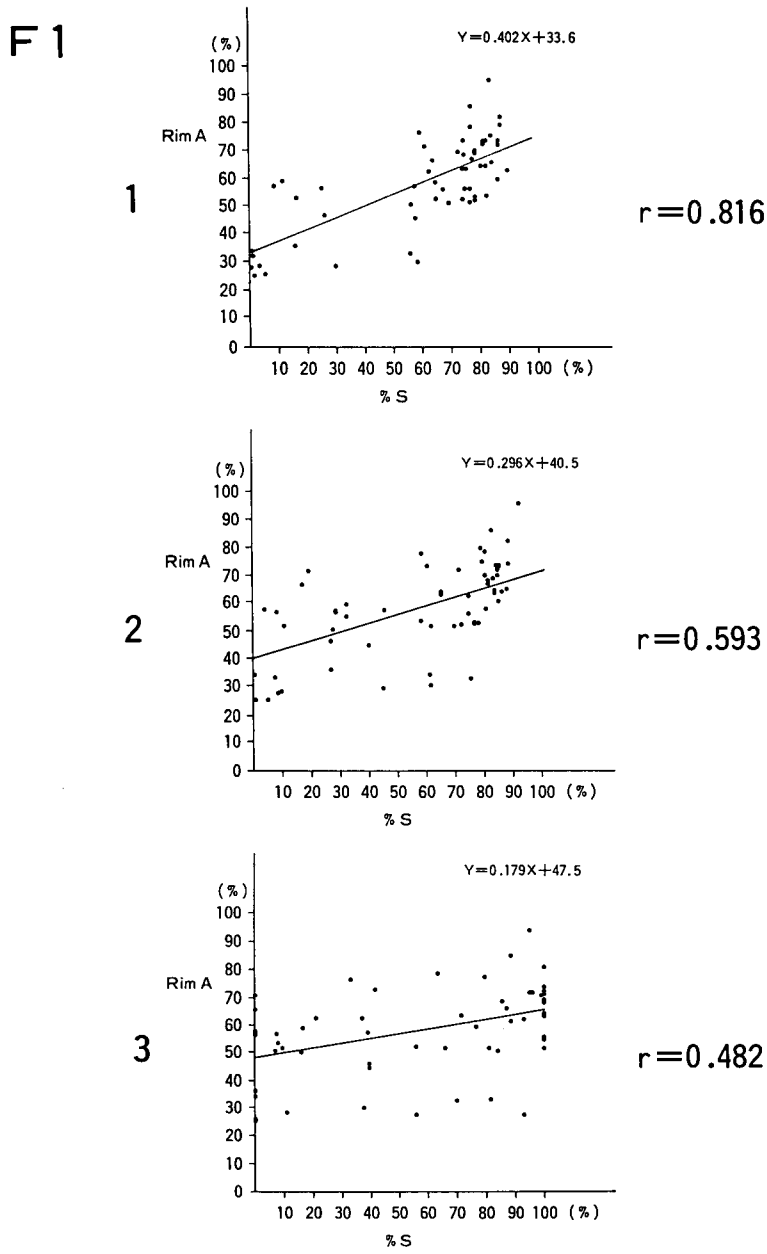

Fig. 6 The correlation between %S and Rim A by subsector in F1 sector.

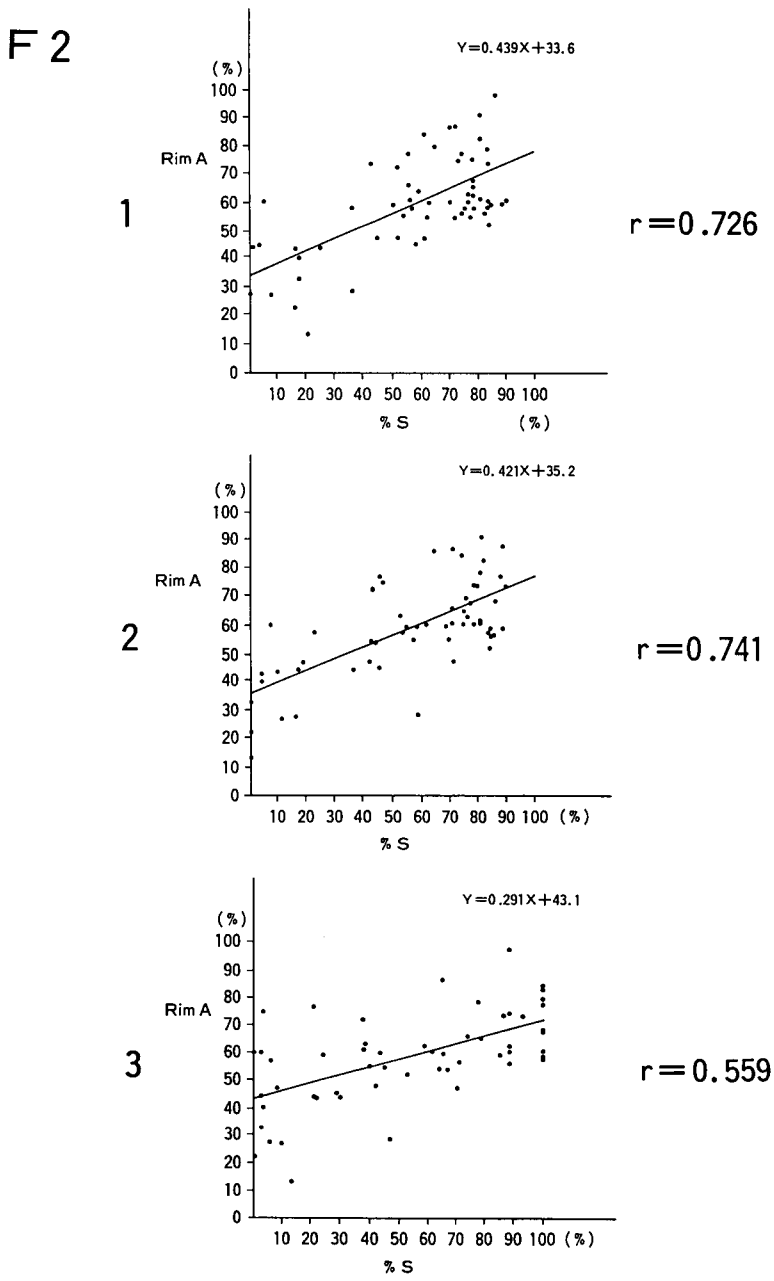

Fig. 7 The correlation between %S and Rim A by subsector in F2 sector.

RESULTS

A. Analysis of retinal sensitivity with glaucomatous NFA

1) Relation between Rim A and %S by each subsector in F1 and F2 sectors (Figs. 6, 7)

The correlation of Rim A and %S was positive with values of 0.653 (F1) and 0.670 (F2), respectively. There was a trend for Rim A to decrease as the %S decreased. The correlation coefficients for F1-1, -2 and -3 were 0.816, 0.593 and 0.482, respectively (Fig. 6), and those for F2-1, -2 and -3 were 0.726, 0.741 and 0.559, respectively (Fig. 7). A closer correlation between Rim A and %S was observed in the region more proximal to the optic disc. The trend was stronger in F1.

2) Relation between the region with decreased retinal sensitivity and the NFA pattern (Figs. 8. 9)

Out of a total of 29 x 4 (=116) sectors in the superior and inferior F1 and F2 sectors of 29 eyes were determined. 50 sectors (43.1%) were judged to occur NFAs. The total NFAs were observed in 31 sectors, the distal NFAs in 12 sectors, and the proximal NFAs in 5 sectors.

The distal NFA group showed a right-declining pattern with a significant decrease in distal %S (Fig. 8). The proximal NFA showed a left-declining pattern in all the cases (Fig. 9).

Case: Male aged 59, right eye (Fig. 10). A proximal NFA was observed in the inferior F1 sector. The decrease in retinal sensitivity at the proximal side was remarkable: %S by subsector in this sector being 55.6% for F1-1, 76.0% for F1-2 and 70.0% for F1-3. A distal NFA was observed in the superior F1 sector. The decrease in retinal sensitivity at the distal side was predominant: F1-1, 2 and 3 being 88.2%, 86.8% and 76.0%, respectively. On the other hand, Rim A showed a remarkable difference of 32.9% for the inferior F1 in which the proximal NFA was observed, and 59.5% for the superior F1 in which the distal NFA was observed. The formation of cupping was large in the region where the decrease in retinal sensitivity was significant in the proximal region.

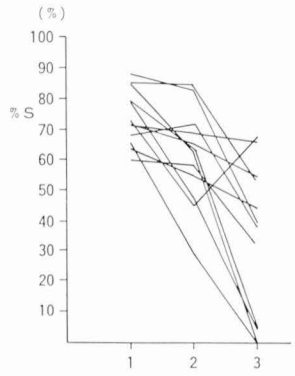

Fig. 8
The relation between the distal NFA pattern and pattern of functional change.

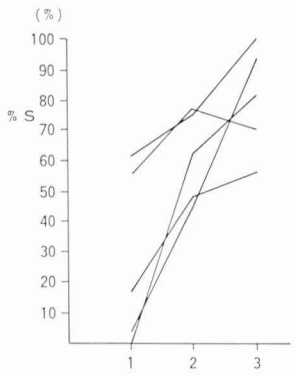

Fig. 9
The relation between the proximal NFA pattern and pattern of functional change.

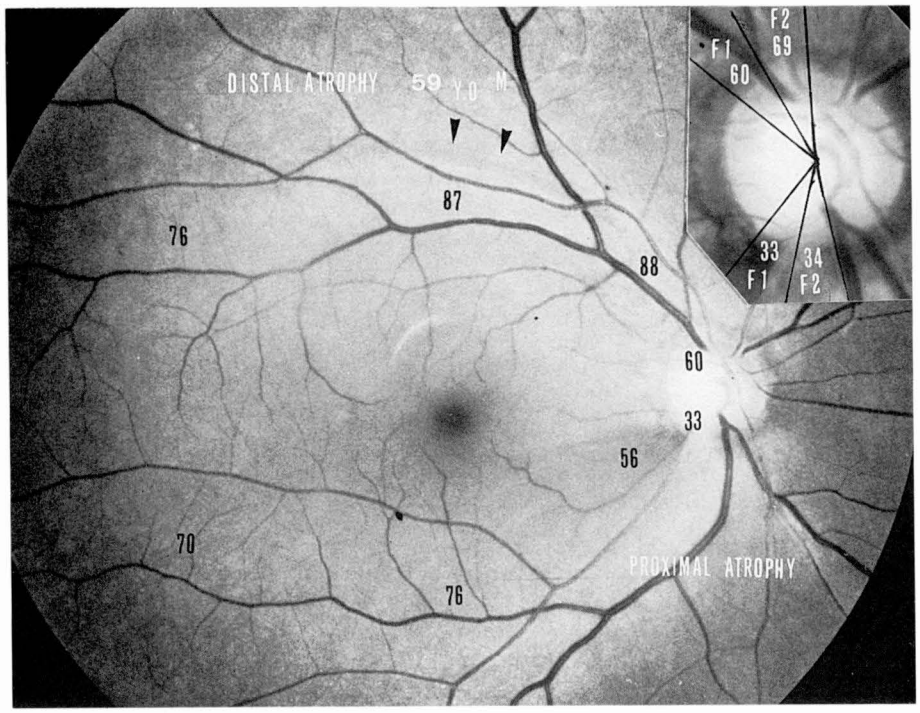

Fig. 10 Male aged 59, right eye. A proximal NFA was observed in the inferior F1 sector and a distal NFA was observed in the superior F1 sector.

B. Comparison of NFA pattern between a glaucomatous eye and a normal eye

1) NFA appearance ratio by age group (Table 1, 2)

NFA was observed both in F1 and F2 sectors in the glaucoma group, being 70.5% in Group C and 9.5% in Group S. NFA appearance ratio in F1 and F2 sectors in Group C showed no difference by age group, but it was observed that there was a trend towards higher ratio in the F2 sector compared with the F1 sector for any age group (Table 1). NFA did not occur in the normal group, but the ratio in the F2 sector increased with aging and was high in Group S compared with Group C for all the age groups. Group C showed a trend towards a decrease in the appearance ratio with aging: 13.3% for 20s, 15.1% for 30s, 16.4% for 40s, 24.2% for 50s and 41.2% for 60s, and it also exhibitied a statistically significant difference in the age groups of 40 and above. Furthermore, a significant difference was observed in the age groups between 20-30s and

Table 1 The glaucoma group. The NFA appearance ratios in F1 and F2 sectors in Group C by age groups.

Age	Eyes	C group(%)	F1/F2
20	4	75.0	0.71
30	9	41.7	0.77
40	11	68.2	0.67
50	13	86.5	0.73
60	13	86.5	0.78
	50		

Table 2 The normal group. The NFA appearance ratios in F2 sector in Group C by age groups. NFA did not occur in F1 sector.

Age	Eyes	C group(%)	S group(%)
20	60	13.3	27.5
30	262	15.1	36.1
40	296	16.4	37.5
50	132	24.2	44.7
60	34	41.2	42.5
	784		

40-60s for the test on difference in the ratio ($p < 0.05$) (Table 2).

No significant difference was observed in the ratio in bilateral eyes and superior and inferior sides, either in the glaucoma group or the normal group.

2) Characteristics of NFA pattern (Table 3, 4)

In Group C of the glaucoma group, a total NFA appearance ratio of Band and Wedge was more than 70% in both sectors. That is to say, Band (49.2%) and Wedge (28.8%) were shown in the F1 sector and Band (37.8%) and Wedge (36.8%) in the F2 sector (Table 3).

Table 3 The glaucoma group. The NFA appearance ratios by pattern in all age groups.

Pattern	F1 (%)	F2 (%)
Fine	3.4	0.0
Rough	15.3	18.3
Slit	3.4	7.3
Band	28.8	37.8
Wedge	49.2	36.6

On the other hand, NFA patterns in Group C in the normal group were Rough in 80-94% for all age groups, and severe NFAs, such as Band or Wedge, were observed in only 6 cases (2.1%) of the entire group (Table 4).

Table 4 The normal group. The NFA appearance ratios by pattern in all age groups.

Age	Fine	Rough	Slit	Band·Wedge (%)
20	0.0	93.8	6.3	0.0
30	8.9	81.0	8.9	1.3
40	5.2	89.7	4.1	1.0
50	0.0	82.8	10.9	6.3
60	0.0	82.1	17.9	0.0
Average	4.2	85.2	8.5	2.1

3) Relation between optic disc cupping and NFA (Table 5)

This assessment was made only for the normal group since there were 82% of cases with cupping 4 in the glaucoma group.

Cupping 4 was observed in 3.1% of the normal group. Regarding the degree of optic disc cupping in the normal group and NFA pattern in Group C, the appearance ratio became higher as the degree of optic disc cupping became stronger with 13.2% for cupping 1 and 33.3% for cupping 4 as seen in Table 5, and a statistically significant difference was observed between cupping 1 and 2 groups and 3 and 4 groups ($p < 0.05$) (Table 5).

Table 5 Normal group. The relationship between cupping size and appearance ratio in Group C.

Cupping	Eyes	C group (%)
1	223	13.2
2	338	16.7 *
3	199	24.4
4	24	33.3
	784	

* $p<0.05$

DISCUSSION

Analyses in (A) were made of the optic disc cupping and the functional change in glaucomatous eye and the functional change associated with a ophthalmoscopic NFA to investigate the relation among the three. To assess cupping, the rim/disc ratio (Rim A) was measured as the ratio was considered to reflect the functional damage directly. And to assess the sensitivity of each site in the retina, the calculation was made from the results of measurements with an Octopus automatic perimeter 500E, which were taken as described in the previous report.[6)]

The correlation between %S and Rim A by the subsector in the F1 and F2 sectors was stronger at the proximal region, compared with the counterpart between %S and Rim A of the subsector at the distal region (Figs. 6, 7). Thus it was confirmed that the more functional damage at the proximal region exerts a large influence on optic disc cupping formation.

The NFA patterns (distal, proximal and total), which could be judged at this time. In the relation between the NFA pattern and the pattern of retinal sensitivity chnage, distal NFA was of the right-declining distal functional damage predominent type

(Fig. 8), i.e., visual field pattern of nasal step, and the proximal NFA was of the left-declining proximal functional damage predominant type (Fig. 9), i.e., the visual field pattern of Bjerrum scotoma. This is ascribable to the fact that the proximal region from the optic disc where the functional damage is present in a greater extent tends to exhibit more NFA than the distal region.

There is a trend for functional damage at the proximal region from the optic disc to exert a larger influence on the formation of optic disc cupping in the distribution of nerve fiber fascicle, showing a proximal NFA, and on the other hand that functional damage on the distal region exerts only a small influence on optic disc cupping, exhibiting a distal NFA from the optic disc.

In animal eyes, Minckler[7] and Radius[10] reported that peripheral ganglion cell axons project through the deeper layers of the peripapillary nerve fiber layer (NFL) and enter the peripheral optic nerve. Conversely peripapillary ganglion cell axons project through those coming from pripheral location to superficial position in the NFL, then to the central optic nerve.

In our results the nerve fiber course has been reaffirmed clinically in the human eyes.

Therefore, nerve fiber drop out that is more proximal from the optic disc tends to be observed clinically as NFA, with a large influence exerted on cupping formation.

We can say that we have successfully enhanced the possibility of estimating with considerable precision the change in function accompanying NFA.

By the way, the fact that NFA is observed in the normal eye has been reported by many researchers, and NFA appearance ratios in the whole retina reported as 3% by Quigley et al.,[9] 17% by Airasksinen et al.,[1] 9.4-15.1% by Sommer et al.,[11] and 12.5% by Iwata et al.[3]

Assessments in (B), we analyzed the charateristics and different points of NFA into those observed in the glaucoma and those in the normal group by arranging NFA into a pattern to assess the mechanism of its occurence.

First, NFAs which were present in connection with or separate from the optic disc were classified into Group C and S, respectively. IN the normal group, the appearance ratio was high

in Group S, but there was a trend for the ratio to increase with aging both in Groups C and S (Table 2). While almost all NFAs in the glaucoma group were in Group C, it was considered to be a possibility of Group C being accompanied by more severe visual field damage. In our assessment, NFA appearance ratios in the arcuate area only in Group C of the normal group were 18.1% and as high as 42% in the patients in the 60s age group.

NFAs in color fundus photographs were classified into 5 patterns from Fine to Wedge, according to the width. Rough and Fine patterns are often corresponded with decreased retinal sensitivity examined by automatic perimeters (Octopus etc.). These patterns have often been recognized in glaucomatous eye that there is a possibility of high morbid state.

The result contrasted to findings that 85% of NFA appearances in the normal group were Rough and that a strong NFA appearance such as Band and Wedge were present in 74-78% of glaucoma gorup. The NFA appearance ratio showed a correlation with aging in the normal group, but it was considered that, in the F1 sector with the thickest retinal nerve fiber layer, NFA is not caused only by nerve fiber dropout due to aging. In addition, there are reports [3,8] that the NFA appearance ratio was significantly high in cases of hypertention, suggesting same action in progress, in glaucoma, of the mechanism causing a strong nerve fiber dropout that differed from aging, such as local circulatory disturbance.

Thus, we can say that we have successfully demonstrated that NFA observed in both the normal eye and glaucoma can be differentiated by its pattern and that glaucomatous NFA are very significant clinically.

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REFFERENCES

1. Airaksienen, P.J., Drance, S.M., Douglas, G.R. and Mawson, D.K.: Am. J. Ophthalmol. 1984. 98. 586/571. Diffuse and localized nerve fiber loss in glaucoma.
2. Hoyt, W.F., Schlicke, B. and Eckelhoff, R.J.: Br. J.

Ophthalmol. 1972. 56. 577/583. Funduscopic appearance of nerve fiber bundle defect.

3. Iwata, K.: Acta. Soc. Ophthalmol. Jpn. 1983. 87. 507/518. Retinal nerve fiber layer abnormality in earliest POAG. - Analysis by cotour synthesizer.
4. Kanatani, I. and Mizokami, K.: Jpn. J. Clin. Ophthalmol. 1986. 40. 725/729. Correlation between retinal nerve fiber bundle atrophy and optic disc cupping.
5. Kanatani, I. and Mizokami, K.: Acta. Soc. Ophthalmol. Jpn. 1987. 91. 1154/1159. Clinical evaluation of retinal nerve fiber layer atrophy.
6. Okubo, K., Katumori, N. and Mizokami, K.: Acta. Soc. Ophthalmol. Jpn. 1984. 88. 332/337. Correlation between glaucomatous optic disc and visual field defects. II. Quantitative evaluation.
7. Minckler, D.S.: Arch. Ophthalmol. 1980. 98. 1630/1636. The organization of nerve fiber bundle in the primate optic nerve head.
8. Nanba, K. and Iwata, K.: Acta. Soc. Ophthalmol. Jpn. 1987. 91. 127/131. Evaluation of retinal fiber layer defects in normal adults.
9. Quigley, H.A., Miller, N.R. and George, T.: Arch. Ophthalmol. 1980. 98. 1564/1571. Clinical evaluation of nerve fiber layer atrophy as an indicater of glaucomatous optic nerve damage.
10. Radius, R. and Anderson, D.R.: Arch. Ophthalmol. 1979. 97. 1154/1158. The course of axons through the retina and optic nerve head.
11. Sommer, A., Quigley, H.A., Robin, A.L., Miller, N.R., Kratz, J. and Arkell, S.: Arch. Ophthalmol. 1984. 102. 1766/1771. Evaluation of nerve fiber layer assessment.