

Fluorescein Filling Defects and Quantitative Morphologic Analysis of the Optic Nerve Head in Glaucoma

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Objectives: To evaluate absolute filling defects of the optic nerve head in normal tension glaucoma (NTG) and primary open-angle glaucoma (POAG) and to compare the filling defects with topographic analysis of the optic disc.

Methods: Twenty-five patients with NTG, 25 patients with POAG, and 25 age-matched controls were included. Fluorescein angiograms were performed by means of a scanning laser ophthalmoscope. The extent of absolute filling defects of the optic nerve head was assessed using digital image analysis of early-phase angiograms. Topographic measurements of the optic disc were acquired using the Heidelberg Retina Tomograph II.

Results: Absolute filling defects were significantly larger ($P=.001$) and were seen more often ($P<.001$) in patients with NTG ($n=18$) and POAG ($n=19$) compared with controls ($n=3$). Rim area ($P=.006$), rim volume

($P=.007$), cup-disc area ratio ($P=.008$), linear cup-disc ratio ($P=.005$), maximum cup depth ($P=.002$), cup shape measure ($P=.03$), and nerve fiber layer thickness ($P=.008$) and cross-sectional area ($P=.006$) were significantly different between patients with glaucoma and controls. Absolute filling defects were significantly correlated with cup area ($r=0.31$; $P=.007$), rim area ($r=-0.38$; $P<.001$), rim volume ($r=-0.35$; $P=.002$), cup-disc area ratio ($r=0.49$; $P<.001$), linear cup-disc ratio ($r=0.48$; $P<.001$), cup shape measure ($r=0.27$; $P=.02$), and nerve fiber layer thickness ($r=-0.33$; $P=.004$) and cross-sectional area ($r=-0.30$; $P=.009$).

Conclusions: Fluorescein filling defects of the optic disc are present in NTG and POAG. The extent of these filling defects is correlated with the morphologic disc damage.

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THE PATHOGENETIC CONCEPTS of glaucoma, defined as a progressive optic neuropathy characterized by optic nerve head excavation and glaucomatous visual field loss, include mechanical and vasogenic mechanisms.¹ A vascular failure leading to perfusion deficits of the optic nerve head, retina, choroid, or retrobulbar vessels, by means of vasosclerosis, small vessel disease, vasospasms, or autoregulatory dysfunction, may contribute to the nerve fiber loss in glaucomatous optic neuropathy.²⁻⁵ The mechanical damage is regarded as intraocular pressure (IOP)-dependent axonal dysfunction and loss. The lamina cribrosa and changes in extracellular matrix seem to have a substantial effect on the mechanical damage.^{6,7}

Fluorescein angiographic studies may describe perfusion alterations of the optic nerve head, retina, and choroid. In different studies,⁸⁻¹⁶ morphologic and dy-

namic perfusion variables demonstrated impaired ocular blood flow in glaucoma.

Fluorescein filling defects of the optic nerve head are areas of hypoperfusion, and they have been described in glaucomatous optic neuropathy since the 1970s.^{8,12,17-29} Absolute filling defects are persistent hypofluorescent areas, and they seem to correspond to capillary dropout in the surface nerve fiber layer of the optic disc.^{8,12,13,20,23,29} In contrast, relative defects are areas of delayed fluorescence, and they show a slower filling pattern with fluorescein.^{8,12,20} The filling defects are interpreted as areas of hypovascularity, as they are reproducible, with no consistent correlation with IOP and systemic blood pressure.^{8,10,12,13}

The number, extent, and topography of fluorescein filling defects correspond to visual field loss, nerve fiber layer defects, and cupping in glaucoma.^{17,20,26-32} Absolute filling defects are larger and of greater number in patients with glaucoma compared with those with ocular hy-

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pertension or controls.^{20,21,29,32} Several investigators^{8,12,33} have reported high specificity of filling defects for glaucoma and anterior ischemic optic neuropathy. Furthermore, the regions of pallor of the disc in optic atrophy seem to result from alterations in the tissue reflectance after axonal loss and from alterations in extracellular matrix and glial tissue rather than from a decrease in microvascular structures.³⁴⁻³⁷ In contrast, O'Day et al²⁴ also reported decreased fluorescence in different types of optic atrophy. In glaucoma, fluorescein filling defects of the optic disc are preferentially located at the margin of the optic disc excavation, mainly inferotemporally and superotemporally, and are more often found at the wall than at the floor of the cup.^{8,12,13,30,38} Several researchers^{8,12,30,29,39,40} emphasize the relevance of fluorescein filling defects in glaucomatous optic neuropathy and postulate that filling defects may be the initial damage in glaucoma.

The Heidelberg Retina Tomograph II (HRT II) (Heidelberg Engineering, Heidelberg, Germany) is a confocal scanning laser ophthalmoscope for quantitative stereometric analysis of the optic nerve head.⁴¹⁻⁴³ The scanning laser technique allows for 3-dimensional assessment of the optic disc based on a digital image of its surface. Differentiation of the neuroretinal rim and the optic nerve head cup requires an operator-dependent contour line-based standard reference plane.⁴¹⁻⁴³ Most stereometric variables depend on this reference plane.⁴¹⁻⁴⁶ The HRT II aims to detect glaucomatous optic disc appearances and structural changes in the retinal nerve fiber layer in glaucoma. Morphologic assessment of the optic disc in detecting early glaucoma may improve diagnostic reliability if structural damage precedes functional damage, as measured by conventional white-on-white perimetry.

The purpose of this study is to investigate the correlation between hypofluorescent areas of the optic disc and morphologic damage in glaucomatous optic neuropathy. Absolute fluorescein filling defects of the optic disc are compared with stereometric variables of the optic nerve head, as measured by confocal scanning laser tomography (HRT II). The filling defects of the optic disc and its stereometric variables are evaluated in patients with normal tension glaucoma (NTG), patients with primary open-angle glaucoma (POAG), and controls. The filling defects and morphologic variables of the optic nerve head are compared among groups and correlated with each other.

METHODS

PATIENTS

Twenty-five patients with NTG, 25 patients with POAG, and 25 age-matched controls are included in this prospective clinical study. For statistical analysis, 1 eye of each participant was randomly chosen. All individuals, including control subjects, provided informed consent. Adherence to the Declaration of Helsinki for research involving human subjects is confirmed.

Patients with NTG and POAG had glaucomatous optic nerve head cupping and glaucomatous visual field defects as defined by the European Glaucoma Society in the absence of retinal or neurologic disease affecting the visual field. The diagnostic criteria for glaucomatous visual field loss are as fol-

lows. Field loss was considered significant when (1) glaucoma hemifield test results were abnormal, (2) 3 points were confirmed with $P < .05$ probability of being normal (one of which should have $P < .01$), not contiguous with the blind spot, or (3) the corrected pattern SD was abnormal with $P < .05$.⁴⁷ All variables were confirmed on 2 consecutive visual field examinations performed using the Humphrey visual field analyzer (model 750; Humphrey-Zeiss, San Leandro, Calif) (full-threshold program 24-2).

All patients with glaucomatous visual field loss underwent diurnal curves of IOP measurements (Goldmann applanation tonometry) at 8 AM, noon, 4 PM, 8 PM, and midnight without any topical or systemic IOP-lowering medication. In patients with NTG, IOP never measured greater than 21 mm Hg.

Visual acuity was 20/40 or better, and no previous laser or surgical treatment had been performed. Patients with refractive aberrations of more than ± 4 diopters, diabetes mellitus, and hypersensitivity to sodium fluorescein were excluded from this study.

Control subjects had no history of ophthalmologic disease. Automatic static white-on-white and short-wavelength automated perimetry did not reveal substantial visual field loss. Nerve fiber layer imaging using a scanning laser ophthalmoscope (SLO; Rodenstock, Ottobrunn, Germany) with blue light (argon-blue 488 nm) indicated a regular nerve fiber layer structure without any nerve fiber bundle defects.

No statistically significant differences between patients with NTG and POAG were found for age, refraction, systolic and diastolic blood pressure, and heart rate. Patients with POAG had a significantly higher IOP compared with patients with NTG ($P = .02$). Seventeen patients with POAG, 16 patients with NTG, and 16 controls had a history of systemic cardiovascular disease, including arterial hypertension, treated with systemic medications. The mean number of local IOP-lowering medications was 1.48 for POAG, 0.64 for NTG, and 0.24 for controls. Six controls were initially treated as patients with NTG but were later reevaluated as controls with physiologic excavation of the optic nerve head. The clinical and demographic characteristics of all individuals included in the study are given in **Table 1**.

PROCEDURES

Patients with POAG, patients with NTG, and control subjects underwent a detailed ophthalmologic examination, videofluorescein angiography using the SLO, and a scanning laser tomographic examination using the HRT II.

Fluorescein angiography of the optic nerve head was performed using the SLO. The confocal video scanning laser ophthalmoscope, with a resolution of 512×512 pixels, detects temporal high-resolution images with high frequencies (25 Hz). To visualize the capillary network of the optic nerve head, the 20° field of observation of the SLO was used. Videofluorescein angiograms permit the selection of images with the best possible visualization of the superficial capillaries.^{15,16,29} To start the angiography, 10% sodium fluorescein dye (2.5 mL) was injected into an antecubital vein. The videofluorescein angiograms were performed with the optic nerve head centered. Images of the early phase (<3 minutes) were digitized visualizing the superficial capillaries of the optic nerve head. The angiograms were analyzed offline using digital image analysis (Matrox Inspector; Matrox Electronic Systems Ltd, Dorval, Quebec). The extent of absolute fluorescein filling defects was measured in relation to the area of the optic nerve head (percentage of the optic disc). Absolute filling defects of the optic nerve head are defined as areas of persistent hypofluorescence during the whole angiogram. During the angiogram, the focus was changed from the neuroretinal rim to the bottom of the cup to avoid artefacts. For evaluation of the hypofluorescent areas of

Table 1. Clinical and Demographic Characteristics of the Patient Groups*

	POAG Group (n = 25)	NTG Group (n = 25)	Controls (n = 25)	P Value†
Age, y	62 ± 9	62 ± 8	58 ± 9	.22
Intraocular pressure, mm Hg	17.2 ± 3.0	15.2 ± 3.0	16.0 ± 3.0	.07
Mean deviation, dB	-8.1 ± 7.5	-7.7 ± 7.4	-0.7 ± 1.4	<.001
Pattern standard deviation, dB	6.7 ± 4.4	6.6 ± 3.8	1.8 ± 0.3	<.001
Spherical equivalent, diopters	-0.9 ± 4.2	-0.3 ± 2.5	0.2 ± 1.7	.49
Systolic blood pressure, mm Hg	143 ± 16	137 ± 18	140 ± 21	.58
Diastolic blood pressure, mm Hg	81 ± 9	79 ± 10	77 ± 9	.50

Abbreviations: NTG, normal tension glaucoma; POAG, primary open-angle glaucoma.

*Data are given as mean ± SD.

†By analysis of variance.

the optic nerve head, the digitized single images were analyzed in a masked manner. Three observers (N.P., A.R., and O.A.) measured the extent of the absolute filling defects in agreement. As a reference for the disc area, digitized red-free images (argon laser 488-nm SLO) of the optic nerve head were used.

Systolic and diastolic blood pressure and heart rate were measured after a 5-minute rest in the sitting position before fluorescein angiography. Nerve fiber layer imaging with a blue laser (argon laser 488 nm) was performed. Nerve fiber layer defects confirmed the diagnosis of POAG or NTG.

Visual field examinations were performed using the Humphrey visual field analyzer and the white-on-white 24-2 full-threshold program. The standard visual field variables of mean deviation, pattern standard deviation, short-term fluctuation, and corrected pattern standard deviation were used for diagnosis and statistical analysis.

All patients and control subjects underwent confocal scanning laser tomography of the optic nerve head using the HRT II (software 2.01). The HRT software analyzes the mean topography of 3 consecutively performed confocal scanning laser images of the optic disc. The variability of the scanning images is expressed by the standard deviation of the topography. The border of the optic nerve head at the level of the Elschnig scleral ring was outlined manually by an experienced examiner (N.P.). Depending on this operator-based contour line, the HRT II software 2.01 calculates a reference plane delineating the neuroretinal layer from the optic cup. Most of the stereometric variables describing the optic nerve head depend on this reference plane. The contour line-based reference plane is located perpendicular to the z-axis, 50 µm below the contour line at 354° to 360° of the optic nerve head circumference. Magnification error was corrected using keratometry values for each individual. For statistical analysis, the following variables were determined: disc area, cup area, rim area, cup volume, rim volume (area above and volume below the reference plane), cup-disc area ratio, linear cup-disc ratio, mean cup depth, maximum cup depth, cup shape measure (the third moment of the frequency distribution of depth values relative to the contour line), height variation contour (maximum minus minimum of the relative height values of the contour line), nerve fiber layer thickness, and nerve fiber layer cross-sectional area (the calculated distance and area between the reference plane and the contour line). Disc area, mean and maximum cup depth, height variation contour, and cup shape measure are independent of the selection of the reference plane.

The fluorescein filling defects and the stereometric variables of the optic disc were compared among groups using analysis of variance. Correlations were tested using the Fisher *r* to *z* test. In all analyses, *P* < .05 was regarded as statistically significant.

RESULTS

Patients with POAG and NTG more often had absolute filling defects of the optic nerve head compared with controls. Absolute filling defects were present in 18 of the 25 patients with NTG, 19 of the 25 patients with POAG, and only 3 of the 25 controls (*P* < .001). The diagnostic validity to differentiate patients with glaucoma from controls was expressed as a specificity of 88% and a sensitivity of 74%. The absolute filling defects of the optic nerve head were significantly larger in patients with NTG and POAG compared with controls (*P* < .01). The extent of the filling defects was not significantly different in POAG and NTG (*P* = .91) (**Table 2**).

The following stereometric variables of the optic nerve head measured by confocal scanning laser ophthalmoscopy (HRT II) differed significantly between patients with glaucoma (POAG and NTG) and controls. Patients with glaucoma had smaller neuroretinal rim areas and rim volumes and larger cup-disc area ratios and linear cup-disc ratios. The maximum cup depth was smaller in patients with glaucoma. The cup shape measure showed significantly less negative values in the glaucoma groups, and the nerve fiber layer thickness and cross-sectional area were smaller. No significant difference between patients with glaucoma and controls was found for disc area, cup area, cup volume, mean cup depth, and the standard deviation of the calculated mean topography of the optic disc. The only variable found to differ significantly between patients with POAG and NTG was the height variation contour (*P* < .05). The results are given in Table 2.

Further analysis was performed to investigate correlations between fluorescein filling defects and stereometric variables of the optic disc. For all participants included in this study, the absolute filling defects were significantly correlated with cup area (*r* = 0.31), rim area (*r* = -0.38), rim volume (*r* = -0.35), cup-disc area ratio (*r* = 0.49), linear cup-disc ratio (*r* = 0.48), cup shape measure (*r* = 0.27), and retinal nerve fiber layer thickness (*r* = -0.33) and cross-sectional area (*r* = -0.30) (*P* < .05 for all) (**Table 3**). No correlations were found for disc area, cup volume, mean and maximum excavation depth, and height variation contour. For patients with POAG, the filling defects were significantly correlated with cup-disc area ratio (*r* = 0.43) and linear cup-disc ratio (*r* = 0.43)

Table 2. Fluorescein Filling Defects of the Optic Nerve Head and Stereometric Variables of the Confocal Scanning Laser Image Analysis*

	POAG Group (n = 25)	NTG Group (n = 25)	Controls (n = 25)	P Value†
Fluorescein filling defects, % of the disc area	12.6 ± 14.8	13.0 ± 16.5	0.7 ± 2.4	.001‡
Disc area, mm ²	2.29 ± 0.7	2.27 ± 0.4	2.39 ± 0.6	.74
Cup area, mm ²	1.20 ± 0.5	1.23 ± 0.5	1.06 ± 0.6	.46
Rim area, mm ²	1.09 ± 0.5	1.01 ± 0.35	1.34 ± 0.3	.006‡
Cup volume, mm ³	0.36 ± 0.2	0.33 ± 0.2	0.38 ± 0.3	.79
Rim volume, mm ³	0.22 ± 0.1	0.22 ± 0.1	0.30 ± 0.1	.007‡
Cup-disc area ratio	0.52 ± 0.1	0.54 ± 0.1	0.42 ± 0.1	.008‡
Linear cup-disc ratio	0.72 ± 0.1	0.73 ± 0.1	0.64 ± 0.1	.005‡
Mean cup depth, mm	0.30 ± 0.1	0.32 ± 0.1	0.35 ± 0.1	.20
Maximum cup depth, mm	0.67 ± 0.2	0.69 ± 0.2	0.81 ± 0.21	.02‡
Cup shape measure	-0.065 ± 0.07	-0.054 ± 0.07	-0.15 ± 0.22	.03‡
Height variation contour, mm	0.33 ± 0.1	0.41 ± 0.2	0.38 ± 0.10	.11
Nerve fiber layer thickness, mm	0.16 ± 0.1	0.18 ± 0.1	0.23 ± 0.10	.008‡
Nerve fiber layer cross-sectional area, mm ²	0.88 ± 0.4	0.97 ± 0.5	1.25 ± 0.40	.006‡
Standard deviation of topography	21 ± 23	19 ± 13	16 ± 8	.60

Abbreviations: NTG, normal tension glaucoma; POAG, primary open-angle glaucoma.

*Data are given as mean ± SD.

†By analysis of variance.

‡Statistically significant difference, NTG and POAG vs controls.

Table 3. Correlations for the Absolute Fluorescein Filling Defects With Stereometric Variables of the Optic Nerve Head for All 75 Participants

Absolute Filling Defects (% of the Optic Disc) and	P Value	Coefficient of Correlation <i>r</i> *
Disc area	.77	0.03
Cup area	.007	0.31
Rim area	<.001	-0.38
Cup volume	.71	0.04
Rim volume	.002	-0.35
Cup-disc area ratio	<.001	0.49
Linear cup-disc ratio	<.001	0.48
Mean cup depth	.57	-0.07
Maximum cup depth	.07	-0.21
Cup shape measure	.02	0.27
Height variation contour	.63	-0.06
Nerve fiber layer thickness	.004	-0.33
Nerve fiber layer cross-sectional area	.009	-0.30

*Correlations were tested using the Fisher *r* to *z* test.

(Table 4). In NTG, the filling defects were significantly correlated with rim area ($r = -0.51$), rim volume ($r = -0.51$), cup-disc area ratio ($r = 0.55$), linear cup-disc ratio ($r = 0.55$), maximum cup depth ($r = -0.40$), and nerve fiber layer thickness ($r = -0.49$) and cross-sectional area ($r = -0.48$) (Table 4). Controls exhibited a significant correlation of the filling defects with the maximum excavation depth only ($r = 0.58$; $P < .01$). None of the other stereometric variables of the controls were statistically significantly correlated with the extent of the filling defects.

COMMENT

Absolute fluorescein filling defects of the optic nerve head were statistically significantly larger and were seen more often in patients with POAG and NTG compared with

controls. These results confirm findings of various previous studies.^{8,12,20,21,29,32} In the present study, filling defects of the optic disc as a tool of differentiation between patients with glaucoma and controls had a specificity of 88% and a sensitivity of 74%. The filling defects observed on fluorescein angiograms reflect an area of hypoperfusion of the superficial nerve fiber layer of the optic nerve head in glaucomatous optic neuropathy and seem to correspond to capillary dropout.^{8,12,29}

Several histologic studies examined changes in the vascular structure of the optic nerve head in glaucoma to study interference of capillary loss and morphologic change of the optic disc. In experimental nonglaucomatous optic atrophy, the number of capillaries remained stable and was expressed as a ratio to the optic nerve tissue. The size and relative volume of the capillaries diminished, whereas fluorescein angiography did not alter.^{36,37,48} The studies of experimental optic disc pallor showed a rearrangement of astrocytes beside ganglion nerve fiber loss. Quigley and Anderson³⁷ and Radius and Maumenee⁴⁸ interpreted these findings as causative for optic disc pallor rather than the vascular alterations because in complete ganglion cell loss, capillaries are still present in a pale optic disc, and fluorescein angiography of the optic disc was not altered. Furthermore, optic atrophy of various causes, including ischemia, is rarely combined with an increasing cup-disc ratio, as in glaucomatous optic nerve degeneration.⁴⁸ Sebag et al⁴⁹⁻⁵¹ found reduced blood volume (approximately 50%) and oxygen delivery (approximately 40%) using vessel oxymetry, laser Doppler technique, and disc reflectometry in experimental optic atrophy. The Doppler measurements were substantiated by histologic studies of microsphere distribution (decrease of 80% in flow in anterior optic atrophy). Again, no abnormalities were detected by fluorescein angiography.⁴⁹⁻⁵¹ In contrast to glaucomatous optic atrophy, optic pallor in optic atrophy seems to result from ganglion cell loss, astrocyte rearrange-

Table 4. Correlations for the Absolute Fluorescein Filling Defects With Stereometric Variables of the Optic Nerve Head for Patients With POAG and NTG

Absolute Filling Defects (% of the Optic Disc) and	POAG Group (n = 25)		NTG Group (n = 25)	
	P Value	Coefficient of Correlation <i>r</i> *	P Value	Coefficient of Correlation <i>r</i> *
Disc area	.43	-0.16	.98	0.003
Cup area	.06	0.38	.08	0.36
Rim area	.52	-0.14	.002	-0.51
Cup volume	.78	0.06	.58	0.12
Rim volume	.83	-0.05	.009	-0.51
Cup-disc area ratio	.03	0.43	.004	0.55
Linear cup-disc ratio	.03	0.43	.003	0.55
Mean cup depth	.40	0.18	.39	-0.18
Maximum cup depth	.70	0.08	.04	-0.40
Cup shape measure	.06	0.38	.06	0.39
Height variation contour	.60	0.11	.48	-0.15
Nerve fiber layer thickness	.62	0.10	.01	-0.49
Nerve fiber layer cross-sectional area	.39	0.18	.01	-0.48

Abbreviations: NTG, normal tension glaucoma; POAG, primary open-angle glaucoma.
*Correlations were tested using the Fisher *r* to *z* test.

ment, or reduced blood volume or oxygen content, alterations not seen with fluorescein angiography.

In glaucomatous optic neuropathy, Elschnig,⁵² Cristini,⁵³ and François and Neetens⁵⁴ found a reduced capillary network in the optic nerve head and choriocapillaries. These qualitative studies⁵²⁻⁵⁴ emphasized capillary rarefaction in glaucomatous optic neuropathy. Kornzweig et al⁵⁵ and Alterman and Henkind⁵⁶ described selective atrophy in radial peripapillary capillaries in post-mortem eyes with chronic glaucoma and in experimental glaucoma. Quigley et al,^{36,37,57} however, stated that in their quantitative histologic studies of experimental glaucoma, capillary atrophy paralleled the nerve fiber loss. They found a stable capillary-tissue ratio in glaucomatous optic neuropathy and could not detect early damage angiographically. Consequently, these alterations in the capillary network of the optic nerve head were assumed to be secondary to nerve fiber tissue loss.^{36,37,57}

In contrast, clinical studies^{8,12,29} dealing with fluorescein angiographic filling defects of the optic nerve head stated that the filling defects, at least in some cases, precede morphologic damage, and vertical studies^{25,29,32} revealed a strong interrelationship to functional defects. The few longitudinal follow-up studies available concluded that filling defects emphasized progressive optic nerve damage,³⁹ and new field defects were related to new filling defects in glaucomatous optic neuropathy.⁴⁰

In the present study, the filling defects were correlated with the stereometric variables of the optic nerve head measured by scanning laser ophthalmoscopy. The statistically significant correlation with cup-disc area ratio and linear cup-disc ratio confirmed previous findings, even more so since in controls no such correlation was found. The filling defects were positively correlated with cup area and cup shape measure and negatively correlated with rim volume and nerve fiber layer thickness and cross-sectional area. In NTG, we found a statistically significant correlation with various variables, although in POAG the filling defects were only statistically significantly correlated with cup-disc area ratio and

linear cup-disc ratio. As patients with POAG and NTG did not differ in the extent of the filling defects and all stereometric variables except height variation contour, this may reflect a stronger relation of vascular and morphologic damage of the optic nerve head in NTG. The question of whether NTG refers to a single disease entity or to a subgroup of open-angle glaucoma with lower tolerance to IOP must be mentioned again. The extent and incidence of fluorescein filling defects of the optic nerve head did not differ in POAG and NTG in the presented study. Therefore, the concept of ischemic damage of the optic nerve head (ie, capillary dropout) in glaucomatous optic neuropathy seems to be applicable to both types of glaucoma. Whether capillary dropout of the optic nerve head precedes or follows neuronal loss needs to be clarified in longitudinal follow-up studies.

Few studies investigated blood flow variables compared with stereometric variables of the optic nerve head or functional data. Ciancaglini et al⁵⁸ found a significant correlation between blood flow variables measured using laser Doppler flowmetry and nerve fiber layer variables of scanning laser ophthalmoscopy. Kuba et al⁵⁹ could not find such correlation comparing laser Doppler flowmetry and scanning laser polarimetry. However, these studies have methodological limitations, as the dependence of blood flow measurement by scanning laser Doppler flowmetry on nerve fiber layer structures and the tissue volume included in the analysis remains unclear. Arend et al¹⁴ investigated fluorescein angiograms of patients with NTG and asymmetrical visual field loss. The altitudinal visual field defects were associated with prolonged arteriovenous passage time.¹⁴ The fluorescein filling defects were highly correlated with the visual field testing in various studies.^{8,12,17,26,29} In a blue field entoptic phenomenon approach, Sponsel et al⁶⁰ measured higher leukocyte velocities in eyes with better visual function, as expressed by the global index mean deviation. In a study by Fontana et al,⁶¹ pulsatile ocular blood flow was lower in NTG eyes with field loss compared with the contralateral normal visual fields. Ciancaglini et al⁶² found a cor-

relation between laser Doppler flowmetry variables of the lamina cribrosa region and visual field defects, although no correlation was found for the neuroretinal rim. In an indocyanine green fluorescence angiography study by Sato et al,⁶³ the watershed zones including the optic nerve head were associated with larger field defects in NTG.

In summary, this study implies a relationship between morphologic damage and superficial capillary loss observed in fluorescein angiography of the optic nerve head in glaucoma. Longitudinal studies are needed to clarify whether this capillary dropout is primary or secondary to nerve fiber tissue loss or functional defects, as clinical and histologic studies revealed different results in the past.

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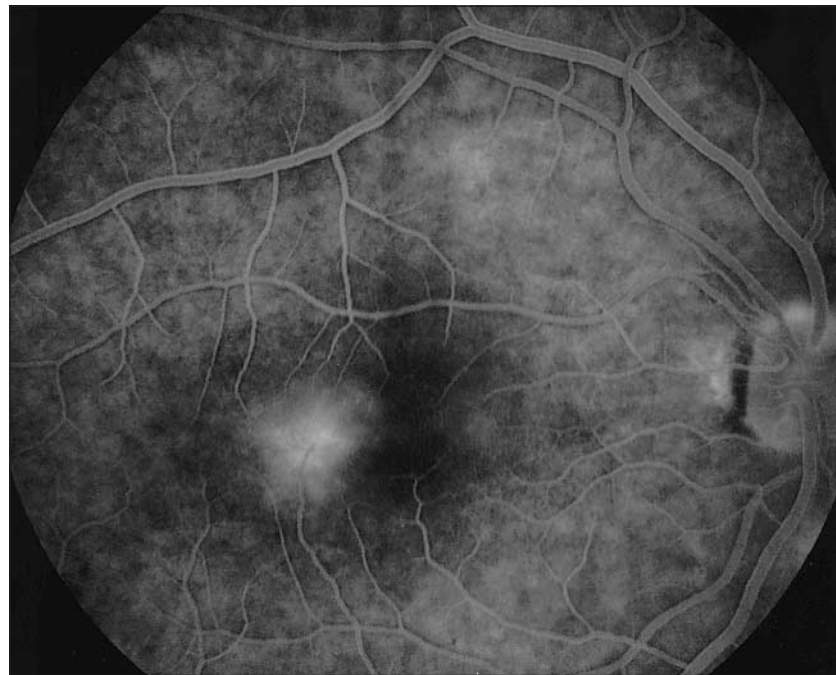
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ARCHIVES Web Quiz Winner

Congratulations to the winner of our October quiz, James A. Kimble, MD, University of Alabama at Birmingham. The correct answer to our October challenge was acquired parafoveal telangiectasis. For a complete discussion of this case, see the Photo Essay section in the November ARCHIVES (Martinez JA. Intravitreal triamcinolone acetonide for bilateral acquired parafoveal telangiectasis. 2003;121:1658-1659).

Be sure to visit the *Archives of Ophthalmology* Web site (<http://www.archophthalmol.com>) and try your hand at our Clinical Challenge Interactive Quiz. We invite visitors to make a diagnosis based on selected information from a case report or other feature scheduled to be published in the following month's print edition of the ARCHIVES. The first visitor to e-mail our Web editors with the correct answer will be recognized in the print journal and on our Web site and will also be able to choose one



of the following books published by AMA Press: *Clinical Eye Atlas*, *Clinical Retina*, or *Users' Guides to the Medical Literature*.