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Topographic changes in the optic disc in eyes with cotton-wool spots and primary open-angle glaucoma *

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Abstract. Changes in the topography of the optic disc in 26 eyes with cotton-wool spots displaying defects in the retinal nerve-fiber layer and in 31 eyes with early primary open-angle glaucoma showing a similar degree of such defects were studied by computer-assisted optic disc analyzer and then compared with 27 controls. Changes in the cup-to-disc ratio, cup volume, and ratio of rim area to disc area were not significant in eyes with cotton-wool spots. The quotient of cup volume divided by cup-to-disc ratio eyes with of primary open-angle glaucoma was greater than that in eyes with cotton-wool spots. For the detection of nerve loss in eyes with cotton-wool spots, the image analyzer, which identified the notches in the horizontally sectioned contour line of the cup, was more sensitive than stereoscopic detection of the notches in the rim ($P<0.05$). The image analyzer enabled the detection of slight nerve-fiber loss by examination of the contour line of the cup in eyes with cotton-wool spots.

Introduction

Increased cup-to-disc ratio (C/D ratio) and decreased neural rim area are early signs of glaucomatous damage; however, there is considerable overlap between normal and glaucomatous eyes [2]. Detection of changes in parameters such as cup volume by the computer-assisted image analyzer may also pose similar problems. Data obtained in previous studies on the cross-sectional contour line of the optic disc cup [12] may be erroneous due to undermining of the cups. The surface height of the nerve-fiber layer [3] shows less variation than the configuration of the optic disc and provides additional evidence of nerve loss; however, the retina is thin, and minute changes may be difficult to detect using the image analyzer. Changes in the surface of the neural rim area are greater than those in the height of the nerve-fiber layer and may be more easily detected by computer-assisted disc analyzer.

In the present study, changes in the neural rim surface were studied by sectioning the cup on a horizontal plane 100 µm below the surface in cases of cotton-wool spots and primary open-angle glaucoma. In eyes with cotton-wool spots, cupping was small despite the discrete defects in the retinal nerve-fiber layer [11] and was different from that in eyes with primary open-angle glaucoma, in which cupping increases either before or concomitantly with the occurrence of nerve-fiber-layer defects.

Patients and methods

Morphometric changes in the optic disc were studied in randomly selected 26 eyes of 26 patients with cotton-wool spots, 31 eyes of 31 subjects with early primary open-angle glaucoma and 27 eyes of 27 controls.

Patients with cotton-wool spots and those with glaucoma showed similar degrees of defects in the retinal nerve-fiber layer but did not have visual acuity measuring $<20/20$, ametropia of >3 diopters or >2 diopters of astigmatism. Subjects with cotton-wool spots did not show leakage from the optic disc as determined by fluorescein angiography, nor did they have retinal edema, large retinal hemorrhages, hard exudation or retinal detachment. Patients with signs of ischemic optic neuropathy, congenital disc anomaly, and a past history of glaucoma or neuro-ophthalmological disease or photocoagulation to the retina were excluded.

Subjects with cotton-wool spots were aged from 44 to 62 years. In all, 5 had hypertensive retinopathy, 19 had diabetic retinopathy and 2 had systemic lupus erythematosus. The severity of the diabetic retinopathy was less level 4 of the modified Airlie House classification [5], and some dot retinal hemorrhages in 13 diabetic patients were small and did not hinder the observation of nerve-fiber defects.

The diagnosis of systemic lupus erythematosus was confirmed by raised anti-nuclear factors and anti-mitochondrial antibodies (type V). Development of the retinal nerve-fiber defects was followed up for 6 months after the appearance of cotton-wool spots.

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The diagnosis of chronic primary open-angle glaucoma was made on the basis of high intraocular pressure ($\geqq 26$ mmHg), open angle, glaucomatous optic disc cupping and visual field defects. Optic discs with oblique insertion and those with extreme cupping (vertical C/D ratio of >0.9) were excluded from the study.

Fundus photographs for the examination of defects in the retinal nerve-fiber layer were taken under red-free light (by Canon 60U fundus camera, Tokyo, and Fuji Neopan SS black-and-white film, Iso 100, Tokyo) and magnified five times. The retinal nerve-fiber defects were examined after the optic discs had been masked and were classified into focal (detectable margins), diffuse (undetectable margins) and mixed types (intermediate, or co-existence of focal and diffuse defects). Photographs for morphometry of the optic disc using a stereoscopic viewer (Asahi Pentax Stereo Viewer II, Asahi Kogaku, Tokyo) were taken with a binocular camera (TRC-SS, Topcon, Tokyo).

The vertical and horizontal C/D ratio (ratio of the vertical and horizontal cup radii to the disc radii) was studied from the photographs, independently from the morphometric study using the optic disc analyzer. Axial length was measured by A-scan ultrasonography, and corneal curvature was measured with a keratometer for computation of the size of the optic disc.

For computer-assisted morphometry of the optic disc, as a first step we marked four coincident control points on the two photographs displayed on the monitor. The vertical and horizontal C/D ratio, contour line of the optic cup, neuroretinal rim area, ratio of neuroretinal rim area to disc area, and cup volume were calculated using the image analyzer, and the size was corrected by Littmann's procedure [9]. We used the Imagenet optic disc analyzer (Topcon, Tokyo, Japan), which is a system almost identical to the PAR IS 2000, details of which have previously been reported [14].

The contour line of the cup was studied at 50, 100 and 150 μm below the surface of the tissues on Elschnig's ring, and we used the 100-μm line as the cup border. The sectional plane was roughly parallel to the frontal plane. The mean height of the tissues on Elschnig's ring was taken as the zero level and the various heights of the tissues were shown on the display.

To examine the undulation of the surface, an arbitrary point could be shown on the display via a mouse device and its absolute height from the zero level could be determined. If necessary, tissue heights can be printed out (see Fig. 1). The degree of undulation of the surface of the optic disc in controls was assessed by measuring the difference between the highest and lowest points within 30° of the circumference of the optic disc in the superior temporal and inferior temporal sectors. In some cases, smoothing of the contour line on the graphics was used to cancel artifacts, but its use was minimized. The vertical C/D ratio was defined as being the ratio of the longest vertical diameter of the cup to the vertical diameter of the optic disc. The optic disc was examined in a masked fashion three times each by the stereoscopic viewer and by Imagenet. Those that were poorly contrasted and/or extremely pale were excluded from the morphometric study.

For the purpose of studying the contour line of the cups, the notching of the neural rim was defined as follows: (1) cases in which the width of the neural rim was focally reduced by half or more within 30° of the circumference; and (2) cases in which small, sharp notches co-existed with grooves in the rim. Diffuse depressions in the temporal part of the optic disc were not considered to represent notches. As studied by Imagenet, the grooves were defined as being continuously depressed areas whose bottom measured ≥ 0.1 mm in depth and not related to the position of vessels.

After the notches had been defined, the possibility of false notches was judged on the display. The dot-like depressions, the small, sharp notches adjacent to the vessels, and the notches caused by steep, abnormal elevation of the wire-frame images on the display were considered to represent possible artifacts, and the groove-like depressions on the surface of the optic disc were considered to represent possible true notches. Abnormally located or sized notches such as the large ones in the papillo-macular bundle area or those extending from the center of the optic disc to its margin are clinically improbable and were excluded as artifacts. The nasal contour line of the cup could have been influenced by vessels and was not included in the study. The final categorization of notches shown on the display into either true notches, which accompany true nerve-fiber loss, or false notches was made by assessing the congruity of their location on the display with that of the retinal nerve-fiber defects on the photographs and with visual field defects and by examination of the notches using the stereoscopic viewer.

The retinal threshold of the posterior retina was examined using program G1 of Octopus 201, and was scanned by program

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                                                [ 90]

                                         7   5   5   5   4   4   5   5
                                 7   7   5   3   3   3   3   3   3   5   5
                         -9   0   3   3   3   1   1   1   1   1   1   3   4   4   2
                     -7 -11 -11   0   0  -3  -4  -5  -5  -4   0   0   1   2   2   1  -3
                    -10 -11 -11 -11 -11 -12 -12 -15 -15 -12  -4  -2   0   1   1   0  -1  -6
                -17 -17 -17 -18 -25 -25 -23 -23 -24 -24 -24 -20 -16  -3   0   0   0  -1  -6
            -17 -17 -17 -18 -34 -38 -43 -48 -50 -56 -56 -41 -34 -30 -26 -19   0   0  -7  -8  -9
            -15 -15 -15 -29 -38 -43 -48 -50 -56 -57 -57 -44 -38 -33 -30 -26 -19 -14  -8  -9  -9
        -13 -15 -13 -13 -29 -36 -41 -43 -48 -50 -56 -49 -42 -35 -31 -30 -29 -26 -19 -17 -12  -9 -13
        -13 -13   0   0 -29 -34 -36 -41 -43 -49 -49 -49 -42 -35 -31 -30 -29 -28 -22 -19 -17 -14 -14
        -12 -10   1   1 -29 -31 -34 -36 -41 -44 -49 -49 -49 -37 -32 -31 -29 -28 -22 -22 -18 -17 -16
        -10  -6   3   3 -29 -30 -32 -33 -36 -44 -49 -53 -52 -44 -36 -33 -33 -29 -25 -22 -18 -17 -17
[180]    -6  -3   3   3 -28 -30 -32 -33 -36 -49 -53 -53 -52 -44 -36 -33 -33 -29 -25 -22 -17 -17 -18      [ 0]
         -6  -3   3   3 -15 -32 -33 -36 -36 -49 -50 -53 -49 -38 -31 -29 -29 -25 -25 -16 -16 -17 -18
         -7  -3   3   3 -15 -32 -32 -36 -36 -36 -49 -49 -38 -31 -27 -25 -25 -25 -25 -16 -16 -16 -17
         -3   1   3   3   3 -27 -32 -32 -28 -28 -32 -36 -32 -27 -25 -18 -18 -19 -19 -14 -14 -16 -17
          1   1   3   3   3  -7 -28 -28 -27 -27 -32 -32 -32 -26 -18 -10  -8  -8 -11 -13 -14 -16 -17
          2   1   1   3   0   0  -7 -14 -14 -25 -32 -32 -31 -26 -10  -4  -2  -2  -9 -11 -13 -15 -18
          2   1   0   0   0   0   0  -1 -10 -14 -25 -29 -29 -14  -4   0   2   0   0  -9 -13 -15 -18
              1   0   0   0   0   0   0  -1  -6 -12 -14 -14  -6   0   2   3   3   0  -3 -12 -18
              0   0   0   0   0   0  -1  -1  -1  -1  -6  -6  -4   0   2   3   3   2   0 -11 -17
                  0   0   0   0   0   1  -1  -1  -1  -1  -1   0   1   2   4   4   4   2  -9
                      0   0   0   2   1   1   1   1   1   1   1   1   2   4   4   4   2
                      0   0   0   2   1   1   1   2   2   2   2   2   2   2   4   3   0
                          2   2   2   1   1   1   2   2   3   3   2   2   2   2   0
                                  2   1   1   1   2   3   3   3   3   2   1
                                          0   0   1   2   3   3   3

                                                [270]
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Fig. 1. An example of the height of optic disc tissues from an eye with chronic high-tension glaucoma, printed in a matrix format. The zero level was the mean height of the nerve tissues on Elschnig's ring. $1 = 10$ μm; −, depression. A groove-like depression appears in the superior temporal sector of the rim (*arrow*). Artifacts caused by vessels were common in the nasal half, which was not included in the study

F of Octopus with a resolution of one degree along the meridians of 45°, 90° and 135° through the fovea. The data on retinal sensitivity from the nonperfusion area were excluded from this study. The short-term fluctuation was <2.5 dB and the pupil size was 3–5 mm in each patient. Subjects were examined more than twice during the first 3 months and the threshold change was examined at intervals of 3 months. The visual field indices of program G1 – mean defect, loss variance, corrected loss variance and short-term fluctuation – have been described by Flammer and associates [6].

The coefficient of variation in computer-assisted morphometry of the optic disc was studied by examining the same eye three times. Statistical analysis was carried out by means of the chi-square test and Student's unpaired *t*-test, and correlation of the C/D ratio with cup volume was analyzed by simple linear regression using a linear correlation coefficient.

Results

The degree of visual field defects found in eyes with cotton-wool spots was similar to that found in patients with primary open-angle glaucoma (Table 1). New nerve-fiber defects developed after the occurrence of 24 of 96 (25%) fresh, solitary cotton-wool spots, 21 of which were of the focal type. When depressions of retinal sensitivity by solitary cotton-wool spots were scanned on the vertical meridian of the fovea centralis by program F, the defects were seen to be small: 5.1 ± 2.1 dB at their deepest points and 2.8° ± 1° in width ($n = 24$). The width of the defective nerve bundle was smaller than the cotton-wool spots. The nerve defects due to single cotton-wool spots were usually mild but may become large with the occurrence of additional cotton-wool spots (Fig. 2a, b).

Table 1. Visual field defects in eyes with cotton-wool spots and primary open-angle glaucoma

Mean defects	Controls ($n = 37$)	CWS ($n = 26$)	POAG ($n = 31$)
0–5 dB	27 (100%)	16 (62%)	17 (55%)
5–10 dB	0	6 (23%)	7 (23%)
10–15 dB	0	4 (15%)	7 (23%)
Mean age (years)	52.3 ± 11.2	54.1 ± 9.7	55.1 ± 13.2

CWS, Cotton-wool spots; POAG, primary open-angle glaucoma; dB, decibels

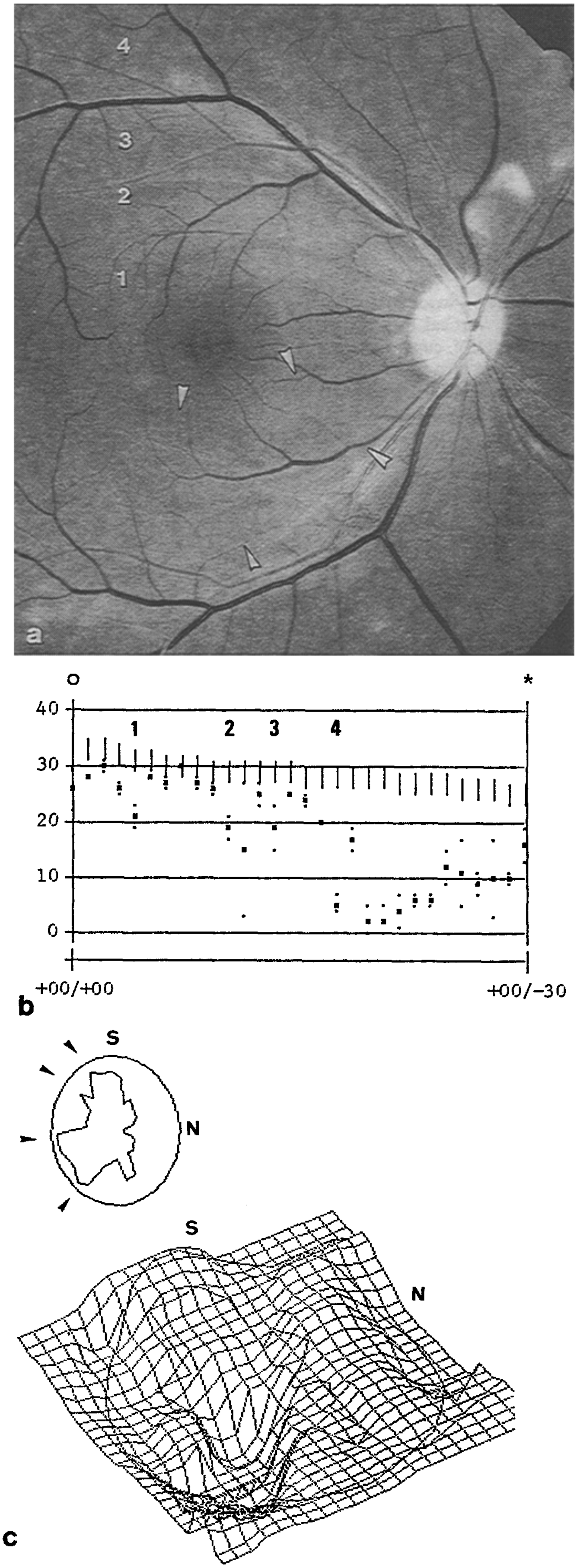

Fig. 2. a Example of defects in the retinal nerve-fiber layer secondary to cotton-wool spots in a patient with systemic lupus erythematosus, showing superior focal (*1–4*) and inferior diffuse defects (*arrowheads*). **b** Depressed retinal sensitivity corresponding to the defects (*1–4*). The retinal sensitivity was scanned using Octopus; program F along the vertical meridian from the fovea (0) to −30° (*). **c** Notches on the contour line of the cup and undulation of the surface of the neural rim as shown by wire-frame display. The defects shown in **a** correspond to the notches (*arrowheads*). The vertical and horizontal C/D ratios were 0.69 and 0.58, respectively, and the mean defect, corrected loss variance and short-term fluctuation values were 14.9 dB, 48.2 dB and 2.5, respectively, but the cup volume (0.17 mm^3) was extraordinarily small. *S*, superior; *N*, nasal side of the optic disc

Table 2. Morphometric parameters of the optic disc cup in eyes with cotton-wool spots and those with high-tension glaucoma

	Control ($n=27$)	CWS ($n=26$)	POAG ($n=31$)
CDR(V)	0.56±0.14	0.57±0.17*3	0.70±0.09*4
CDR(H)	0.48±0.16	0.47±0.21*3	0.63±0.16*4
CV	0.19±0.14	0.24±0.23*3	0.47±0.27*4
RA	1.63±0.42	1.66±0.36*1	1.42±0.45
RA/DA	0.68±0.13	0.68±0.15*2	0.54±0.13*4
MD(dB)	0.1 ±0.39	6.9 ±6.2	6.2 ±5.5*4

CWS, cotton-wool spots; POAG, primary open-angle glaucoma; CDR(V), vertical cup-to-disc ratio; CDR(H), horizontal cup-to-disc ratio; CV, cup volume (mm^3); RA, rim area (mm^2); RA/DA, ratio of rim area to disc area; MD; mean defects (dB)
Comparison between the CWS and POAG groups: *1 $P<0.05$; *2 $P<0.01$; *3 $P<0.001$
Comparison between the control and POAG groups: *4 $P<0.001$

Nerve-fiber-layer defects in eyes with primary open-angle glaucoma were rarely multiple and more diffuse, and the border line between the healthy area and pathological area was not clear. Their deepest points measured 14±6.8 dB and defective areas below 3 dB were 12.5°± 5.8° in width, which was broader than defects found in eyes with cotton-wool spots ($P<0.001$). Examination of the control eyes revealed that the temporal part of the optic disc was 150±57 μm deeper than the zero level and that the undulation of the superior temporal and inferior temporal sectors (the difference between the highest and lowest points of the optic disc within 30° of the circumference) measured 49.5±41.2 μm ($n=21$).

The vertical and horizontal C/D ratios of control eyes analyzed by Imagenet were 0.56±0.14 and 0.48± 0.16, respectively (Table 2), which were greater than the respective values of 0.37±0.13 and 0.36±0.14, determined by direct measurement on the photographs ($P<0.001$). In spite of the retinal nerve-fiber and visual field defects, there was no significant difference in C/D ratio, cup volume, rim area or ratio of rim area to disc area between eyes with cotton-wool spots and control eyes. The vertical C/D ratio, horizontal C/D ratio, cup volume, rim area and ratio of rim area to disc area in cases of cotton-wool spots were significantly smaller than those found in eyes with primary open-angle glaucoma that showed a similar degree of visual field defects ($P<0.001$, $P<0.01$, $P<0.001$, $P<0.05$ and $P<0.01$ respectively; Table 2).

The linear correlation coefficient between C/D ratio and cup volume in eyes with primary open-angle glaucoma and those with cotton-wool spots were $r=0.60$ and $r=0.78$ respectively, and the unpaired t-test showed a statistically significant correlation ($P<0.001$) between these parameters in both groups. The quotient of cup volume divided by C/D ratio was greater in eyes with primary open-angle glaucoma. The simple linear-regression line calculated using the method of least squares was $Y=1.94X-0.89$ for eyes with primary open-angle glaucoma and $Y=1.09X-0.38$ for those with cotton-wool spots, where Y represents the cup volume and X,

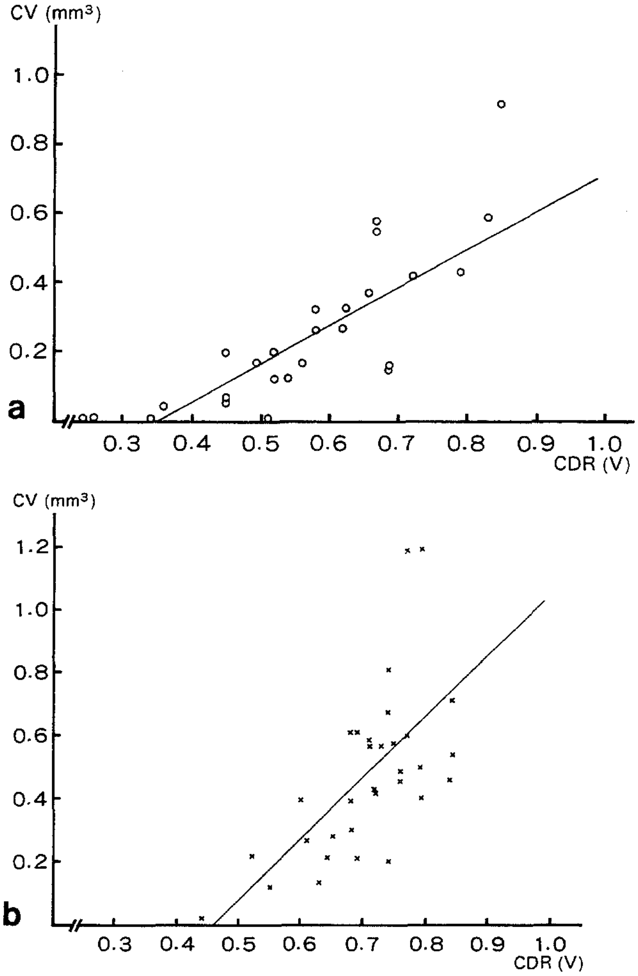

Fig. 3a, b. Relationships between the vertical C/D ratio [*CDR(V)*] and cup volume (*CV*) in eyes with **a** cotton wool spots and **b** primary open-angle glaucoma (POAG). The C/D ratio ($P<0.001$), cup volume ($P<0.01$), ratio of rim area to disc area ($P<0.001$) and rim area ($P<0.05$) in eyes with POAG were significantly greater or smaller than those in eyes with cotton-wool spots (Table 2). The quotient obtained by dividing the cup volume by the vertical cup-to-disc ratio was greater in the POAG group ($P<0.001$)

the vertical C/D ratio (Fig. 3a, b). The numerical value obtained by dividing the cup volume by the vertical C/D ratio in eyes with primary open-angle glaucoma was 0.71±0.41, which was significantly greater than the value of 0.41±0.25 obtained for eyes with cotton-wool spots ($P<0.001$).

When the temporal contour line of the cup was studied using the image analyzer, 18 of 26 (69%) eyes with cotton-wool spots showed 28 notches in the neuroretinal rim (Fig. 2c). In all, 10 of the 18 eyes (56%) had only 1 notch and others had ≥2. However, 7 of the 28 notches on the display were judged to be false. Among the residual 21 notches, 13 notches in 11 patients corresponded to the retinal nerve-fiber or visual field defects and were thus assessed as being true notches (Table 3).

All 26 patients with cotton-wool spots showed nerve-fiber defects by the examination under red-free light; thus, the detection of notches by image analysis (11/26; 42%) was less sensitive than that by examination under

Table 3. Evaluation of the notches in each group

	Control ($n=27$)	CWS ($n=26$)	POAG ($n=31$)
Total number of notches found by Imagenet	27/17 eyes	28/18 eyes	27/17 eyes
False notches judged on the display	11	7	4
Candidates for true notches after judgment based on the display by the image analyzer	16/10 eyes	21/15 eyes	23/15 eyes
False notches not corresponding to actual nerve-fiber loss	16/10 eyes**	8/6 eyes	9/7 eyes
True notches corresponding to actual nerve-fiber loss	0	13/11 eyes*	14/12 eyes
Notches found by stereoscopic examination	0	3/3 eyes	11/8 eyes

CWS, cotton-wool spots; POAG, primary open-angle glaucoma

* Significantly greater than value obtained by stereoscopic examination ($P<0.05$); ** significantly greater than value obtained for CWS ($P<0.05$)

red-free light ($P<0.001$). Three patients showed notches during stereoscopic examination of their optic discs, and these notches were detected using both the stereoscope and Imagenet in two eyes (8%). Thus, Imagenet (11/26; 42%) was more sensitive than stereoscopic examination (3/26, 12%) in detecting nerve loss in the neuroretinal rim ($P<0.05$). In eyes with primary open-angle glaucoma, notches corresponding to nerve loss were found in 12 of 31 eyes (39%) by Imagenet and in 8/31 eyes (26%) by stereoscopic examination, and the detection rate was similar for both techniques.

The number of eyes with false notches that did not correspond to true nerve-fiber loss in controls, patients with cotton-wool spots and those with primary open-angle glaucoma were 10/27 (37%), 6/26 (23%) and 7/31 (23%), respectively, and the differences were not significant. However, total number of false notches per total number of eyes examined was 16/27 (59%), 8/26 (31%) and 9/31 (29%), respectively, and that in controls was slightly higher ($P<0.05$; Table 3). Of 23 eyes with artifacts, 16 (70%) had vessels either running horizontally across the neural rim or emerging from half-lucent nerve tissues adjacent to the artifacts on the display. The poorly focused points on the photographs and the low contrast of the optic disc itself were the other causes of the artifacts.

The coefficient of variation for morphometry of the vertical C/D ratio, horizontal C/D ratio, cup volume, rim area and ratio of rim area to disc area as determined three times by Imagenet was 6.5%, 8.3%, 8.9%, 6.5% and 8.9%, respectively. The notches were examined five times and the variation in reproducibility was <2%.

Discussion

The development of defects in the nerve-fiber layer of patients with cotton-wool spots is well known [7, 8, 10]. The defects are focal and contrast highly with the surrounding retina. In many cases, they are the first clinical sign of nerve damage, whereas changes in classic indices such as the C/D ratio, cup volume, rim area and ratio of rim area to disc area are small and do not represent early signs of nerve damage in eyes with cotton-wool spots [11]. This contrasts with findings in glaucomatous eyes, in which the previously mentioned parameters are affected early. The difference in the relationship between cup volume and C/D ratio in patients with cotton-wool spots as opposed to glaucomatous eyes may be useful in distinguishing non-glaucomatous from glaucomatous optic disc cupping in cases in which differentiation by examination of photographs is difficult [13].

Detection of slight nerve-fiber loss is a subject of clinical importance. If the optic disc analyzer is sensitive enough, slight changes in eyes with cotton-wool spots should be detected; however, in the present study and other investigations [1, 14], the coefficients of variation for measurement of optic disc parameters by computer-assisted morphometry were moderately large. Small changes in the area or volume of the optic cup in these patients might have been ignored because of the large variance of data obtained using the image analyzer. The pale and poorly contrasted neural rim in these cases may be another reason why it was difficult to detect changes in the optic disc using this system.

The classic indices for cup volume and disc area were not useful in eyes with cotton-wool spots; however, morphometric analysis of the optic disc cup based on its horizontally sectioned contour line was valuable in detecting early nerve-fiber loss in such cases. The small cup drop (100 μm in the present study) may produce a C/D ratio larger than the clinically determined value; however, the sectional plane near the surface of the optic disc can reveal slight undulations or grooves on the surface of the optic disc in eyes with cotton-wool spots that can hardly be detected by straightforward examination.

The most serious problem in interpreting the contour lines of optic disc cupping involved the differentiation of artifacts. Depth measurement of the optic nerve head varies interphotographically, and 95% confidence intervals of 166 and 252 μm have been reported for ten photographs of healthy optic discs [4]. However, intraphotographic variation of data is low, and a setup of 100 μm drop was large enough to exclude artifacts in the present study. Tilted or largely excavated optic discs may cause erroneous displays of the image [15, 16], and should be excluded.

In the present study, 70% of the false notches were correlated with vessels, and the abundance of vessels in the neural rim in less excavated eyes may cause a higher incidence of artifacts, especially when the vessels emerge from half-lucent nerve tissues or run across the cupped area. This may explain the high prevalence of false notches in the well-vascularized optic disc of controls. The present image analyzer was not precise enough to exclude all artifacts; moreover, the detection of the latter largely depends on the experience of the operator. Acquisition of high-quality images from high-quality cameras, e.g. "High Vision" of the NHK Co., Tokyo, may eliminate artifacts.

We studied the 100-μm line below the zero level to determine the surface changes, because the 50-μm line had a higher prevalence of artifacts and the 150-μm line was less sensitive for the detection of surface changes. In primary open-angle glaucoma, the sensitivity of Imagenet and that of stereoscopic examination in the detection of focal nerve-fiber loss were similar. The cupping was deep and large and the cup walls were steep in eyes with primary open-angle glaucoma, and focal defects in the neural rim were easily detected by stereoscope. The nerve defects in eyes with cotton-wool spots were smaller than those in eyes with primary open-angle glaucoma; this might explain the difference in sensitivity for the detection of nerve loss by stereoscopic examination between patients with cotton-wool spots and those with primary open-angle glaucoma.

In conclusion, despite the difficulties we encountered in interpreting the data, by examination of the horizontally sectioned contour line of the cup, the image analyzer was useful in detecting slight nerve-fiber loss secondary to cotton-wool spots.

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