Detection of Structural Damage From Glaucoma With Confocal Laser Image Analysis

Hideya Uchida, Luca Brigatti, and Joseph Caprioli

Purpose. To determine which structural optic nerve head parameters measured with confocal scanning laser image analysis that best discriminate between normal persons and those with glaucoma.

Methods. One randomly selected eye of 53 patients with early open-angle glaucoma (average visual field mean deviation = -4.8 dB) and of 43 age-, race-, and refractive error-matched normal subjects were studied. The performance of nine structural measures was evaluated with linear multivariate analysis and a neural network: cup area, cup to disc area ratio, rim area, height variation contour, cup volume, rim volume, cup shape measure, mean retinal nerve fiber layer thickness, and retinal nerve fiber layer cross-section area. A discriminant function was derived with two thirds of the sample and its discriminant power tested on the remaining one third. This was repeated twice so that the entire sample was used for training and testing. A neural network was trained and tested in the same way. Stereoscopic color optic nerve photographs of the same eyes were evaluated qualitatively by three experienced, masked observers. Receiver operating characteristic (ROC) curves of discriminant function, neural network results, and qualitative evaluation were plotted. Comparisons of the areas under the ROC curves were performed with nonparametric statistics.

Results. There were statistically significant differences between the normal and glaucoma groups for all measures (P < 0.007) except for height variation contour, mean retinal nerve fiber layer thickness, and retinal nerve fiber layer cross-section area. Cup shape measure provided the single best measure to distinguish between normal subjects and those with early glaucoma and had a diagnostic precision of 84%. Neural network diagnostic precision, when all measures were used, was 92% and decreased to 82% when cup shape measure was omitted. The area under the ROC curve when all measures were combined was 0.94; it was significantly lower (P = 0.04) when cup shape measure was omitted (area = 0.84). The area under the ROC curve for qualitative optic disc evaluation by experienced observers was 0.93. There was no statistically significant difference between qualitative evaluation and neural network performance (P = 0.80).

Conclusions. Cup shape measure, the statistical third moment of the distribution of depth values of the optic nerve head obtained with confocal laser image analysis, can be used to discriminate between normal persons and those with early glaucomatous damage with high diagnostic precision. Invest Ophthalmol Vis Sci. 1996; 37:2393-2401.

Structural changes to the optic nerve and nerve fiber layer usually precede glaucomatous achronic visual field loss as currently measured.1-7 Careful detection of structural changes to the optic nerve–nerve fiber layer complex is important for the diagnosis and follow-up of eyes with early or suspected glaucoma. The importance of elevated intraocular pressure as a risk factor for glaucoma has been shown, but its diagnostic precision for glaucoma is less powerful than that of structural or functional measures.8-11

In recent years, scanning confocal laser tomography has been used to make quantitative measurements of optic nerve head and nerve fiber layer structures. The reproducibility and potential advantages over other techniques have been described.12-16 In this study, we examine the ability of optic nerve head structural measurements provided by confocal scanning laser image analysis to discriminate between normal persons and those with early glaucoma.
A group of patients with glaucoma and a group of normal subjects were defined as follows: two or more adjacent points with a 5-dB (Octopus) or 10-dB (Humphrey) loss or greater in one or more arcuate areas, compared with perimeter-results (less than 15% false-positive and 15% false-negative responses). Typical early glaucomatous visual field defects, optic nerve appearance consistent with the visual field defect, and absence of other disorders affecting the optic disc or visual field. When both eyes of a patient qualified, one was chosen randomly by coin toss for inclusion in the study.

All patients had previous experience with static threshold automated perimetry and reliable visual field results (less than 15% false-positive and 15% false-negative responses). Typical early glaucomatous visual field defects were defined as follows: two or more contiguous points with a 10-dB (Octopus) or \( P < 0.01 \) (Humphrey) loss or greater in superior or inferior arcuate areas, compared with perimetric-stored age-matched control subjects, or three or more contiguous points with a 5-dB (Octopus) or \( P < 0.05 \) (Humphrey) loss or greater in superior or inferior arcuate areas, or a 10-dB (Octopus and Humphrey) difference across the nasal horizontal midline in two or more adjacent locations.

Cases with more advanced visual field defects (mean deviation \( < -10 \) dB) or high ametropia (spherical equivalent \( < -5 \) D or \( > 3 \) D) were excluded. Optic disc tomography (Heidelberg Retinal Tomography; Heidelberg Engineering GmbH, Germany) and visual field examinations were performed within 6 months of each other. The tenets of the Declaration of Helsinki were followed with regard to study subjects. The study was approved by the Human Investigation Committee of the Yale University School of medicine, and informed consent was obtained from each subject before enrollment in this study.

Nine optic disc measures obtained with confocal laser image analysis were analyzed: cup area, cup-to-disc area ratio, rim area, height variation contour, cup volume, rim volume, cup shape measure, mean retinal nerve fiber layer height, and retinal nerve fiber layer cross-section area.\(^{17}\) Mean topographic images, having less than 30 \( \mu m \) of average variability (average of the standard deviations of the topographic values of each pixel in the three images) were used. A statistical software package (SPSS for Windows; Version 6.0, SPSS, Chicago, IL) was used to perform the statistical analyses. Probability plots were used to evaluate the distribution of the data; if the data were distributed normally, a Student's t-test for paired data was used for hypothesis testing; otherwise, the nonparametric Wilcoxon rank-sum test was used.

Linear model coefficients of the multivariate data set were estimated. The nine optic disc variables were used in combination and separately in the logistic regression analysis. Our sample was randomly divided into three subsets (A, B, and C). The proportion of normal and glaucomatous eyes in each subset was maintained constant. Two subsets (for example, A and B) were used to calculate the discriminant functions. The values of 0 for normal eyes and 1 for eyes with glaucoma were assigned to diagnosis as a dependent variable, and the multivariate linear coefficient models were estimated. The discriminant function thus derived was applied to the remaining subset (in this example, C) to assess the ability of the function to classify the data. The results were tested, in turn, on each of the subsets after the discriminant function was derived with the other two. To test the results on subsets A, B, and C, the functions were derived from B and C, A and C, and A and B, respectively. A classification was thereby obtained for each eye in this study.

The same procedure was used to train a back propagation neural network (Neural Works Professional II, Neural Ware, Pittsburgh, PA) and to test its performance. The back propagation structure used had three layers, nine elements in the input layer (one per structural measure), four in the intermediate (hidden) layer and one in the output layer. Neural networks are distinguished from conventional programs or other forms of artificial intelligence (such as expert systems) because they are not programmed, but are rather "trained" by examples. The training is performed by submitting a series of data together with the expected answer; the neural network will detect a relationship between the input and the output data, without the operator having to specify (or even know) the details of this relationship. Neural networks can solve non-linearly separable problems, problems in which two categories are not separable by a continuous line described by a function. This may explain the better results obtained by neural networks compared to those obtained by linear discriminant analysis on the same pool of data.\(^{18-21}\) To find which structural measure contributed the most to the neural network result, we repeated the training and test procedures after eliminating from the data set those measures that showed the best discrimination power in the linear logistic regression model.

Sensitivity, specificity, and diagnostic precision of
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Each discriminant function was calculated and the corresponding receiver operating characteristic (ROC) curves were plotted. The same was done for the neural network results. The ROC curve is a plot of the false-positive rate (1-specificity) against the true-positive rate (sensitivity). It is a useful way to display the continuous relation between sensitivity and specificity for a test or measure. The closer the ROC curve runs to the upper left-hand corner of the plot, the higher the diagnostic precision of the test, because at that location, the true-positive rate approaches 1 and false-positive rate approaches 0. A test with no diagnostic value would plot a straight diagonal line from lower left to upper right. The area under the curve is a numeric value that provides a measure of the diagnostic capability of a test. A perfect test would have an area of 1 (100% specificity and 100% sensitivity at the appropriate cutoff value), whereas a test with no diagnostic value would have an area of 0.5. The area under the ROC curves was calculated; it provides a way to quantify the ability of each test to discriminate normal subjects from those with early glaucoma.22,23 Statistical comparisons of the areas under the ROC curves were performed with nonparametric statistics.24

To compare the diagnostic ability of confocal scanning laser tomography with that of clinical disc assessment, a qualitative evaluation of stereoscopic color optic nerve photographs was undertaken. Three experienced masked, independent observers evaluated each subject’s standard color stereoscopic optic disc photographs, taken on the same day as the scanning confocal laser images, and assessed the probability of glaucomatous structural damage. An evaluation scale was defined as follows: 1 = definitely normal; 2 = probably normal; 3 = uncertain; 4 = probably glaucoma; 5 = definitely glaucoma. The average of the three observers’ scores was calculated, and the corresponding ROC curve was plotted. Sensitivity, specificity, diagnostic precision, and area under the ROC curve of the qualitative evaluations were calculated.

Octopus visual field indexes (mean defect and corrected pattern standard deviation) were converted to Humphrey visual field index format (mean deviation and corrected pattern standard deviation) according to the method described by Zeyen et al.25 Finally, we calculated the correlations between the morphologic measurements and the visual field indexes mean deviation and corrected pattern standard deviation with Spearman’s correlation coefficient. To account for multiple comparisons, Bonferroni’s corrected probabilities were calculated. P < 0.05 was considered statistically significant.

RESULTS

Forty-three normal subjects recruited from staff members or spouses and friends of patients, and 53 patients TABLE 1. Characteristics of the Study Population: Mean ± SD

<table>
<thead>
<tr>
<th></th>
<th>Normal (n = 43)</th>
<th>Glaucoma (n = 53)</th>
</tr>
</thead>
<tbody>
<tr>
<td>Age (years)</td>
<td>50.9 ± 13.6</td>
<td>56.1 ± 10.0</td>
</tr>
<tr>
<td>Refractive error (D)</td>
<td>-0.3 ± 1.5</td>
<td>-0.6 ± 2.0</td>
</tr>
<tr>
<td>Mean deviation (dB)*</td>
<td>-0.4 ± 1.6</td>
<td>-4.8 ± 3.4</td>
</tr>
<tr>
<td>Corrected pattern standard deviation (dB)*</td>
<td>0.8 ± 1.0</td>
<td>30.2 ± 39.0</td>
</tr>
</tbody>
</table>

* Statistically significant difference between normal and glaucoma patients (P ≤ 0.001).

with open-angle glaucoma with early visual field defects were examined. In the group with open-angle glaucoma, there were 43 eyes with primary open-angle glaucoma, seven eyes with pigment dispersion syndrome, two eyes with pseudo-exfoliation syndrome, and one eye with secondary open-angle glaucoma. Average visual field mean deviation and corrected pattern standard deviation were statistically different in the normal and glaucoma groups (P < 0.001 and P = 0.001, respectively); there were no statistically significant differences for age, race, and refractive error. The characteristics of the study population are detailed in Table 1. Cup-to-disc area ratio, rim area, cup shape measure, mean retinal nerve fiber layer thickness, and retinal nerve fiber layer cross-section area were distributed normally; the other measures were not.

There were no significant differences between the two diagnostic groups for height variation contour, mean retinal nerve fiber layer thickness, and retinal nerve fiber layer cross-section area. The remaining six measures were significantly different (P = 0.007) between the groups. The results are detailed in Table 2. Table 3 lists the results of linear discriminant analysis. When all measures were used together, diagnostic precision, sensitivity, and specificity were 81%, 81%, and 81%, respectively. Cup shape measure and cup-to-disc area ratio showed the highest diagnostic precision of all the measures when considered separately. When cup shape measure alone was used for testing, diagnostic precision was 84%, sensitivity was 83%, and specificity was 86%. When cup-to-disc area ratio alone was used, diagnostic precision, sensitivity, and specificity were 84%, 77%, and 93%, respectively.

The neural network analysis provided similar results. When all measures were used, the diagnostic precision, sensitivity, and specificity were 92%, 91%, and 92%, respectively. If cup shape measure was omitted, diagnostic precision, sensitivity, and specificity decreased to 84%, 91%, and 77%, respectively; when cup-to-disc area ratio was omitted, the diagnostic precision, sensitivity, and specificity decreased to 81%, 81%, and 81% (Table 4). Figure 1 shows the ROC
TABLE 2. Confocal Scanning Laser Measurements of the Optic Nerve Head in Normal and Open Angle Glaucoma: Mean ± SD

<table>
<thead>
<tr>
<th>Parameter</th>
<th>Normal</th>
<th>Glaucoma</th>
<th>P Value</th>
</tr>
</thead>
<tbody>
<tr>
<td>Cup area (mm²)</td>
<td>0.47 ± 0.26</td>
<td>1.03 ± 0.46</td>
<td>&lt;0.001</td>
</tr>
<tr>
<td>Cup-to-disc area ratio</td>
<td>0.23 ± 0.11</td>
<td>0.45 ± 0.15</td>
<td>&lt;0.001</td>
</tr>
<tr>
<td>Rim area (mm²)</td>
<td>1.53 ± 0.28</td>
<td>1.20 ± 0.36</td>
<td>&lt;0.001</td>
</tr>
<tr>
<td>Height variation contour (mm)</td>
<td>0.37 ± 0.07</td>
<td>0.35 ± 0.09</td>
<td>NS</td>
</tr>
<tr>
<td>Cup volume (mm³)</td>
<td>0.10 ± 0.08</td>
<td>0.33 ± 0.24</td>
<td>&lt;0.001</td>
</tr>
<tr>
<td>Rim volume (mm³)</td>
<td>0.37 ± 0.11</td>
<td>0.28 ± 0.14</td>
<td>0.002</td>
</tr>
<tr>
<td>Cup shape measure</td>
<td>-0.24 ± 0.07</td>
<td>-0.09 ± 0.08</td>
<td>&lt;0.001</td>
</tr>
<tr>
<td>Mean RNFL thickness (mm)</td>
<td>0.23 ± 0.05</td>
<td>0.20 ± 0.06</td>
<td>NS</td>
</tr>
<tr>
<td>RNFL cross-sectional area (mm²)</td>
<td>1.17 ± 0.27</td>
<td>1.07 ± 0.37</td>
<td>NS</td>
</tr>
</tbody>
</table>

NS = not significant; RNFL = retinal nerve fiber layer.

curves plotted for individual measures. The area under the ROC curve for cup shape measure was 0.93. The ROC curves with the neural network analysis are plotted in Figure 2A. The area under the curve for the neural network analysis (all measures combined) was 0.94. The area under the ROC curve, when cup shape measure was omitted, was 0.84; these two areas were statistically, significantly different (P = 0.04). The area under the ROC curve, when cup-to-disc area ratio was omitted, was 0.90; the area was not statistically significantly different from all measures combined (P = 0.29).

The diagnostic precision, sensitivity, and specificity of qualitative optic disc evaluation were 87%, 86%, and 89%, respectively. The corresponding ROC curve is shown in Figure 2B. The area under the ROC curve for qualitative disc evaluation was 0.93. There were no statistically significant differences between the areas under the ROC curves for qualitative evaluation and neural network performance (P = 0.80).

Several structural measurements correlated with the visual field indexes mean deviation and corrected pattern standard deviation (Table 5). Cup shape measure showed the strongest correlations with mean deviation (r = -0.61; P < 0.001) (Fig. 3) and corrected pattern standard deviation (r = 0.61; P < 0.001).

DISCUSSION

Structural alterations of the optic disc-nerve fiber layer complex provide the earliest reliable signs of damage from glaucoma.1-7 Accurate and objective quantitative measurements of the optic nerve head and nerve fiber layer are required to improve our ability to regularly recognize early glaucomatous damage. The quest for more accurate and objective methods has caused several qualitative and quantitative systems to be proposed to detect optic disc changes.

Quantitative methods have the advantage of obtaining numerical values that easily can be analyzed and compared. Airaksinen et al.26 used planimetry to measure the neuroretinal rim area in normal subjects, glaucoma suspects, and patients with glaucoma from enlarged stereophotographs.26 Balazsi et al.27 evaluated the correlation between cup-to-disc ratio and rim area with visual function in normal, ocular hypertensive, and early open-angle glaucomatous eyes with stereophotographs.27 They found significant correlations between the neuroretinal rim area and several visual function tests, whereas the cup-to-disc ratio showed a weak correlation with visual functions. Lichter28 showed the limited usefulness of the cup-to-disc ratio estimates to indicate whether a disc is normal or not. Photogrammetry is a technique that allows the measurements of three-dimensional structures from stereoscopic photographs for which the stereoscopic base separation is known. Schwartz29 and associates measured optic disc cupping and pallor with manual photogrammetry of stereoscopic color photographs. They found that ocular hypertensive eyes showed significantly greater pallor but not cupping when com-

TABLE 3. Sensitivity, Specificity, and Diagnostic Precision of the Discriminant Function for Structural Optic Nerve Head Measures

<table>
<thead>
<tr>
<th>All Measurements</th>
<th>81</th>
<th>83</th>
<th>77</th>
</tr>
</thead>
<tbody>
<tr>
<td>Cap Shape Measure</td>
<td>81</td>
<td>86</td>
<td>93</td>
</tr>
<tr>
<td>Cup-to-Disc Area Ratio</td>
<td>81</td>
<td>84</td>
<td>84</td>
</tr>
</tbody>
</table>

* Not significantly different from cup shape measure (P = 0.37).
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TABLE 4. Sensitivity, Specificity, and Diagnostic Precision of the Neural Networks Trained With Different Measures

<table>
<thead>
<tr>
<th></th>
<th>All Measurements</th>
<th>All But Cup Shape Measure</th>
<th>All But Cup-to-Disc Area Ratio</th>
<th>All But Cup Shape Measure and Cup-to-Disc Area Ratio</th>
</tr>
</thead>
<tbody>
<tr>
<td>Sensitivity (%)</td>
<td>92</td>
<td>91</td>
<td>81</td>
<td>85</td>
</tr>
<tr>
<td>Specificity (%)</td>
<td>91</td>
<td>77</td>
<td>81</td>
<td>84</td>
</tr>
<tr>
<td>Diagnostic precision (%)</td>
<td>92</td>
<td>84</td>
<td>81</td>
<td>84</td>
</tr>
<tr>
<td>Area under the receiver operating characteristic curve</td>
<td>0.94</td>
<td>0.84*</td>
<td>0.90</td>
<td>0.82†</td>
</tr>
</tbody>
</table>

* Significantly different from all measures combined (P = 0.04).
† Significantly different from all measures combined (P = 0.02).

pared with normal eyes. They also reported reversal of cupping and pallor of the optic disc after intraocular pressure reduction. Portney compared cup volume, cup depth, cup area, and cup volume asymmetry in normal subjects, ocular hypertensives, and patients with glaucoma with photogrammetric measurements and showed that only cup volume asymmetry was a diagnostically useful parameter. Johnson et al reported that cup volume, cup area, and cup depth measurements did not separate normal subjects and patients with glaucoma well, but that the cup area–cup depth relation had better diagnostic ability.

Digitized simultaneous stereoscopic videographic images have been used to make measurements of the optic nerve head and peripapillary nerve fiber layer. They provide quantitative measures like disc area, rim area, cup-to-disc ratio, and cup volume without the need of extensive training for the technician. The reproducibility of these devices was reported by several investigators. A novel measure, relative nerve fiber layer height, was shown to detect the presence of early structural glaucomatous damage better than measurements of rim area, cup-to-disc ratio, or cup volume and had a stronger correlation with visual field loss than these other measures.

More recently, confocal scanning laser image analysis has been applied to the problem of identifying structural damage to the optic nerve and the nerve fiber layer. Several instruments are being used to provide images and derive measurements to quantify the topography of the optic nerve head and peripapillary nerve fiber layer. The reproducibility of confocal scanning lasers has been reported.

In the current study, we found significant differences between normal subjects and patients with early glaucoma damage with regard cup area, cup-to-disc area ratio, rim area, cup volume, rim volume, and cup shape measure. Estimation of the linear discriminant

FIGURE 1. (A) Receiver operating characteristic (ROC) curves of optic disc parameters. The area under each curve is shown in parentheses. The area under the ROC curves of cup shape measure (0.93) and cup-to-disc area ratio (0.89) did not show a statistically significant difference (P = 0.37). (B) The ROC curves of disc rim and nerve fiber layer parameters. The area under each curve is shown in parentheses.
model coefficients identified cup shape measure and cup-to-disc area ratio as the most powerful diagnostic measure. The decrease in performance of the artificial neural network after deletion of these measures from the training and test sets confirmed the relative importance of these measurements.

The ROC curves of the tested measures provide a graphic representation of their ability to discriminate between normal eyes and those with early glaucoma. The ROC curve is a plot of the false-positive rate (1 - specificity) against the true-positive rate (sensitivity). It is a useful way to display the continuous relation between sensitivity and specificity for a test or measure. The closer the ROC curve runs to the upper left-hand corner of the plot, the higher the diagnostic precision of the test, because at that location, the true-positive rate approaches 1 and false-positive rate approaches 0. A test with no diagnostic value would plot a straight diagonal line from lower left to upper right. The area under the curve is a numeric value that provides a measure of the diagnostic capability of a test. A perfect test would have an area of 1 (100% specificity and 100% sensitivity at the appropriate cutoff value), whereas a test with no diagnostic value would have an area of 0.5 (50% specificity and 50% sensitivity).

<table>
<thead>
<tr>
<th>Topographic Measures</th>
<th>Mean Deviation</th>
<th>Corrected Pattern Standard Deviation</th>
</tr>
</thead>
<tbody>
<tr>
<td>Cup area (mm²)</td>
<td>-0.34*</td>
<td>0.50†</td>
</tr>
<tr>
<td>Cup-to-disc area ratio</td>
<td>-0.43†</td>
<td>0.54†</td>
</tr>
<tr>
<td>Cup shape measure</td>
<td>-0.61†</td>
<td>0.61†</td>
</tr>
<tr>
<td>Height variation contour (mm)</td>
<td>0.43†</td>
<td>NS</td>
</tr>
<tr>
<td>Mean retinal thickness (mm)</td>
<td>0.46*</td>
<td>NS</td>
</tr>
<tr>
<td>Rim area (mm²)</td>
<td>NS</td>
<td>NS</td>
</tr>
<tr>
<td>Retinal cross-sectional area (mm²)</td>
<td>NS</td>
<td>NS</td>
</tr>
<tr>
<td>Cup volume (mm³)</td>
<td>NS</td>
<td>NS</td>
</tr>
<tr>
<td>Rim volume (mm³)</td>
<td>0.44†</td>
<td>-0.40*</td>
</tr>
</tbody>
</table>

NS = not significant.
* P < 0.05.
† P < 0.01.
cup shape measure and cup-to-disc area ratio had the ROC curves with the highest diagnostic values. The area under the ROC curves did not show a significant difference between cup shape measure and cup-to-disc area ratio \((P = 0.37)\) (Fig. 1A, Table 3). The performance of the neural network after deletion of cup shape measure showed a statistically significant decrease \((P = 0.04)\). Conversely, the performance of the neural network after deletion of cup-to-disc area ratio did not show a statistically significant decrease \((P = 0.29)\). This result suggests that cup shape measure is the best discriminator between normal eyes and those with early glaucoma. When all measures were used with the neural network analysis, the diagnostic precision, sensitivity, specificity, and area under the ROC curve of qualitative optic nerve disc evaluation were 0.87, 0.86, 0.89, and 0.93, respectively. Because there was no statistically significant difference between the area under the ROC curve of qualitative optic nerve disc evaluation and that of neural network performance \((P = 0.80)\), quantitative measurements obtained with confocal scanning laser and analyzed with neural networks seemed to have a similar diagnostic ability to qualitative disc evaluation by experienced observers for the detection of structural damage in early glaucoma.

The structural index cup shape measure (the normalized third moment of the central distribution of cup structures depths) is a measure of the skewness of the frequency distribution of depth values that belong to that portion of the image selected by the operator (in this case, the optic disc). Its value typically is negative in normal eyes (relatively small, shallow cups where small depth values are most frequent) and less negative or positive in glaucomatous eyes (steep slopes, deep cup, high values frequent). In mathematical terms, it is obtained by dividing the square of the third moment of the distribution by the third power of the second moment (variance):

\[
\text{Cup shape measure} = \frac{\sum (X - \bar{X})^3 / n}{\left[\sum (X - \bar{X})^2 / n\right]^{3/2}}
\]

where \(X = \) mean depth, \(X_i = \) depth of each point, and \(n = \) number of points measured within the disc margin.

This numerical description of the cup shape has the advantage of summarizing in one number the structure of the cup and takes into account its depth variation and steepness of the cup walls. It also emphasizes the value of points of extreme depth inside the cup because the cubed differences between the depth of each point and the mean depth will be sensitive to
FIGURE 5. (A) Example of a glaucomatous disc: cup area = 0.83 mm², cup-to-disc area ratio = 0.36, rim area = 1.49 mm², cup volume = 0.16 mm³, cup shape measure = -0.10. Despite the fact that cup area and cup volume of this eye are smaller than the mean for normal eyes, cup shape measure shows a significantly abnormal value; 95% of normal eyes have cup shape measure $\leq -0.10$. (B) Clinical optic nerve photograph of the same glaucoma disc.

a few points far from the mean and relatively insensitive to points closer to it. Moreover, the cup shape measure does not depend on a reference plane, the definition of which can be problematic.\[8\]

Cup volume was significantly different between the two groups, but it was not found to be an important discriminating parameter, because its values widely overlap in the two groups. This is not unexpected, because cup volume depends on disc size.\[40\] Cup shape measure, conversely, is independent of the disc size. The area under the ROC curves were statistically significantly different between cup shape measure and cup volume ($P = 0.04$).

Characteristic early glaucomatous optic disc changes may appear as focal atrophy, concentric atrophy, and deepening of the cup with laminar bowing and compression.\[41\] When comparing cups with approximately the same volume but different shapes, in a mathematically modeled optic disc, the cup shape measure of a cylindrically shaped cup is larger than that of a conically shaped cup.\[38\] Figures 4 and 5 show examples of a normal and an early glaucomatous optic disc in which the structural measurements are all similar except for cup shape measure.

We found a correlation between the visual field indexes and several structural parameters, the strongest of which was present between cup shape measure and mean deviation ($r = -0.61$). Also, cup shape measure showed the strongest significant correlation with corrected pattern standard deviation ($r = 0.61$). This confirms the findings reported in a previous study on a different set of patients.\[38\]

At present, an important issue concerning confocal scanning laser image analysis is the instability of its reference plane for depth measurements. This can be affected by the refractive error and changes in retinal thickness with progressive damage from glaucoma. Because many of the measured variables depend on the reference plane, they may be more unstable and not reliable when longitudinal follow-up of a disc is sought. Cup shape measure is independent of the reference plane and represents a sensitive and specific measure to detect early glaucomatous damage. The relative values of the various structural parameters to detect progressive damage currently are being evaluated longitudinally.

Key Words
confocal scanning laser, cup shape measure, early glaucoma, neural networks, receiver operating characteristic curves

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References


