Correlation of Pattern Electroretinogram with Optic Disc Cup Shape in Ocular Hypertension

Tommaso Salgarello, Alberto Colotto, Benedetto Falsini, Luca Buzzonetti, Luca Cesari, Giancarlo Iarossi, and Luigi Scullica

PURPOSE. To evaluate the correlation of pattern electroretinogram (PERG), an index of inner retinal function, with confocal scanning laser (CSLO) optic disc structural parameters in ocular hypertension (OHT).

METHODS. Thirty-four patients with OHT, normal white-on-white (Humphrey 30-2) perimetry, and normal clinical optic discs were examined with PERG and CSLO disc analysis. Two groups of normal subjects (n = 38 and 18, for PERG and CSLO, respectively) and a group of 12 patients with early open-angle glaucoma (EOAG) were also tested. Pattern electroretinogram amplitudes were measured in response to sinusoidal gratings of variable spatial frequency (0.58–5.8 cycles/degree), modulated in counter-phase at 7.5 Hz. Morphometric optic disc parameters were obtained by the Heidelberg Retina Tomograph (HRT), either globally or from predefined disc sectors. In addition to standard parameters, the cup shape measure, an index of depth variation and steepness of the cup walls, was determined.

RESULTS. In individual OHT patients, PERG amplitudes at 2.6 cycles/degree were negatively correlated with cup shape measures (r = −0.43, P < 0.01) obtained from analysis of the inferotemporal (IT) sector. No significant correlations were found for the other parameters. On average, the cup shape measures derived from IT sector or global analysis were significantly (P < 0.01) worse, and closer to the measures of EOAG patients, in OHT patients with abnormal PERG compared with those with normal PERGs. The cup shape measure displayed a low sensitivity (20%) and a high specificity (100%) in predicting PERG abnormalities in individual OHT patients.

CONCLUSIONS. The results indicate that in OHT there is a significant although weak correlation between PERG amplitude and the shape of the optic disc cup, suggesting a parallel involvement of both function and morphology. Combined PERG and optic disc cup structural analysis is of potential diagnostic value to detect early damage to optic nerve head in individual OHT patients.


In glaucoma, structural changes to the optic nerve head are usually associated with deterioration of function.1–3 In ocular hypertension (OHT), morphologic signs of early optic nerve damage usually precede the onset of typical visual field loss, although subtle functional deficits may be revealed by refined psychophysical and electrophysiologic techniques.4 Morphologic optic disc abnormalities have been described in OHT by computer-assisted planimetric analysis of the optic disc (see, for example, Ref. 5) and, more recently, by confocal scanning laser ophthalmoscopy (CSLO),6–7 which has provided three-dimensional analysis of the optic disc structure. Reproducibility and potential advantages of the CSLO tomography over other techniques have been described elsewhere.8–11 Functional deficits in OHT have been reported by measuring luminance and chromatic contrast sensitivities,12–15 motion detection perimetry,14 blue-on-yellow perimetry,15,16 and luminance and chromatic pattern electroretinograms (PERGs).13,17,18

Although the correlation between CSLO and functional losses has been well documented in glaucomatous eyes (see, for example, Refs. 1 and 3), the same relationship has not been clearly established in OHT eyes. An approach to evaluate the correlation is to compare CSLO parameters of the optic disc with a sensitive test of retinal ganglion cell function (i.e., the PERG).19,20 The PERG has been reported to be abnormal in a substantial proportion of OHT eyes13,17,18,21–23 and of predictive value for the development of early field losses in OHT eyes.24,25 A quantitative association between losses in CSLO and PERG measurements would indicate that structural and functional damage to the optic nerve develops in parallel in early stages of disease. Lack of correlation, on the other hand, would mean that a certain amount of structural damage is necessary for functional deficits to become detectable (as previously suggested26) or that functional deficits may precede structural damage. Clinically, evaluating the relationship between structural and functional damage in OHT could help to better delineate the boundaries between healthy and pathologic optic nerve heads in glaucoma-risk eyes. The present study was designed to evaluate the correlation between CSLO optic disc and PERG measurements in a cohort of OHT patients with normal conventional white-on-white perimetry. Morphy-
metric and functional results of OHT eyes were also compared with those obtained from normal control subjects or patients with early, clinically-defined, glaucoma.

**METHODS**

**Subjects**

Thirty-four patients with a diagnosis of OHT (intraocular pressure, IOP ≥ 21 mm Hg on two or more separate occasions, normal optic disc appearance, normal Goldmann and Humphrey 30-2 threshold test perimetry, best corrected visual acuity ≥20/20) were examined with both PERG and CSLO tomography. Normal appearance of the optic disc, on routine stereoscopic examination with slit-lamp biomicroscopy and 78 diopter (D) lens, was defined as a vertical cup-to-disc diameter ratio less than or equal to 0.5, with no asymmetry (±0.2, explained by side differences in disc size), excavation, thinning of the rim, notching, hemorrhages, nerve fiber layer defects, or parapapillary atrophy. Two independent groups of normal subjects (n = 38 and 18 evaluated by PERG and CSLO, respectively) and a group of 12 early open-angle glaucoma (EOAG) patients were also tested. Diagnosis of EOAG was established on the basis of an elevated IOP (>21 mm Hg on two separate occasions), an open angle, the presence of abnormal white-on-white topographic images for each eye, according to Weinreb et al.29 Details of this instrument and its reproducibility have been published.10,11,28–30 Test-retest variability of the three measurements of each point, expressed by the average of the standard deviations of the topographic values of each pixel in the three images, was 13.47 ± 4.39 μm (range: 7.3 to 23.38 μm) for the normal group. 12.48 ± 4.43 μm (range, 6.7 to 24.25 μm) for the OHT group, and 14.37 ± 4.13 μm (range, 7.31 to 23.01 μm) for the EOAG group. Each mean topography image was automatically corrected for horizontal and vertical tilt.31 The margin of the optic disc was manually drawn on the image as a contour line around the inner edge of the peripapillary scleral ring of Elschnig, using a computer mouse system by a trained operator (TS). Two axial boundaries, the curved

**Apparatus and Procedure**

Electroretinograms were recorded according to a previously published technique.23 Briefly, stimuli were vertical sinuisoidal gratings of variable spatial frequency (0.58, 0.88, 1.3, 1.7, 2.6, and 5.8 cycles/degree), modulated in counter–phase at 7.5 Hz and electronically generated on a high-resolution TV monitor (contrast: 90%; mean luminance: 80 candela [cd]/m2; field size: 14° [width] × 24° [height]). Subjects were fixated at the center of the stimulating field with natural pupils, and size was measured. No differences in pupil size were observed between patients and control subjects or between the two patient groups. Electroretinograms were recorded by a Ag/AgCl electrode taped on the skin of the lower eyelid. A similar electrode, placed over the eyelid of the contralateral unstimulated eye was used as reference.17,19,23 Responses were amplified (100,000), filtered (1–30 Hz), sampled with a resolution of 12 bits and averaged (400 events) with automatic artifact rejection. Two replications were obtained for each record to verify reproducibility. The amplitude (in microvolts) of the Fourier analyzed response 2nd harmonic was measured and plotted as a function of spatial frequency.

CSLO tomography of the optic disc was performed by the Heidelberg Retina Tomograph (HRT; Heidelberg Engineering GmbH, Heidelberg, Germany), by analyzing the mean of three 10° topographic images for each eye, according to Weinreb et al.29 Details of this instrument and its reproducibility have been published.10,11,28–30 Test-retest variability of the three
surface and the reference plane, were used by the 2.01 HRT software to generate the optic nerve head measurements. Most of two- and three-dimensional data (e.g., cup and rim area, cup and rim volume) were obtained with respect to the standard reference plane, placed by the current software 50 μm posterior to the mean height of the disc margin contour line at the papillomacular bundle, more precisely in a temporal segment between 350° and 356°. Other topographic optic disc parameters (e.g., cup shape measure and maximal cup depth) were automatically measured relative to the curved surface. This surface is bound by the disc contour line and follows the height variation of the retinal surface along the contour line, whereas the height of its center equals the mean height of the optic disc margin; all connecting lines from the center to a boundary point are straight lines. For each optic disc, the following morphometric parameters were evaluated either globally or for the predefined HRT disc sectors: disc area, cup area, cup-to-disc area ratio, rim area, cup volume, rim volume, maximal cup depth, and cup shape measure. The cup shape measure is a measure of the skewness of the frequency distribution of depth values of disc cupping. It summarizes in numerical terms the structure of the cup, taking into account both depth variation and steepness of the cup walls. Unlike other structural cup or rim parameters, it is independent of reference plane. The parameter has a negative value for a flat or nearly flat excavation and turns to positive values if the slope at the edges of the excavation increases. In normal eyes cup shape measure is typically negative, whereas glaucomatous eyes tend to be less negative or positive. Magnification error was automatically corrected by using patients’ keratometry readings. The optic disc sectors included in the analysis were: superotemporal (ST, 45°), superonasal (SN, 45°), nasal (N, 90°), inferonasal (IN, 45°), inferotemporal (IT, 45°), and temporal (T, 90°). Disc sector analysis was dictated by specific sectors of the disc, including mainly superior and inferior poles.

### Statistical Analysis

Pattern electroretinogram and HRT data from only one eye, randomly selected, per subject or patient were included in the analysis. Between-group comparisons (including normal, OHT, and EOAG eyes) were performed by univariate and multivariate ANOVAs, with multiple contrasts. A P < 0.05 was considered significant. Correlations between PERG amplitudes (dependent variables) and HRT parameters (predictor variables) derived from OHT eyes were performed by multiple linear regression analyses, which evaluated the effect of a single variable while correcting for the effects of the disc size, given its well-known analyses, which evaluated the effect of a single variable while randomly selected, per subject or patient were included in the study population. Data from global and sectorial analyses were obtained with respect to the curved surface and the reference plane, placed by the current software 50 μm posterior to the mean height of the disc margin contour line at the papillomacular bundle, more precisely in a temporal segment between 350° and 356°. Other topographic optic disc parameters (e.g., cup shape measure and maximal cup depth) were automatically measured relative to the curved surface. This surface is bound by the disc contour line and follows the height variation of the retinal surface along the contour line, whereas the height of its center equals the mean height of the optic disc margin; all connecting lines from the center to a boundary point are straight lines. For each optic disc, the following morphometric parameters were evaluated either globally or for the predefined HRT disc sectors: disc area, cup area, cup-to-disc area ratio, rim area, cup volume, rim volume, maximal cup depth, and cup shape measure. The cup shape measure is a measure of the skewness of the frequency distribution of depth values of disc cupping. It summaries in numerical terms the structure of the cup, taking into account both depth variation and steepness of the cup walls. Unlike other structural cup or rim parameters, it is independent of reference plane. The parameter has a negative value for a flat or nearly flat excavation and turns to positive values if the slope at the edges of the excavation increases. In normal eyes cup shape measure is typically negative, whereas glaucomatous eyes tend to be less negative or positive. Magnification error was automatically corrected by using patients’ keratometry readings. The optic disc sectors included in the analysis were: superotemporal (ST, 45°), superonasal (SN, 45°), nasal (N, 90°), inferonasal (IN, 45°), inferotemporal (IT, 45°), and temporal (T, 90°). Disc sector analysis was dictated by specific sectors of the disc, including mainly superior and inferior poles.

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## Results

In Table 2 the mean (±SD) PERG amplitudes at the different spatial frequencies are reported for normal, OHT, and EOAG eyes. Mean amplitudes of OHT eyes were significantly lower [multivariate F(6,65): 3.3, P = 0.01] than those of normal eyes, with greatest losses at medium spatial frequencies (1.3–2.6 cycles/degree). Comparison between OHT and EOAG eyes also showed that in the latter PERG amplitudes at 1.3 cycles/degree were on average smaller [univariate F(1,39): 4.2, P = 0.05] than those observed in the former. Among individual OHT eyes, PERG amplitudes were found to be abnormal (i.e., lower than 95% confidence limits at one or more spatial frequencies, see also the Results section) and compared with that of PERG abnormalities by 2 × 2 tables. For the purposes of this analysis, limited to OHT eyes with a normal visual field, the PERG was considered as a functional “gold standard”. It should be noted, however, that the technique, as the HRT analysis, is still an experimental procedure and cannot be considered as a gold standard in clinical terms.

### Table 2. PERG Results in Normal, OHT and EOAG Eyes

<table>
<thead>
<tr>
<th>Spatial Frequency (cycles/degree)</th>
<th>Normal (n = 38)</th>
<th>OHT (n = 34)</th>
<th>EOAG (n = 12)</th>
</tr>
</thead>
<tbody>
<tr>
<td>0.58</td>
<td>0.55 (0.06)*</td>
<td>0.41 (0.21)</td>
<td>0.31 (0.15)</td>
</tr>
<tr>
<td>0.88</td>
<td>0.66 (0.06)</td>
<td>0.47 (0.23)</td>
<td>0.41 (0.16)</td>
</tr>
<tr>
<td>1.3</td>
<td>0.85 (0.13)</td>
<td>0.57 (0.28)</td>
<td>0.41 (0.13)</td>
</tr>
<tr>
<td>1.7</td>
<td>1.05 (0.25)</td>
<td>0.61 (0.30)</td>
<td>0.48 (0.16)</td>
</tr>
<tr>
<td>2.6</td>
<td>0.66 (0.12)</td>
<td>0.58 (0.28)</td>
<td>0.47 (0.28)</td>
</tr>
<tr>
<td>5.8</td>
<td>0.48 (0.12)</td>
<td>0.41 (0.18)</td>
<td>0.33 (0.14)</td>
</tr>
</tbody>
</table>

* Means (standard deviation).
Table 3. HRT Results in Normal Subjects, OHT and EOAG Patients

<table>
<thead>
<tr>
<th>Disc Area</th>
<th>Normal (n = 18)</th>
<th>OHT pooled (n = 34)</th>
<th>OHT (normal PERG) (n = 19)</th>
<th>OHT (abnormal PERG) (n = 15)</th>
<th>EOAG (n = 12)</th>
</tr>
</thead>
<tbody>
<tr>
<td>Total</td>
<td>1.98 (0.35)*</td>
<td>2.21 (0.33)</td>
<td>2.26 (0.32)</td>
<td>2.14 (0.35)</td>
<td>2.18 (0.29)</td>
</tr>
<tr>
<td>Supero-temporal</td>
<td>0.26 (0.05)</td>
<td>0.29 (0.05)</td>
<td>0.30 (0.04)</td>
<td>0.28 (0.06)</td>
<td>0.28 (0.04)</td>
</tr>
<tr>
<td>Supero-nasal</td>
<td>0.25 (0.05)</td>
<td>0.28 (0.04)</td>
<td>0.29 (0.04)</td>
<td>0.27 (0.05)</td>
<td>0.28 (0.04)</td>
</tr>
<tr>
<td>Nasal</td>
<td>0.48 (0.09)</td>
<td>0.54 (0.09)</td>
<td>0.54 (0.09)</td>
<td>0.52 (0.08)</td>
<td>0.53 (0.08)</td>
</tr>
<tr>
<td>Infero-nasal</td>
<td>0.24 (0.05)</td>
<td>0.27 (0.05)</td>
<td>0.28 (0.04)</td>
<td>0.26 (0.05)</td>
<td>0.27 (0.04)</td>
</tr>
<tr>
<td>Infero-temporal</td>
<td>0.28 (0.06)</td>
<td>0.30 (0.05)</td>
<td>0.31 (0.05)</td>
<td>0.29 (0.05)</td>
<td>0.29 (0.04)</td>
</tr>
<tr>
<td>Temporal</td>
<td>0.48 (0.09)</td>
<td>0.53 (0.09)</td>
<td>0.54 (0.09)</td>
<td>0.52 (0.08)</td>
<td>0.53 (0.07)</td>
</tr>
<tr>
<td>Rim Area</td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Total</td>
<td>1.58 (0.21)</td>
<td>1.55 (0.27)</td>
<td>1.60 (0.22)</td>
<td>1.48 (0.32)</td>
<td>1.36 (0.25)</td>
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<tr>
<td>Supero-temporal</td>
<td>0.20 (0.03)</td>
<td>0.19 (0.04)</td>
<td>0.20 (0.04)</td>
<td>0.18 (0.05)</td>
<td>0.17 (0.06)</td>
</tr>
<tr>
<td>Supero-nasal</td>
<td>0.23 (0.03)</td>
<td>0.21 (0.04)</td>
<td>0.22 (0.04)</td>
<td>0.20 (0.04)</td>
<td>0.19 (0.06)</td>
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<td>Nasal</td>
<td>0.45 (0.06)</td>
<td>0.43 (0.08)</td>
<td>0.44 (0.08)</td>
<td>0.42 (0.09)</td>
<td>0.39 (0.07)</td>
</tr>
<tr>
<td>Infero-nasal</td>
<td>0.23 (0.04)</td>
<td>0.23 (0.03)</td>
<td>0.23 (0.05)</td>
<td>0.22 (0.04)</td>
<td>0.20 (0.04)</td>
</tr>
<tr>
<td>Infero-temporal</td>
<td>0.23 (0.06)</td>
<td>0.21 (0.05)</td>
<td>0.23 (0.04)</td>
<td>0.20 (0.05)</td>
<td>0.18 (0.02)</td>
</tr>
<tr>
<td>Temporal</td>
<td>0.27 (0.06)</td>
<td>0.27 (0.08)</td>
<td>0.28 (0.07)</td>
<td>0.25 (0.09)</td>
<td>0.23 (0.06)</td>
</tr>
<tr>
<td>Cup Shape Measure</td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Total</td>
<td>−0.26 (0.08)</td>
<td>−0.18 (0.08)</td>
<td>−0.21 (0.07)</td>
<td>−0.15 (0.08)</td>
<td>−0.15 (0.07)</td>
</tr>
<tr>
<td>Supero-temporal</td>
<td>−0.21 (0.11)</td>
<td>−0.10 (0.14)</td>
<td>−0.13 (0.12)</td>
<td>−0.06 (0.15)</td>
<td>−0.07 (0.12)</td>
</tr>
<tr>
<td>Supero-nasal</td>
<td>−0.27 (0.14)</td>
<td>−0.16 (0.11)</td>
<td>−0.18 (0.12)</td>
<td>−0.14 (0.11)</td>
<td>−0.07 (0.24)</td>
</tr>
<tr>
<td>Nasal</td>
<td>−0.30 (0.15)</td>
<td>−0.20 (0.14)</td>
<td>−0.23 (0.15)</td>
<td>−0.17 (0.13)</td>
<td>−0.20 (0.06)</td>
</tr>
<tr>
<td>Infero-nasal</td>
<td>−0.31 (0.18)</td>
<td>−0.16 (0.12)</td>
<td>−0.18 (0.13)</td>
<td>−0.14 (0.12)</td>
<td>−0.11 (0.11)</td>
</tr>
<tr>
<td>Infero-temporal</td>
<td>−0.19 (0.13)</td>
<td>−0.15 (0.11)</td>
<td>−0.19 (0.10)</td>
<td>−0.10 (0.10)</td>
<td>−0.09 (0.08)</td>
</tr>
<tr>
<td>Temporal</td>
<td>−0.13 (0.10)</td>
<td>−0.09 (0.08)</td>
<td>−0.11 (0.07)</td>
<td>−0.06 (0.08)</td>
<td>−0.08 (0.04)</td>
</tr>
</tbody>
</table>

* Means (standard deviation).

normal and EOAG eyes [univariate F(1,26): 13]. HRT parameters of individual OHT eyes were compared with the 95% confidence limits established for normal eyes with disc areas in the ranges 1 to 2 and 2 to 3 mm². Cup-to-disc area ratio was abnormal in 14 (41.2%), rim area in 8 (23.5%), and cup shape measure in 3 (8.8%) of 34 OHT patients.

In individual OHT eyes, significant PERG abnormalities at low and medium spatial frequencies tended to be associated with more positive values of cup shape measure. These trends were observed when the parameter was derived either from the global analysis or the analyses of temporal disc sectors. Figure 1 shows the PERG and HRT results obtained from the right eye of three representative patients: an OHT with normal PERG, an OHT with abnormal PERG, and an EOAG patient. In Figure 1A, PERG amplitudes of the patients are plotted as a function of spatial frequency. The continuous and dotted lines in the plots indicate the mean and the lower 95% confidence limits, respectively, established for the different amplitudes in normal subjects. Figure 1B shows the HRT reflectance images of the optic discs from each patient and the corresponding z-profiles taken along oblique meridians (indicated by the thick lines) crossing both SN and IT sectors. Each cupping profile has been selected as the most representative (i.e., that closest to the average) of all the profiles at the IT sector. It can be noted that the steepness of the cup profile is substantially greater in the OHT eye with abnormal PERG compared with that of the OHT eye with normal PERG, although similar to that of the EOAG eye. The differences in cup profiles between OHT patients with normal or abnormally reduced PERGs are quantified by differences in cup shape measures, which were −0.24 and −0.11 in the OHT eyes with normal and abnormal PERGs, respectively. The cup shape measure in the EOAG eye was −0.07.

Figure 2 shows a scattergram of PERG amplitudes recorded individually from OHT eyes at 2.6 cycles/degree and plotted as a function of the corresponding cup shape measures at the IT sector. The negative correlation was statistically significant (multiple regression: r = −0.43, coefficient for cup shape measure: −1.03, P < 0.01). No other significant correlations were found between PERG amplitudes and HRT measures in OHT eyes.

Figure 3 shows the frequency distribution histograms of the three HRT parameters (i.e., cup-to-disc area ratio, rim area, and cup shape measure) gathered from the sectorial analysis (IT sector) in the different groups of the study population. For OHT eyes, the data are separately plotted for the group with normal PERG amplitude (n = 19) and for that with abnormally reduced PERGs (n = 15). It can be seen that in OHT eyes with...
abnormal PERGs, but not in those with normal PERGs, the
distribution of cup shape measure tends to be more similar to
those of EOAG eyes than to those of normal subjects. The
distributions of cup-to-disc area ratio and neuroretinal rim area
do not show similar differences across the patient group. A
multivariate ANOVA, including simultaneously cup-to-disc area
ratio, rim area, and cup shape measure as dependent variables,
showed significant differences between OHT eyes with normal
and abnormal PERGs \( \text{multivariate } F(3,29): 4.6, P \leq 0.01 \).
Univariate F tests, however, reached the significance level only
for the cup shape measures \( F(1,31): 10.44, P < 0.01 \). The
difference in cup shape measure distributions between OHT
eyes with normal and those with abnormal PERGs was also
observed in the global disc analysis [not shown, univariate
\( F(1,31): 12.04, P < 0.01 \)].

In Table 4 incidences of HRT parameter and PERG abnor-
malities in individual OHT patients are compared by \( 2 \times 2 \)
tables. The functional parameter PERG was considered in this
analysis the gold standard of reference (see also the Methods
section). It can be noted that all three HRT parameters (cup-
to-disc area ratio, rim area, and cup shape measure, derived
from global disc analysis) displayed a low sensitivity and a
relatively high specificity in predicting corresponding PERG
abnormalities. Among the parameters, the highest specificity
and positive predictive value was displayed by cup shape
measure.

**DISCUSSION**

The goal of the present study was to evaluate in eyes with
OHT, normal conventional automated perimetry, and normal
clinical appearance of the optic nerve head, the relationship
between early PERG losses and structural optic disc parameters
derived from CSLO analysis. Analysis of correlations between
PERG and HRT parameters showed that PERG amplitudes at
medium spatial frequencies (i.e., responses previously re-
ported as specifically vulnerable in OHT) tended to de-
crease significantly as the cup shape measure of individual eyes
moved toward the abnormal range \( (> -0.10) \). This was de-
monstrable when amplitudes were compared with cup shape
measures calculated separately for the IT disc sector, which
has been found to be the most frequently affected in early
glaucoma. The correlation did not attain statistical signifi-

**Figure 1.** (A) Plots of PERG amplitudes at different spatial frequencies obtained from three representative patients’ eyes (from top to bottom): an OHT patient with normal PERG, an OHT with abnormal PERG, and an EOAG patient. In each plot, the continuous and dotted lines indicate the normal mean values and 95% confidence limits, respectively, established for the different response amplitudes. (B) HRT reflectance images of the optic discs of the same eyes whose PERGs are reported in (A). To the right of each image, the corresponding z-profiles of the cupping (taken along oblique meridians and crossing both SN and IT sectors) are also shown. Each cupping profile has been selected as that closest to the average of all profiles at the IT sector. Dashed lines in the z-profiles plots indicate the level of the reference plane.
cance when the structural parameter was derived from global
disc analysis. However, a significant difference in the distribu-
tions of parameter values was found when eyes with normal or
abnormal PERGs were compared, with the latter showing av-
erage values closer to those found in a glaucomatous pop-
ulation.

In the past, only a few studies have evaluated the corre-
lation between PERG and disc morphometry in OHT. 40,41
None of these found, in cross-sectional evaluations, a signifi-
cant association between PERG amplitudes or latencies and
disc parameters. Longitudinal evaluations provided contrasting
results. In a 6-month follow-up study, Bach and Funk40 found
that PERG amplitude losses in glaucoma suspect eyes were
significantly correlated with progressive rim area losses. In
contrast, in a longer longitudinal study, Bo¨mer et al.41 reported
a poor value of the PERG in predicting the worsening of
morphometric parameters in glaucoma suspects. None of the
previous studies evaluated the relationship between PERG and
the shape of the optic disc cup, expressed quantitatively by the
cup shape measure.

Recent clinical evidence 2 indicates that the cup shape
measure can be used with high diagnostic precision to discrim-
inate between normal and glaucomatous eyes. Studies evaluat-
ing in glaucomatous eyes the relationship between visual field
loss and structural damage to the optic nerve found that the
cup shape measure showed the strongest correlations with
mean deviation or corrected pattern SD values obtained from
white-on-white 1–3 or blue-on-yellow 3 perimeties. Taken to-
gether, these previous findings support the suggestion that an
abnormality in the cup shape measure reflects indirectly glau-
comatous damage to retinal ganglion cells and optic nerve
axons. 1 This is in agreement with histologic findings, 42 dem-
onstrating that morphologic changes in the lamina cribrosa are
correlated with neural loss in open-angle glaucoma, and clin-
ical belief 3 that increased cupping of the disc is a manifestation
of glaucomatous neural damage. It should be emphasized,
however, that the amount of correlation we found was rather
weak \( r = –0.43 \), with the structural parameter accounting
for no more than 20% of the PERG variance. Comparable
results were found in the previous studies correlating perimet-
ric sensitivities with HRT parameters when only the popula-
tions of OHT and EOAG patients were considered. 3 The weak-
ness of the association may have different causes that are
detailed below (see the next paragraph) and indicates that in

![Figure 2. Pattern electroretinogram amplitudes, recorded from individual OHT eyes at 2.6 cycles/degree, plotted as a function of corresponding
cup shape measures obtained from analysis of IT disc sector (multiple regression with cup shape measure and disc area as dependent variables:
\( r = –0.43 \), coefficient cup shape measure = −1.03, \( P < 0.01 \)).](image-url)
the clinical setting a full characterization of the status of the optic nerve head in OHT requires both functional tests and morphologic disc analysis.

A subset of the OHT eyes evaluated in this study showed significant abnormalities of PERG, HRT parameters, or both. PERG alterations tended to be more frequent than those of

**Table 4.** Sensitivity and Specificity of HRT Parameter Abnormalities in Predicting PERG Abnormalities in Individual OHT Eyes

<table>
<thead>
<tr>
<th>Abnormal PERG (n = 15)</th>
<th>Normal PERG (n = 19)</th>
</tr>
</thead>
<tbody>
<tr>
<td>Abnormal CDA* (n = 14)</td>
<td>8</td>
</tr>
<tr>
<td>Normal CDA (n = 20)</td>
<td>7</td>
</tr>
<tr>
<td>Abnormal RA† (n = 8)</td>
<td>5</td>
</tr>
<tr>
<td>Normal RA (n = 26)</td>
<td>10</td>
</tr>
<tr>
<td>Abnormal CSM‡ (n = 3)</td>
<td>3</td>
</tr>
<tr>
<td>Normal CSM (n = 31)</td>
<td>12</td>
</tr>
</tbody>
</table>

* CDA = cup-to-disc area ratio; † RA = rim area; ‡ CSM = cup shape measure.
fibers, which may develop before the occurrence of changes in the cup structure. Recent clinical observations showing that PERG amplitude in OHT eyes was inversely correlated with the thickness of the peripapillary nerve fiber layer as measured by OCT imaging, lend support to this hypothesis. Second, the normal values for most HRT parameters are strongly dependent on the size and shape of the optic disc (see for example Ref. 38), resulting in an increased variability and low clinical sensitivity in borderline cases. Interestingly, cup-to-disc area ratio, rim area, and cup shape measure displayed a low sensitivity but a relatively high specificity in predicting PERG losses in individual eyes. The highest predictive value was shown by the cup shape measure. This raises the possibility that when used in combination PERG and cup shape measure could help in defining the limits between normal and pathologic optic discs, strengthening an otherwise uncertain diagnosis of optic nerve damage in individual OHT eyes. Clearly, only longitudinal studies evaluating the rate of development of field losses in different subcategories of OHT eyes will clarify the clinical relevance of the present findings.

In summary, the results of this study show that in OHT there is a significant, although weak, correlation between the PERG, an index of inner retinal function, and optic disc structure. In individual eyes, abnormalities in the shape of optic disc cup may be highly predictive for the presence of ERG losses. These data suggest a parallel involvement of both structure and function in OHT and a potential clinical value of combined PERG and CSLO optic disc analysis in detecting eyes at increased risk for glaucoma damage.

References


