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Diagnostic Accuracy of Pattern Electoretinogram Optimized for Glaucoma Detection

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Abstract

Purpose—To assess the ability of the new pattern electoretinogram optimized for glaucoma detection (PERGLA) paradigm to discriminate between healthy individuals and individuals with glaucomatous optic neuropathy (GON).

Design—Cross-sectional study.

Participants—One hundred forty two eyes of 71 participants (42 healthy and 29 with GON in at least one eye) enrolled in the University of California, San Diego, Diagnostic Innovations in Glaucoma Study (DIGS) were studied. Healthy individuals were those recruited as healthy with healthy appearing optic disc by examination and masked stereoscopic optic disc photograph evaluation. GON was defined based on stereo-photograph assessment.

Methods—PERGLA (Glaide Elettronica, Pisa, Italy) recordings were obtained within six month of standard automated perimetry (SAP) testing. Dependent variables were PERGLA amplitude, phase, amplitude asymmetry, and phase asymmetry and SAP pattern standard deviation (PSD) and mean deviation (MD).

Main Outcome Measures—Diagnostic accuracy (sensitivity and specificity) of the PERGLA normative database for classifying healthy and glaucoma individuals was determined. In addition, performance (areas under receiver operating curves, AUC) of PERGLA amplitude and phase for classifying healthy (n=84) and GON (n=50) eyes was determined. Results from both analyses were compared to those from SAP.

Results—Sensitivity and specificity of the PERGLA normative database were 0.76 and 0.59, respectively, compared to 0.83 and 0.77 for SAP. AUCs for PERGLA amplitude and phase were 0.75 and 0.50 (chance performance), respectively. AUCs for SAP PSD and mean MD were 0.83 and 0.78, respectively.

Conclusions—Pattern electoretinograms recorded using the PERGLA paradigm can discriminate between healthy and glaucoma eyes, although this technique performed no better than SAP at this task. Low specificity of the PERGLA normative database suggests that the distribution of recordings included in the database is not ideal.

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Keywords

Glaucoma; Electrophysiology; Pattern Electroretinogram; Perimetry; Discrimination

The diagnostic accuracy of the pattern electroretinogram (PERG) for discriminating between healthy and glaucoma eyes has been investigated for over twenty-five years¹⁻³ and recent work suggests that it is useful for this task.⁴⁻⁶ The PERG response is massed primarily from the electrical potentials of retinal ganglion cells⁷⁻¹⁰ and it is ganglion cell damage that is the underlying cause of glaucoma-related decreases in visual sensitivity.¹¹ The PERG stimulus isolates the ganglion cell response using a reversing (i.e., contrast modulated) checker-board or grating pattern that carries no change in overall luminance over time (space-averaged luminance). Depending on the reversal rate of the stimulus, the resulting electrical response profile appears as an isolated triple inflection-point waveform (transient PERG) or a continuous sinusoidal waveform (steady-state PERG).

Because the PERG response is very small, its success for discriminating between healthy and glaucoma eyes relies on a complex interaction of stimulus and recording parameters. Variable adherence to PERG recording/analysis standards and the expertise required to assess PERG results possibly have hampered this technique from developing into a clinically useful tool for the general ophthalmologist.

Recently, a user-friendly PERG measurement paradigm designed specifically for glaucoma detection has been introduced that employs optimized stimulus parameters for boosting signal to noise ratio. It compares response amplitude and phase to an internal normative database (Glaid PERGLA, Lace Elettronica, Pisa, Italy) to aid in clinical interpretation of responses. Preliminary studies suggest that PERG measurements using this technique are repeatable (with coefficients of variability on the order of 10 percent for amplitude measurements)¹²⁻¹⁵, show acceptable signal to noise ratio (SNR) to detect early to moderate decreases in response amplitude (e.g., 5 to 13 in healthy eyes)¹²⁻¹⁵, and are sensitive to glaucoma-related decreases in signal when comparisons are made to the internal normative database.⁴

The current study assesses the ability of PERGLA (pattern electroretinogram optimized for glaucoma detection) measurements (amplitude, phase, amplitude asymmetry, phase asymmetry) to distinguish between healthy individuals and those with glaucomatous optic neuropathy (GON). Results are compared to those from standard automated perimetry (SAP).

METHODS

Subjects

142 eyes of 71 participants enrolled in the University of California, San Diego, Diagnostic Innovations in Glaucoma Study (DIGS) were included in this study. All eyes had good quality stereo-photography (TRC-SS, Topcon Instruments Corp. of America, Paramus, NJ) of the optic disc and reliable (false positives, fixation losses and false negatives $\leq 33\%$ with no observable testing artifacts) standard automated perimetry (SAP, Humphrey Field Analyzer II with Swedish Interactive Thresholding Algorithm, Carl Zeiss Meditec, Dublin CA) testing within 6 months of PERG testing.

In addition, each study participant underwent a comprehensive ophthalmologic evaluation including review of medical history, best-corrected visual acuity testing, slit-lamp biomicroscopy, intraocular pressure (IOP) measurement with Goldmann applanation tonometry, gonioscopy, and dilated slit lamp fundus examination with a 78 diopter lens. To be included in the study, participants had to have a best-corrected acuity better than or equal to

20/40, spherical refraction within $\pm 5.0D$ and cylinder correction within $\pm 3.0D$, and open angles on gonioscopy. Eyes with coexisting retinal disease, uveitis, or non-glaucomatous optic neuropathy determined on examination or stereo-photograph assessment were excluded.

Because the PERGLA paradigm involves simultaneous binocular testing in the clinic and its software employs an inter-eye asymmetry comparison to the internal normative database, recordings from both eyes of each study participant were assessed. Participants were classified either as glaucoma patients ($n=29$) or as healthy controls ($n=42$) to investigate PERGLA diagnostic accuracy.

For this study, glaucoma patients were defined as individuals recruited from our clinic (i.e., being treated or followed for glaucoma or suspicion of glaucoma) with GON in at least one eye based on masked assessment of stereo-photographs of the optic disc by two experienced observers (at least one a fellowship-trained glaucoma specialist). In cases of disagreement between observers, a third observer adjudicated the decision (in these cases, at least two of three observers were fellowship-trained glaucoma specialists). A study diagnosis of GON required marked violation of the "ISNT Rule" of distribution of neuroretinal rim thickness (defined by contour, not color), presence of focal thinning disrupting the contour of the neuroretinal rim, and/or the presence of diffuse or focal (wedge-shaped) RNFL atrophy wider than the width of the largest observed vessel and evidenced by light-dark-light patterns of reflectivity in superior or inferior arcuate bundles.

Of the 29 patients, 25 were treated with pressure lowering medications in at least one eye at the time of testing. Eight were on prostaglandins only, four were on beta-blockers only, two were on steroid drops only, one was on a carbonic anhydrase inhibitor, and 10 were on a combination of medications. Average (95% C.I.) presenting IOP in treated patients was 25.0 (22.2, 27.8) mmHg. IOP in the four untreated patients ranged from 17 mmHg to 24 mmHg.

Healthy controls were defined as individuals recruited from the general population with healthy appearing optic discs by examination and masked stereo-photograph assessment up to six months before or at the time of enrollment, with no history of elevated IOP ≥ 22 mmHg. Because we intended to assess the sensitivity and specificity of SAP, visual field results were not part of the inclusion/exclusion criteria for either group.

The average (95% C.I.) age of healthy individuals was 63.4 (60.3, 66.6) years and the average age of glaucoma patients was 65.7 (61.2, 70.1) years [$p(t) = 0.389$]. Twenty-nine (67%) healthy individuals were female and 17 (61%) patients were female [$p(\chi^2) = 0.562$]. IOP at the time of PERGLA recording was similar in healthy and glaucoma eyes [15.0 (14.5, 15.6) mmHg and 15.0 (13.7, 16.3) mmHg, respectively; $p(t) = 0.969$].

All study methods adhered to the provisions of the Declaration of Helsinki guidelines for research involving human participants and the Health Insurance Portability and Accountability Act (HIPAA).

PERG Testing

A commercially available modification of the Glaid (Lace Elettronica, Pisa, Italy, software version 2.1.14) electrophysiology instrument, called PERGLA was used to measure the PERG response.^{4,12} The PERGLA stimulus is a black and white (contrast 98%, mean luminance 40 cd/m²), horizontal square wave grating (1.6 c/deg), counter-phasing at 8.14 Hz, presented on a computer monitor (14.1 cm diameter circular field). At a viewing distance of 30 cm, the display subtends 25 deg centered on the fovea. Responses from both eyes are measured simultaneously. Electrical signals from silver-chloride skin electrodes (9 mm adhered with conductive cream and tape) (both lower eyelids active, both temples reference, forehead

ground) are fed into a two-channel differential amplifier, amplified (100,000 fold), filtered (1–30 Hz), then digitized with 12-bit resolution at 4169 Hz. Before testing, the electrode impedance is monitored automatically and an on-screen indicator signals acceptable impedance ($\leq 5 \text{ k}\Omega$). Additionally, an on-screen oscilloscope displays background noise.

The PERGLA software obtains each waveform by averaging 600 artifact-free time-periods (i.e., sweeps) of 122.8 msec each, synchronized with the contrast alternation of the stimulus grating. Two independent response blocks of 330 sweeps each are recorded and separated by a user-defined inter-stimulus interval (approximately one minute). For each block, the first 30 sweeps are rejected from the average to eliminate onset effects from the steady-state recording. Sweeps containing spurious signals attributable to blinks and eye movements are rejected over a threshold voltage of $\pm 25 \mu\text{V}$. Resulting steady-state PERGs take the form of near-sine waves that are Fourier transformed to isolate the harmonic component at the contrast reversal rate (16.28 Hz, 2 contrast reversals per cycle). In addition, a noise response is obtained by multiplying alternate sweeps by 1 and -1 before averaging. The noise response also is Fourier transformed at 16.28 Hz to allow calculation of SNR.

Resulting response amplitudes and latencies (i.e., phase shifts) were recorded as independent study variables. In addition, these values were compared to results from a manufacturer provided normative database to classify individuals as within or outside of normal limits (see below).

Each participant was tested by the same operator (AT) twice, approximately one hour apart. Test time was approximately 4 minutes per test. Preparation and electrode placement added approximately 5 to 10 minutes to each examination. All eyes were refracted, appropriate corrections for viewing distance were made and near acuity was J1 or better for all participants.

Visual field testing

Individuals were tested using the Humphrey HFAII (software version 4.1, Carl Zeiss Meditec, Dublin, CA) 24-2 protocol with Swedish Interactive Thresholding Algorithm (SITA). This instrument and its operation have been described in detail elsewhere.¹⁶

Analyses

First, the diagnostic accuracies of PERGLA and SAP measurements were determined and compared in healthy and glaucoma individuals using normative databases. Individuals were considered outside of normal limits (ONL) by PERGLA if the PERG amplitude (either eye), phase (either eye), inter-ocular amplitude asymmetry, or phase asymmetry was outside of normal limits (defined as outside 2 S.D. of normal variability, depressed or retarded for amplitude and phase, respectively) on two consecutive tests. Abnormality by SAP was defined as either Glaucoma Hemifield Test (GHT) outside normal limits or PSD outside of 95% normal limits (i.e., $\leq 5\%$) in either eye, also on two consecutive tests.

Next, continuous measures of PERGLA amplitude and phase and SAP MD and PSD were compared between healthy eyes ($n = 84$ of 42 healthy individuals) and GON eyes ($n = 50$ of 29 individuals with GON). PERGLA results from the first of two trials and SAP results from the SAP test closest to the PERG test were chosen for analysis. Diagnostic accuracy of these parameters was assessed by reporting the areas under receiver operating characteristic curves (AUC). Significant differences between AUC were determined using the method of De Long.¹⁷ Because overall AUC can be influenced by areas of the curve where specificity is very poor (i.e., right-hand side of the curve), we also determined sensitivity at set specificities of 0.75, 0.85 and 0.95.

RESULTS

Using the normative database and criteria of abnormality of repeatable amplitude (at least one eye), phase (at least one eye), amplitude asymmetry or phase asymmetry ONL, PERGLA sensitivity was 0.76 (C.I. = 0.56, 0.89; 22/29 glaucoma patients correctly classified) and specificity was 0.56 (C.I. = 0.43, 0.74; 25/42 healthy patients correctly classified). Sensitivity of SAP was 0.83 (C.I. = 0.63, 0.93; 24/29) and specificity was 0.79 (C.I. = 0.63, 0.89; 33/42), respectively. PERGLA accuracy (percent correct classification) was 0.66 and SAP accuracy was 0.80. Agreement between techniques was fair (69% agreement, $K = 0.38$, C.I. = 0.17, 0.60).

PERGLA (amplitude and phase) and SAP (MD and PSD) measurements are compared for healthy and GON eyes in Table 1. Significant differences (t-test, all $p \leq 0.001$) were found for all parameters except PERGLA phase ($p=0.582$). PERGLA amplitude was decreased by approximately 33% in GON compared to healthy eyes.

ROC curve areas for discriminating between healthy and GON eyes were greatest for SAP PSD (0.83), followed by SAP MD (0.78), PERGLA amplitude (0.75) and PERGLA phase (0.50). The AUC for PERGLA phase was not significantly different from chance (asymptotic significance = 0.952) and was significantly lower than AUCs for all other parameters (method of De Long, all $p < 0.001$) (Table 2, Figure 1). AUCs for PERGLA amplitude, SAP PSD and SAP MD were statistically similar (method of De Long, all $p \geq 0.110$). Qualitatively, sensitivities at or near the chosen specificities of 0.75, 0.85 and 0.95 were generally better for SAP than for PERGLA parameters based on examination of 95% confidence intervals (especially at higher specificities, Table 2).

DISCUSSION

For a new diagnostic instrument to be clinically useful its measurements must be acceptably reproducible and they must be able to identify the target disease. Previous studies indicate that PERGLA measurements are highly reproducible.^{12–15} In the current study, the sensitivity of PERGLA measurements was quite good when the internal normative database was employed. However, specificity was poor suggesting that the current normative database may not be ideal. Regardless of the normative database, however, PERGLA amplitude showed acceptable diagnostic accuracy, described by AUC, similar to that of SAP MD but lower than SAP PSD. This was not the case for PERGLA phase, which performed at the level of chance.

Because the phase measurement performed no better than chance at discriminating between healthy and GON eyes, we conducted a *post hoc* analysis of PERGLA normative database accuracy with this parameter excluded (i.e., an ONL result required repeatable phase and/or phase asymmetry abnormality). The exclusion of phase increased specificity by 0.12 from 0.59 to 0.71 (95% CI = 0.55, 0.84) but decreased sensitivity by 0.14 from 0.76 to 0.62 (95% CI = 0.42, 0.79) resulting in no overall gain in accuracy. Because the PERG amplitude from both eyes of healthy individuals are highly correlated¹² and early glaucoma might manifest as a significant decrease in this correlation before a significant intraocular amplitude defect is detectable, the classification performance of amplitude asymmetry alone also was determined. Sensitivity and specificity of this parameter alone were 0.56 (95% CI = 0.34, 0.79) and 0.65 (95% CI = 0.51, 0.78), respectively.

PERGLA amplitude is negatively correlated with IOP and age in healthy eyes.¹² Differences in IOP between healthy and GON eyes could have contributed to decreases in diagnostic accuracy in the current study if IOP was higher in the control group compared to the GON group at the time of testing, but this was not the case (IOP was the same between groups). Similarly, any between-group effect of age on diagnostic accuracy was ruled out because age

in both groups was similar. The relatively poor specificity (compared to sensitivity) of the normative database in our population might be explained by the fact that our healthy controls were significantly older than those whose measurements compose the PERGLA normative database. Average age of healthy individuals in our study was 63.3 years compared to 43.8 years (S.D. = 18.0 years, range: 22 to 85 years) in the PERGLA normative database as described by Porciatti and Ventura.¹² Although the PERGLA normative data is age-corrected, this correction could be somewhat inaccurate because of a larger number of younger individuals compared to older ones included in the original analysis.

Because of instrument calibration differences, the International Society for Clinical Electrophysiology of Vision recommends that each laboratory should ideally derive its own normative values.¹⁸ The use of an external normative database possibly gathered on a differently calibrated instrument may have had some impact on the performance of this database in our study population. The normative database provided for the PERGLA instrument includes data from only one clinical site. In addition, data from a relatively small number of healthy individuals is included. However, for an instrument to be widely usable for general ophthalmologists who presumably are unlikely to gather their own normative data, an instrument specific normative database is needed. Increasing the size of the PERGLA normative database by including recordings from other centers could increase its generalizability and performance. This is a relatively straightforward task that would require a software upgrade to update database comparisons for previously obtained individual tests.

The first clinical study reporting PERGLA results by Ventura and colleagues⁴ described a sensitivity of 0.52 in glaucoma suspect patients (n = 200, those with apparent GON by stereoscopic photograph assessment and visual fields within normal limits) and 0.69 in glaucoma patients (n = 42, with abnormal SAP and/or progressive optic disc changes by photograph assessment). Similar to our study, this study classified patients as outside normal limits on PERGLA if they showed amplitude or phase ONL in either eye or amplitude or phase asymmetry ONL between eyes. Sensitivity for detecting individuals with GON (regardless of the visual field sensitivity) in the current study was better (0.76). However, specificity for detecting healthy study participants in our study was low (0.59). In the earlier study⁴, specificity was not directly reported presumably because the majority of the healthy participants also contributed to the data set used to define outside of normal limits measurements (i.e., the reported specificity would be artificially high). In general, reporting sensitivity without reporting specificity is not recommended because the false positive rate of the test in question is unknown. Because of this, our results are not directly comparable to those of the earlier study.⁴

Many previous studies have shown significant differences in PERG amplitude between healthy and glaucoma (and ocular hypertensive, OHT) eyes using both steady-state and transient stimuli (see¹⁹ for a recent review) with some evidence that the steady-state response is more susceptible to what are presumed glaucomatous changes.^{20,21} Recently, Parisi and colleagues examined the ability of the transient PERG to discriminate between healthy eyes and treated OHT eyes. Based on the cut-offs applied, sensitivity in OHT eyes was approximately 0.85 for P50 implicit time and 0.69 for P50 to N95 amplitude in the absence of visual field abnormality by SAP, possibly indicating detection of early functional deficits (although this rate of abnormality is much greater than the number of OHT eyes expected to later develop glaucoma). The reported specificity for these parameters was 1.00, (however, this value is biased upward by definition because the same set of eyes used to define the outside normal limits/within normal limits cut-offs were used to assess them). When assessing the sensitivity/specificity trade-offs using receiver operating characteristic analyses, AUCs approached 1.0. It is unlikely based on the study design that very large AUCs were the result of differences in IOP (although IOP at testing among groups was not reported) or age between healthy and other experimental

groups (groups were nearly age matched). Dramatic differences in results between this study and ours might be attributable in part to differences in severity in the glaucoma groups (average SAP MD = -8.43 dB in the former, -2.48 dB in the latter), differences in PERG measurement techniques (transient versus steady state PERG) and/or parameters measured.

In related studies suggesting early detection of functional defects using PERG, Bayer and colleagues²² detected decreased amplitude in SAP-normal eyes of glaucoma patients with unilateral visual field defects and Bach⁵ and colleagues detected decreased PERG ratios (ratio of response to check size 0.8 deg/0.16 deg) in OHT eyes approximately 2 years before these eyes developed SAP defects. In the latter study, 95 eyes of 54 treated ocular hypertensives (although 3 had glaucoma in the fellow eye so were not strictly OHT) were tested every 6 months for a median of 8 years. At the end of the study, eyes were divided into converted (based on change in MD or changed clusters of points, $n = 8$) and non-converted ($n = 87$). The authors described the AUC for discriminating between converted and non-converted eyes every six months. Three years prior to the study's end, the AUC was 0.60 (chance). This value increased to approximately 0.70 two years, and to approximately 0.80 one year prior, indicating early detection of change using PERG. Results of this study should be interpreted with caution, however, because of the very small number of conversions observed (as is expected in an OHT population).

If the PERG response is measuring retinal ganglion cell activity, it should be associated with the number of ganglion cells in the retina. Optic disc topography and retinal nerve fiber layer (RNFL) thickness measured using optical imaging techniques have been suggested as *in vivo* surrogates for assessing ganglion cell counts. Therefore, PERG measurements should be associated with these measurements and this is the case. A significant but modest association between temporal neuroretinal rim area measured using confocal scanning laser ophthalmoscopy and PERG amplitude has been shown²³, as have significant associations between RNFL thickness measured using optical coherence tomography and transient PERG²⁴ and steady-state PERGLA.²⁵ These results suggest that PERG is at least somewhat representative of the ganglion cell count. The somewhat weak correlations among electrophysiological and imaging results reported may be attributable to the presence of sick (i.e., unresponsive) cells yet to drop out and influence topography.

To our knowledge, this is the first study comparing PERGLA results to standard automated perimetry results. In the current study, PERG was outperformed somewhat by SAP. One possible reason for this result is that the PERG stimulus is presented to the central visual field and glaucomatous defects usually first manifest peripherally. It is possible that the majority of our early glaucoma patients had primarily local, peripheral defects and PERG is more sensitive to diffuse loss. However, recent evidence suggests that PERG can detect centrally measured defects that are not present with SAP testing.²⁶ This might be due to redundancy of ganglion cell representation in the macula. Moreover, PERG results are very abnormal in some glaucoma eyes with mild visual field defects (PERG results also can be normal in eyes with severe field defects, however)²⁷ and multi-focal PERG results suggest that PERG and SAP defects are not co-localized.²⁸ These results suggest that PERG may be recording ganglion cell activity that is not linearly related to visual function. If this is the case, results showing little association between PERG and SAP results are not surprising and it is possible that these techniques provide complementary information. In the current study, 30 eyes showed PERGLA abnormality but not SAP abnormality and 18 eyes showed SAP abnormality but not PERGLA abnormality. Of the 30 eyes with abnormal PERG and normal SAP, only 5 were classified as GON. Of the 18 eyes with abnormal SAP and normal PERG, 9 were classified as GON. These results suggest that PERG is identifying dysfunction attributable to causes other than glaucoma such as age.

It is possible that in the current study the diagnostic accuracy of SAP testing was artificially elevated relative to PERGLA testing. This is because we required reliable SAP results and made no such requirement of PERGLA results. SAP software incorporates complex staircase- and fixation monitor-based algorithms to assure test reliability and no such algorithms currently are available for PERGLA, though the PERGLA paradigm does require acceptable electrode impedance and it employs techniques to remove noise from recordings (see Methods). The great majority of our study participants were inexperienced with electrophysiological testing of visual function, so the tests used for analyses were their initial tests. However, learning effects similar to those observed in initial SAP testing are not expected for electrophysiology tests because electrophysiology tests are largely objective.

Overall, our results suggest that while PERG measured using the PERGLA paradigm can discriminate between healthy and glaucoma eyes, and PERG amplitude is significantly different between healthy eyes and those with glaucoma defined based on disc appearance, the specificity of the PERGLA normative database for identifying healthy individuals is not ideal. Moreover, the sensitivity of PERGLA amplitude is lower than that of SAP global indices at high specificities and PERGLA discrimination performance is no better than SAP MD and probably worse than SAP PSD based on receiver operating characteristic curve analyses. It is likely that PERGLA recordings, like standard PERG recordings, are influenced by factors such as IOP, age and lens opacities (and stimulus/recording variables) and the effects of these variables need to be more thoroughly dissociated from disease related effects.

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Figure 1.

Receiver operating characteristic curves (AUC) for discriminating between healthy eyes and eyes with glaucomatous optic neuropathy (GON) for PERGLA amplitude and phase and SAP pattern standard deviation (PSD) and mean deviation (MD). The reference line describes chance discrimination (i.e., AUC = 0.50). AUC for PERGLA phase is significantly smaller than for other parameters that have statistically similar AUCs. PERGLA = pattern electroretinogram optimized for glaucoma detection, SAP = standard automated perimetry.

Table 1

Comparing pattern electroretinogram optimized for glaucoma detection (PERGLA) and standard automated perimetry (SAP) parameters between glaucomatous optic neuropathy (GON) and healthy eyes.

	GON eyes (n = 50)	Healthy eyes (n=84)	P(t)=
<i>PERGLA Amplitude (μV) (95% CI)</i>	0.532 (0.466, 0.598)	0.775 (0.715, 0.836)	< 0.0001
<i>PERGLA Phase (π rad) (95% CI)</i>	1.82 (1.79, 1.85)	1.81 (1.79, 1.84)	0.582
<i>SAP PSD (dB) (95% CI)</i>	4.35 (3.30, 5.41)	1.67 (1.53, 1.81)	< 0.0001
<i>SAP MD (dB) (95% CI)</i>	-2.48 (-3.34, -1.62)	-0.11 (-0.33, 0.10)	< 0.0001

CI = confidence interval

PSD = pattern standard deviation

MD = mean deviation

Table 2

Receiver operating curve areas (AUC) and sensitivities at approximately 0.95, 0.85 and 0.75 specificity for pattern electroretinogram optimized for glaucoma detection (PERGLA) amplitude and phase and standard automated perimetry (SAP) pattern standard deviation (PSD) and mean deviation (MD).

Parameter	AUC (95% CI)	Sensitivity (95% CI), specificity (95% CI) at ≈ 0.95 specificity	Sensitivity (95% CI), specificity (95% CI) at ≈ 0.85 specificity	Sensitivity (95% CI), specificity (95% CI) at ≈ 0.75 specificity
<i>PERGLA amplitude</i>	0.75 (0.66, 0.83)	0.18 (0.09, 0.32) 0.95 (0.87, 0.98)	0.44 (0.30, 0.59) 0.85 (0.75, 0.91)	0.66 (0.51, 0.78) 0.76 (0.66, 0.84)
<i>PERGLA phase</i>	0.50 (0.40, 0.61)	0.08 (0.03, 0.20) 0.96 (0.88, 0.99)	0.22 (0.12, 0.36) 0.84 (0.74, 0.90)	0.34 (0.22, 0.49) 0.75 (0.65, 0.83)
<i>SAP PSD</i>	0.83 (0.76, 0.90)	0.42 (0.28, 0.57) 0.96 (0.89, 0.99)	0.66 (0.51, 0.78) 0.85 (0.75, 0.91)	0.74 (0.59, 0.85) 0.74 (0.63, 0.82)
<i>SAP MD</i>	0.78 (0.69, 0.86)	0.48 (0.34, 0.62) 0.96 (0.89, 0.99)	0.60 (0.45, 0.73) 0.86 (0.77, 0.92)	0.68 (0.53, 0.80) 0.75 (0.65, 0.83)

CI = confidence interval