Humphrey matrix frequency doubling perimetry for detection of visual-field defects in open-angle glaucoma

C I Clement, I Goldberg, P R Healey, et al.

Br J Ophthalmol 2009 93: 582-588 originally published online July 31, 2008
doi: 10.1136/bjo.2007.119909

Updated information and services can be found at:
http://bjo.bmj.com/content/93/5/582.full.html

These include:

References
This article cites 32 articles, 10 of which can be accessed free at:
http://bjo.bmj.com/content/93/5/582.full.html#ref-list-1

Article cited in:
http://bjo.bmj.com/content/93/5/582.full.html#related-urls

Email alerting service
Receive free email alerts when new articles cite this article. Sign up in the box at the top right corner of the online article.

Topic collections
Articles on similar topics can be found in the following collections

Angle (691 articles)
Intraocular pressure (689 articles)
Glaucoma (710 articles)
Epidemiology (4930 articles)

Notes

To order reprints of this article go to:
http://bjo.bmj.com/cgi/reprintform

To subscribe to British Journal of Ophthalmology go to:
http://bjo.bmj.com/subscriptions
Humphrey matrix frequency doubling perimetry for detection of visual-field defects in open-angle glaucoma

C I Clement, I Goldberg, P R Healey, S Graham

ABSTRACT

Aim: Matrix perimetry uses frequency-doubling technology (FDT) incorporated into a 5° test target. This permits testing of the same number of locations within a defined visual field as standard automated perimetry (SAP) and may improve performance compared with original FDT perimetry. This study investigates the performance of Humphrey Matrix perimetry for detecting glaucomatous visual-field loss.

Design: Prospective case control study.

Methods: We recruited 115 participants with glaucomatous visual-field loss and 33 normal controls from an urban glaucoma practice. Each participant performed SITA 24-2 SAP then threshold 24-2 Matrix perimetry. Severity of visual-field loss was defined using SAP mean deviation (MD) as early (MD > -6 dB), moderate (MD > -6 to -12 dB) or advanced (MD < -12 dB). The sensitivity and specificity of Humphrey Matrix perimetry were calculated for different automated indices.

Results: The matrix perimetry sensitivity and specificity were up to 100% for moderate and advanced glaucomatous visual-field loss. A receiver operator characteristic area under the curve (AUC) analysis revealed MD to be slightly better than pattern standard deviation (PSD) for defining moderate (AUC: MD 0.997; PSD 0.987) and advanced defects (AUC: MD 1.000; PSD 0.987). Matrix was less sensitive (up to 87.3%) for detecting early glaucomatous visual-field loss compared with SITA 24-2 SAP (AUC: PSD 0.948; MD 0.910).

Conclusions: Matrix perimetry is excellent for detection of moderate to advanced glaucomatous visual-field loss but may miss some early defects. It may be well suited to following progression of early to moderate field loss because of a smaller target size compared with original FDT perimetry.

Glucomatous visual-field loss is associated with visual-field defects and visual impairment. Accurate assessment of this field loss is vital to diagnose and to monitor glaucoma management.

Historically, the “gold standard” for visual-field testing has been standard automated perimetry (SAP) because of relative reproducibility and accuracy. However, up to 50% of RGCs are lost before a scotoma is detected with SAP. This may reflect redundancy within the visual pathways stimulated by white-on-white perimetry and highlights the need for more focused testing methods.

Frequency-doubling technology (FDT) was developed on the premise that it may detect RGC damage earlier in glaucoma. It uses the frequency-doubling illusion (FDI), which places Μγ (magnocellular subtype) RGCs into a high gain state and possibly generates non-linear response properties within this subpopulation. My cells are relatively sparse, with reduced redundancy; selectively testing their function may permit earlier detection of RGC damage clinically.

The first commercially available frequency-doubling perimeter used a 10° stimulus to assess 17 zones in the central 24° of vision. FDT performance appears to be excellent for moderate to advanced defects. Its ability to detect early field loss is also good, but there is a tendency to miss small defects.

The Humphrey “Matrix” perimeter uses the FDI with a 5° stimulus to assess 55 zones in the central 24° of vision. Reduction of the FDI target has been achieved without compromising the test performance and allows Matrix perimetry to test the same number of zones as points tested by SAP. Comparison with standard FDT perimeter suggests that Matrix perimetry may have a higher sensitivity for early glaucomatous loss and better characterisation of the pattern of visual-field loss. Thus, Matrix perimetry may provide additional benefits for monitoring subtle progression in glaucomatous field defects.

We assessed Matrix perimetry against SAP to determine its ability to detect early, moderate and advanced glaucomatous visual-field loss.

METHODS

Patient selection

Patients were prospectively enrolled at an urban glaucoma practice between April and September 2004 with informed consent obtained from each participant. The South East Sydney Area Health Service human research ethics committee reviewed and approved the study protocol. Only patients with open-angle glaucoma (OAG) with reproducible visual-field defects on SAP tested within 12 months of this study were included. One of three ophthalmologists (IG, SLG or PRH) diagnosed OAG on the basis of typical optic disc changes and the presence of glaucomatous visual-field loss using SITA standard 24-2 perimetry (SAP: Humphrey Field Analyzer, Zeiss/Humphrey systems, Dublin, California) according to previously described criteria.

Patients were excluded if the best-corrected visual acuity was <0.5 in the tested eye, if refractive error was greater than ±6 dioptres sphere, if they had ocular surgery within the preceding 3 months or if they had a history of other conditions that might affect visual-field testing (including diabetic retinopathy, age-related
macular degeneration, stroke, retinal artery or vein occlusion and/or cataract).

Control patients were recruited from relatives/friends of patients who attended the same glaucoma practice. They were required to have neither a personal nor a family history of glaucoma and to satisfy all other exclusion criteria. During a single clinic visit, control subjects performed SAP and Matrix perimetry then had applanation tonometry, slit-lamp examination, fundus examination and optic disc photography. If a potential control subject had either IOP > 21 mm Hg or an optic disc suspicious for glaucoma, they were not included in the analysis.

Visual-field testing
Testing was performed using the Matrix perimeter (Humphrey Matrix, Zeiss/Humphrey systems, Dublin, California; Welch Allen, Skaneateles Falls, New York). We used the 24-2 threshold test algorithm consisting of 55 test locations within the central 24° of the visual field using a 5° square stimulus with 0.25 cycles per degree sinusoidal grating counter flickering at 25 Hz.

Subjects were instructed on the use of the Matrix perimeter, shown the FDI on a card and then shown the fixation target and stimulus in simulation mode. Testing was performed in a dimly lit room with correction as required. The right eye was routinely tested first, except where only the left eye was suitable for inclusion in the study. All testing was supervised by the same person (CIC) and was stopped if the false-positive or false-negative rates reached 33% or fixation losses reached 20%. At this stage, patients were re-instructed, and then testing was recommenced. If the false-negative or false-positive rates remained higher than 33% or fixation losses higher than 20% at the end of the test, the patient was excluded from the study.

Table 1 Baseline characteristics

<table>
<thead>
<tr>
<th>Disease severity</th>
<th>Criteria</th>
<th>Control</th>
<th>Early</th>
<th>Moderate</th>
<th>Advanced</th>
</tr>
</thead>
<tbody>
<tr>
<td>No</td>
<td></td>
<td>33</td>
<td>53</td>
<td>33</td>
<td>29</td>
</tr>
<tr>
<td>Mean age (years)</td>
<td>62.46 (8.11)</td>
<td>66.43 (14.15)</td>
<td>70.03 (10.26)</td>
<td>68.89 (11.78)</td>
<td></td>
</tr>
<tr>
<td>Male</td>
<td>16 (48%)</td>
<td>22 (42%)</td>
<td>19 (58%)</td>
<td>15 (52%)</td>
<td></td>
</tr>
<tr>
<td>Right eye</td>
<td>33 (100%)</td>
<td>37 (67%)</td>
<td>26 (76%)</td>
<td>24 (83%)</td>
<td></td>
</tr>
<tr>
<td>Mean visual acuity</td>
<td>1.02 (0.10)</td>
<td>0.91 (0.26)</td>
<td>0.86 (0.27)</td>
<td>0.73 (0.26)</td>
<td></td>
</tr>
<tr>
<td>SAP MD (dB) (SD)</td>
<td>−1.69 (2.93)</td>
<td>−3.36 (1.68)</td>
<td>−8.59 (1.87)</td>
<td>−17.98 (4.54)</td>
<td></td>
</tr>
<tr>
<td>SAP PSD (dB) (SD)</td>
<td>2.78 (3.05)</td>
<td>4.74 (2.76)</td>
<td>8.91 (2.07)</td>
<td>10.75 (2.17)</td>
<td></td>
</tr>
<tr>
<td>Matrix glaucoma hemifield test (abnormal)</td>
<td>2 (6%)</td>
<td>45 (84.9%)</td>
<td>32 (97%)</td>
<td>29 (100%)</td>
<td></td>
</tr>
<tr>
<td>Matrix MD (dB) (SD)</td>
<td>0.95 (2.03)</td>
<td>−4.08 (3.55)</td>
<td>−9.94 (4.21)</td>
<td>−16.53 (4.88)</td>
<td></td>
</tr>
<tr>
<td>Matrix PSD (dB) (SD)</td>
<td>2.58 (0.65)</td>
<td>5.12 (1.77)</td>
<td>6.71 (1.93)</td>
<td>6.53 (2.40)</td>
<td></td>
</tr>
<tr>
<td>Matrix time (s) (SD)</td>
<td>309.57 (9.87)</td>
<td>314.86 (12.28)</td>
<td>314.76 ± 13.92</td>
<td>305.24 (11.0)</td>
<td></td>
</tr>
</tbody>
</table>

MD, mean deviation; PSD, pattern standard deviation; SAP, standard automated perimetry.

Disease severity Criteria Sensitivity (%) Specificity (%)

Early GHT 79.5 95.7
MD p<5 44.6 100
PSD p<5 79.5 95.7
Moderate GHT 96.9 94.1
MD p<5 91.7 100
PSD p<5 100 94.3
Advanced GHT 100 89.3
MD p<5 100 89.3
PSD p<5 100 89.3

GHT, glaucoma hemifield test; MD, mean deviation; PSD, pattern standard deviation.

RESULTS
One hundred and forty-eight patients were included in the final analysis (control, N = 33; early, N = 53; moderate, N = 33; advanced, N = 29). Baseline characteristics for each group are shown in table 1. Compared with controls, all glaucoma groups had significantly worse visual acuity and the moderate glaucoma group were significantly older.

Matrix perimetry sensitivity and specificity compared with standard SAP are summarised in tables 2, 3. MD p<5% demonstrated a low sensitivity for early field loss but a very high sensitivity and specificity for moderate and advanced visual-field loss. PSD p<5% was the most useful index for detection of early visual-field loss with sensitivity 79.5% and specificity 95.7%.

AUC analysis showed excellent performance for Matrix perimetry compared with SAP (table 3, fig 1). AUC ranged from 0.948 for early glaucoma to 0.987 for advanced glaucoma when using PSD. The performance was not as good for early

Data analysis
Statistical analysis was performed using GraphPad Prism 4.0c for Macintosh. Results from only the right eye were analysed unless not affected by glaucoma or not meeting the inclusion/exclusion criteria, in which case the results from the left eye were used. Glaucoma severity was stratified based on SAP results into early (mean deviation (MD) > −6 dB), moderate (MD −6 to −12 dB) or advanced (MD < −12 dB).

Baseline visual performance between groups was compared using an unpaired Student t test. Differences in gender distribution, side used and Matrix glaucoma hemi-field test (GHT) were analysed using the χ² test.

Three strategies were used to discriminate glaucomatous from healthy eyes using Matrix perimetry: (1) abnormal GHT, (2) MD with a significance 0.05 or (3) pattern standard deviation (PSD) with a significance 0.05. Sensitivity and specificity were calculated for each strategy. In addition, receiver operator characteristic area under the curve (AUC) was calculated for MD and PSD.

Agreement between SAP and Matrix perimetry was evaluated in terms of MD and PSD using linear regression and Bland–Altman scatter plots.¹⁴

Distinguishing healthy eyes from those with early glaucoma is of particular interest. Therefore, parameters that may distinguish between these two groups were examined using the Student t test with Bonferroni correction for multiple comparisons.

Clinical science
glaucoma when MD was used (0.910) but was ideal for detecting advanced glaucoma (1.000).

Scatter plots demonstrated good agreement between SAP and Matrix for both MD and PSD (fig 2). The linear regression analysis showed a higher $R^2$ value for MD ($R^2 = 0.71$; $p < 0.001$) compared with PSD ($R^2 = 0.57$; $p < 0.001$), indicating a stronger correlation for MD. The Bland–Altman scatter plots suggested good agreement for MD for all defect severities, whereas agreement was good for PSD for early to moderate defects but less so for advanced defects.

Subcategory analysis failed to identify predictors of abnormal Matrix perimetry in the early OAG group (table 4).

Direct comparison of SAP and Matrix within groups showed differing results for controls and early glaucoma (table 5). The control group had a significantly better MD on Matrix compared with SAP (0.95 dB vs −1.69 dB; $p < 0.02$), whereas no significant difference in Matrix and SAP was seen in the early glaucoma group.

Table 4 Performance characteristics for early glaucoma patients with and without abnormal Matrix perimetry

<table>
<thead>
<tr>
<th>Characteristic</th>
<th>Glaucoma hemifield test</th>
<th>MD</th>
<th>PSD</th>
</tr>
</thead>
<tbody>
<tr>
<td></td>
<td>Normal</td>
<td>Abnormal</td>
<td>p Value</td>
</tr>
<tr>
<td>No</td>
<td>6</td>
<td>47</td>
<td>NA</td>
</tr>
<tr>
<td>Mean age (years)</td>
<td>55.7</td>
<td>67.8</td>
<td>0.50</td>
</tr>
<tr>
<td>Mean visual acuity</td>
<td>1.05</td>
<td>0.90</td>
<td>0.16</td>
</tr>
<tr>
<td>SAP mean MD (dB)</td>
<td>−2.76</td>
<td>−3.44</td>
<td>0.39</td>
</tr>
<tr>
<td>SAP mean PSD (dB)</td>
<td>3.62</td>
<td>4.86</td>
<td>0.47</td>
</tr>
<tr>
<td>Matrix mean MD (dB)</td>
<td>−1.07</td>
<td>−4.4</td>
<td>0.20</td>
</tr>
<tr>
<td>Matrix mean PSD (dB)</td>
<td>2.89</td>
<td>5.32</td>
<td>0.10</td>
</tr>
<tr>
<td>Matrix time (s)</td>
<td>312.3</td>
<td>315.2</td>
<td>0.57</td>
</tr>
<tr>
<td>Mean fixation errors</td>
<td>8%</td>
<td>5%</td>
<td>0.52</td>
</tr>
<tr>
<td>Mean false positive</td>
<td>2%</td>
<td>2%</td>
<td>0.77</td>
</tr>
<tr>
<td>Mean false negative</td>
<td>3%</td>
<td>2%</td>
<td>0.68</td>
</tr>
</tbody>
</table>

Bold values highlight comparisons that reached significance. *p Value calculated with the Student t test. MD, mean deviation; PSD, pattern standard deviation; SAP, standard automated perimetry.

DISCUSSION

We anticipated that Matrix perimetry would be equal to or better than SAP for detecting early glaucomatous visual-field loss. The Matrix perimeter uses the FDI which places M\(c\) RGCs into a high gain state and may also preferentially stimulate them. Selective M\(c\) RGC loss as a feature of early glaucoma has support: (1) cells with large diameter axons may be preferentially affected by glaucoma; (2) they project to the M\(c\) layers of the lateral geniculate nucleus; and (3) M\(c\) layers of the lateral geniculate nucleus have reduced cell density in glaucoma patients. Reduced redundancy of M\(c\) also may explain earlier detection of visual loss by this technology. However, this study found that Matrix perimetry missed some early visual-field defects with a sensitivity of 79.5% (tables 2, 3; figs 1, 3, 4). Others have reported similar results.

Multiple factors may have contributed to reduced sensitivity for early glaucomatous visual-field loss. My RGCs may be difficult to differentiate from koniocellular RGCs anatomically and may be equally affected early in glaucoma. Both have large diameter axons, large dendritic fields and are relatively few in number. In addition, perimeter designed to selectively isolate deficiencies in the koniocellular network (short wavelength automated perimetry) has been effective for detection of early glaucomatous visual-field loss. Other studies do not support selective loss of M\(c\) RGCs in early glaucoma. Rather, animal models of glaucoma have shown either selective loss of parvocellular RGCs or no selective loss at all. Isolation of parvocellular RGC damage in early glaucoma using high-pass resolution perimetry (HRP) supports these findings.
Figure 1  Receiver operator curves for Matrix perimetry. The figure compares the mean deviation (MD) and pattern standard deviation for early, moderate and advanced glaucoma. The area under the curve (AUC) is indicated.

Figure 2  Scatter plots showing linear regression analysis (A, B) and Bland–Altman analysis (C, D) comparing SAP with Matrix perimetry. Comparisons of MD (A, C) and PSD (B, D) are shown. MD, mean deviation; PSD, pattern standard deviation; SAP, standard automated perimetry.
Such disagreement is attributable to differences in study populations and possibly in definitions of glaucoma. Selective M\textsubscript{c}RGC loss may occur in some individuals with glaucoma but not others. Patients in this study were selected on the basis of reproducible visual-field defects on SAP. This may represent selection of patients in whom selective M\textsubscript{c}RGC loss is not a feature. Interestingly, in studies where patients were selected on the basis of optic disc changes alone, FDT perimetry was superior for detection of early glaucomatous functional loss compared with SAP.\textsuperscript{26, 27} Further, original FDT perimetry can identify visual-field defects well in advance of SAP visual-field loss in some individuals but not others.\textsuperscript{5} Interestingly, separate studies\textsuperscript{28, 29} have recently found both FDT and Matrix perimetry: (1) are able to identify visual-field defects in individuals with structural evidence of glaucomatous optic neuropathy but with consistently normal SAP; (2) identified most, but not all, early glaucomatous field loss in individuals with diagnostic changes on SAP.

Reduction of the FDT target size from 10\textdegree{} to 5\textdegree{}, the basis of Matrix perimetry, seems to have no adverse effect on performance.\textsuperscript{13, 0} Our results confirm this observation and suggest that performance for detection of early and moderate glaucomatous visual-field loss may have been marginally improved. Further improvement in this area may be achieved by analysing specific clusters of grouped points of reduced contrast sensitivity matching well-defined glaucomatous visual-field defects. This has been shown to be effective in the past, and preliminary work looking at its influence on Matrix perimetry demonstrates promising results.\textsuperscript{18} Brusini et al\textsuperscript{28} have examined the cluster analysis for the Matrix 30-2 and found the best combination to be: PSD <5% and/or GHT outside normal limits.

**Figure 3** Examples of grey scale and pattern deviation plots of early, moderate and advanced glaucomatous visual-field defects on Humphrey Matrix perimetry. MD, mean deviation; PSD, pattern standard deviation.

**Figure 4** Total deviation and pattern deviation plots comparing standard automated perimetry (SAP) and Matrix perimetry in the left eye of a 30-year-old male with early glaucoma. Early superior arcuate scotoma is demonstrated on SAP but not detected using Matrix perimetry.
and/or a cluster of \( \geq 2 \) areas with \( p < 5\% \). With this, a specificity of 75% with a sensitivity of 84.3%, 93.1% and 100% for early, moderate and severe glaucoma, respectively, was achieved. Interestingly, this is no better than our own results when PSD < 5% was used alone.

The pattern of field loss in our patients with early glaucoma included nasal steps, arcuate and para-central scotomas in both hemifields. While the pattern of field loss detected by Matrix perimetry was comparable in this group, this did not always register as a defect according to PSD (table 2, fig 2). PSD was excellent at indicating defects that were discrete and/or deep but was less successful for detecting shallow and more diffuse defects. PSD was unlikely to be abnormal if early defects were mirrored on either side of the horizontal meridian (eg, superior and inferior early arcuate scotomas) compared with isolated defects. This points to the potential of alternative interpretive strategies such as cluster analysis.

PSD is a measure of the variance in defects having subtracted the effects of MD and may be more sensitive in early glaucoma than other indices (table 2). While SAP PSD demonstrates a linear rise from 4.74 dB in early glaucoma to 10.75 dB in advanced glaucoma (table 1), this is not seen with Matrix perimetry. Instead, Matrix PSD rapidly rises to 5.12 dB for early glaucoma and then plateaus around 6.5 dB thereafter (table 1). This would be what was expected of a perimeter better suited for detecting early glaucomatous visual-field loss. While this notion is in conflict with the sensitivity/specificity data from this study and others,\(^ {37} \) it highlights the potential capabilities of this technology and stresses the need for further work on strategies for interpreting Matrix perimetry.

That performance on both SAP\(^ {31} \) and FDT perimetry\(^ {32} \) improves with experience raises this as a potential source of bias in this study. All glaucoma patients had prior experience with SAP but were first-time users of Matrix perimetry. It is not known whether experience with SAP translates into more reliable performance on the Matrix perimeter. That control patients had unchanged PSD and improved MD on Matrix perimetry (table 4) suggests that this effect, if present, is likely to be minor.

We also do not know to what extent fatigue may have reduced performance. As Matrix perimetry was always performed after SAP in the same sitting, the phenomenon of declining performance due to consecutive perimeter testing may have applied.\(^ {33} \) Comparison within groups found no difference in performance between SAP and Matrix perimetry with the exception of a significantly better MD on Matrix perimetry for the control group (table 5). This may have occurred because perimeters using FDT are less susceptible to this phenomenon in part because of shorter testing times.\(^ {34} \) Interestingly, results from studies\(^ {35} \) in which SAP and Matrix testing were randomised are identical to those reported here. However, despite this, we are unable to completely discount the effect of fatigue as a source of bias.

The performance of Matrix perimetry compares well with SAP in patients with perimetric glaucoma. Advantages relate to its compact size and reduced cost compared with some automated perimeters. It takes less time to perform in patients with glaucoma compared with SAP and is less technically challenging to use for both patient and technician. The test–retest reliability has been reported to be better for perimeters using FDT compared with automated perimetry,\(^ {36} \) and the reduced target size compared with standard FDT perimetry may allow for detection of more subtle changes in glaucomatous visual-field loss. Saturation of indices towards advanced field defects suggests it is less well suited for following progression of severe disease. Detection of field defects not seen with SAP remains a potential benefit of Matrix perimetry, but further research is needed to specifically address this question.

Competing interests: None.

Ethics approval: Ethics approval was provided by South East Sydney Area Health Service human research ethics committee.

Patient consent: Obtained.

REFERENCES


