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ORIGINAL ARTICLE

Measuring Visual Function in Age-Related Macular Degeneration with Frequency-Doubling (Matrix) Perimetry

Andrew John Anderson*, Chris A. Johnson†, and John S. Werner*

ABSTRACT

Purpose. To determine the agreement between the Humphrey Matrix perimeter 10-2 test and the 10-2 Humphrey Field Analyzer (HFA) test when assessing visual function in patients with age-related macular degeneration (AMD).

Methods. Forty-two eyes of 42 subjects with AMD (average 75.0 years, SD = 6.2: median visual acuity in logarithm of the minimum angle of resolution of 0.26, range, −0.12 to 1.04) were evaluated with the Matrix and HFA 10-2 visual field tests. Mean deviation (MD), pattern standard deviation, and test time were recorded. We calculated spatial concordance of individual test locations, being the proportion of spatially agreeing locations with identical classification (normal vs. abnormal, $p < 5\%$) on the pattern deviation plot. As multiple HFA stimuli overlapped with some Matrix locations, several criteria for grouping HFA data into locations were investigated.

Results. Both MD and pattern standard deviation were significantly correlated for the two devices ($r^2 = 0.79$ and $r^2 = 0.80$, respectively, $p < 0.0001$). Using our standard criterion for abnormal HFA locations (≥50% stimuli abnormal), the median spatial concordance was 0.76, with 95% of tests giving a concordance of ≥0.59. A small, but significant, increase in concordance occurred when a stricter criterion (all stimuli abnormal at a location) was applied. Median fixation loss percentages were 7 and 0% for the HFA and Matrix, respectively. Visual acuity in logarithm of the minimum angle of resolution showed modest correlations with both defect depth (HFA MD: $r^2 = 0.39$, $p < 0.0001$) and size of defect (number of abnormal points on the HFA: $r^2 = 0.24$, $p < 0.0001$).

Conclusions. Using a simple metric to calculate spatial concordance, the Matrix 10-2 test quantifies the spatial extent of significant depression of the central visual fields in AMD in a manner similar to the HFA 10-2. The spatial extent and depth of central visual field loss in AMD are only modestly predicted by visual acuity measurements.

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Key Words: age-related macular degeneration, automated perimetry, visual field, psychophysics, frequency doubling, visual acuity, contrast

Frequency Doubling Technology (FDT) perimetry (Carl Zeiss Meditec, Dublin CA, and Welch Allyn, Skaneateles, NY) is a relatively new visual field test procedure that is designed to evaluate visual field loss in glaucoma and other ocular and neurological diseases affecting the visual pathways.[1] The coarse, flickering sinusoidal grating targets used in the FDT perimeter are comparatively large (10° square), however, and so limit the spatial resolution of the test. More recently, a second-generation device—the Humphrey Matrix perimeter—has been released that uses smaller targets that are more closely spaced across the visual field,[2] allowing the spatial extent and shape of visual field defects to be better characterized.

There are several stimulus presentation patterns available in the Matrix. The 30-2 and 24-2 test strategies arrange stimuli in a similar way to the test patterns of the same name in the Humphrey Visual Field Analyzer (HFA),[3] and the utility of these test patterns for assessing visual field loss in glaucoma and other ocular and neurologic diseases has been investigated.[4–7] The Matrix also provides two further test stimulus presentation patterns (10-2 and Macula) for assessing more central areas of the visual field.[1]

In this article, we assess the ability of the Matrix 10-2 to characterize central visual field loss resulting from age-related macular

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degeneration (AMD). Flickering targets have been successfully used to measure compromised visual function in AMD.[8–10] In particular, some evidence suggests that sensitivity to non-flickering lights remains normal whereas sensitivity to flickering lights is decreased,[10] suggesting that early disease may preferentially depress flicker sensitivity. There is also evidence that losses in flicker sensitivity can predict which eyes will develop wet AMD.[11] The efficacy of flicker testing may depend on the way in which sensitivity is assessed. However, although changes in contrast detection thresholds appear sensitive to AMD,[8–10] Maier et al.[12] suggest changes in critical flicker-fusion frequency are of no diagnostic benefit.

As AMD is a spatially inhomogeneous disease that can worsen both through increased sensitivity loss in abnormal areas of the visual field as well as through the development of abnormal sensitivity in previously normal areas, perimetric assessment of the macular area provides valuable information about both the depth and spatial extent of any changes in visual function. In addition to assessing how visual field summary indices compare between the Matrix and HFA perimeters, in this article, we assess the spatial concordance of the visual field defects found using each device to determine whether similar sized defects are identified in observers with AMD.

METHODS

Participants

Forty-two eyes of 42 subjects (average 75.0 years, SD = 6.2) with AMD were used in the study. Both dry and wet forms of the disease were included, with the diagnosis of AMD being confirmed by a retinal specialist from an eye examination within 6 months of performing visual fields. Each subject had a visual acuity of better than 6/90 (20/300) in the selected eye. Subjects with a history of other ocular, neurological, or systemic diseases known to affect vision were excluded, along with subjects who had had laser therapy to the macular region. Cataract was graded and no subject had more than 2+ nuclear sclerosis, being a change consistent with vision of ~6/9 (20/30) or better.[13] The degree of nuclear sclerosis does not appear to strongly correlate with the number of abnormal points in FDT perimetry, in contrast to other cataract types such as posterior subcapsular cataract.[14] It is a common finding that clinically significant cataract (i.e., that for which surgery is subsequently performed) can significantly decrease the mean deviation (MD) index in FDT perimetry,[15–19] although the pattern standard deviation (PSD) index appears robust to change[15,17–19] or may decrease slightly.[16] Findings for the HFA are somewhat more equivocal: e.g., Carrillo et al.[20] found cataract did not significantly alter MD, whereas Kook et al.[19] found significant decreases in MD on both the HFA (decreased 3.54 dB) and FDT (decreased 4.93 dB). In our study, when any type of cataractous change other than nuclear sclerosis was noted (eight subjects), visual acuities were always better than 6/12 (20/40) except in one subject (two letters missed at 6/12). The median visual acuity of the group in logarithm of the minimum angle of resolution was 0.26 (range, −0.12 to 1.04). Controlled hypertension and/or migraine were not grounds for exclusion. The study complied with the tenets of the Declaration of Helsinki and was approved by the appropriate institutional human experimentation committee where subject recruitment and testing took place. All subjects gave written informed consent before participation.

Testing Procedure

Subjects performed a 10-2 Matrix and a 10-2 HFA examination (SITA-Standard), with the spatial layout of the stimuli in each test shown in Fig. 1. All testing was done on a single day, with the order of testing randomized and rest breaks given between tests. Although the majority of subjects performed tests on both eyes, we only analyzed results from one randomly selected eye when both eyes met the eligibility criteria outlined above. The appearance of perimetric stimuli was demonstrated as required, however, no dedicated practice run was provided and subjects were not required to have previous perimetric experience: as such, our data collection was similar to that expected in a clinical setting. The Matrix perimeter estimates losses of fixation by the Heijl-Krakau blind spot method,[3] in which a small, high-contrast stimulus is periodically presented at the expected location of the physiological blind spot.[21] The percentage of times this stimulus is detected is termed the fixation loss percentage or fixation loss index. We recorded fixation loss percentages for all subjects, with all subjects except one using the conventional central fixation marker for each test. One subject (visual acuity of $20/200^{2+}$) used the central fixation marker for the HFA (fixation loss percentage = 5%) and peripheral fixation markers ("alternate fixation" option in the device) for the Matrix (fixation loss percentage = 0%). Qualitative evaluation of fixation behavior can also be accomplished by the test administrator by viewing a video camera image of the patient's eye that is being tested.

Matrix 10-2 tests were performed on prototype versions of the Humphrey Matrix perimeter whose display hardware and test strategy were identical to that available for the commercial version of the instrument.[2] Summary indices (MD and PSD) and probability plots [total deviation and pattern deviation (PD)] were not available as print-outs from these instruments, and so were calculated subsequently from a normative database of 277 subjects described previously.[2] The normative database for the commercial device was derived from a large subset (265) of these data, and so our calculations should be very close to those available for the commercial device. The algorithm used to calculate MD and PSD values was identical to that used in the HFA.[2]

Statistical Analyses

We calculated the spatial concordance between the Matrix and HFA using:

concordance = spatially agreeing locations/total test locations

Spatially agreeing locations were defined as those that were either normal on both tests or abnormal (outside the 5% limit) on both tests, based on the PD plots. As the spatial arrangement of stimuli in each test differed (Fig. 1), HFA stimuli were grouped into 44 locations according to the Matrix stimulus they overlapped, and each grouped location was then declared abnormal if at least one-half its stimuli were abnormal on the PD plot. To deter-

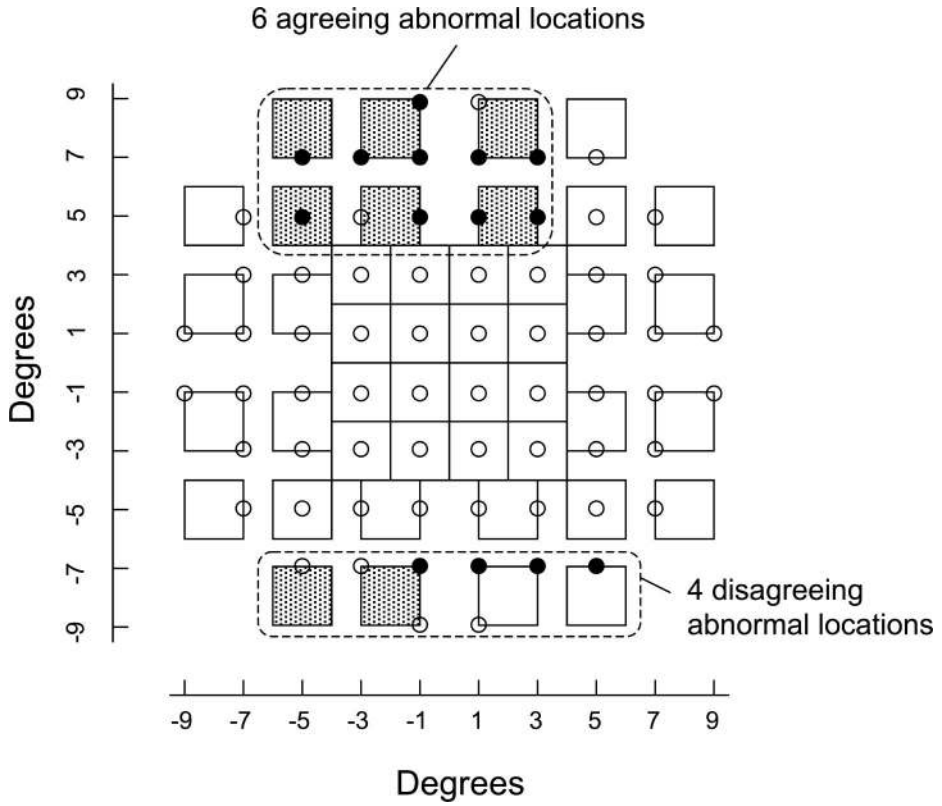

FIGURE 1.

Spatial layout of the test stimuli in the HFA 10-2 (circles) and the Matrix 10-2 (squares) tests. Matrix stimuli were 2° square grating patches (0.5 c/°, 12 Hz) and HFA stimuli 0.43° diameter circular luminous increments. For the purposes of calculating spatial concordance, HFA test stimuli were grouped into 44 locations based on the Matrix test stimulus they overlapped, with the location being judged as abnormal if at least 50% of the HFA stimuli at the locations returned abnormal thresholds (filled circles). The above hypothetical example shows eight abnormal Matrix locations (shaded squares) and eight abnormal HFA locations, with six abnormal locations in agreement between the two tests (i.e., abnormal on both HFA and Matrix). Thirty-four locations are normal on both HFA and Matrix. The spatial concordance is 0.91, indicating that the classification of locations into abnormal vs. normal is in agreement between tests for 91% of locations. We also performed two additional analyses where a location was deemed abnormal on the HFA if any stimuli (liberal criterion) or if all stimuli (strict criterion) returned abnormal thresholds: concordance is 0.91 and 0.89 using these criteria respectively in the above example.

mine the effect of this criterion—hereafter called the standard criterion—for abnormality, we also performed two additional analyses where a location was declared abnormal if either any stimuli (liberal criterion) or if all stimuli (strict criterion) were abnormal on the HFA's PD plot. A concordance value of one indicates that there is complete agreement in the location of all normal and abnormal locations between the two tests, and a concordance value of 0 indicates no agreement in the location of all normal and abnormal locations.

Because there is measurement error in the summary indices (MD & PSD) returned from both the Matrix and the HFA, a conventional linear regression on these data—where error is assumed only along the y axis—is inappropriate. We therefore used Deming regressions,[22] where errors along the x- and y axes are assumed and which minimize the sum of the squared perpendicular distances between each datum and the regression line (for an easily accessible reference, see also http://en.wikipedia.org/wiki/Deming_regression). Deming regressions require the ratio of x- and y axis errors to be estimated, although it has been shown that regression slopes are increasingly robust to estimate errors of this ratio as the correlation between x and y values increases[23]: because test/retest data were not available for our subjects, the measurement variability from each device was assumed to be the same. A runs test[22] was used to determine if there was any significant deviation from linearity. All statistical analyses were performed using the software program Prism (version 4.0c for Macintosh, GraphPad Software, San Diego, DA).

Contrast Metrics

Weber contrast ($\Delta L/L$) is typically used to describe spatially aperiodic targets like those used by the HFA, whereas Michelson contrast $[(L_{max} - L_{min}]/[L_{max} + L_{min})]$ is typically used to describe spatially periodic targets like those used in the Matrix.[24] Although it is possible to determine a Weber contrast value for Matrix targets, the relationship between this value and the Michelson contrast will depend on the assumptions made in the Weber contrast calculation. For example, the method used by Sun et al.[25] [Weber = $(L_{max} - L_{mean})/(L_{mean})$] produces identical values for both Weber and Michelson contrast, whereas the method given by Shapley and Enroth-Cugell[26] [Weber = $(L_{max} - L_{min}]/[L_{min})$] produces a non-linear relationship between the two values, with Michelson contrast being approximately half the Weber value at low contrast levels (Fig. 2, upper panel). The depth of a Weber contrast sensitivity defect for a grating, in terms of $\log_{10}$ units, therefore will also depend on the conversion technique chosen. For

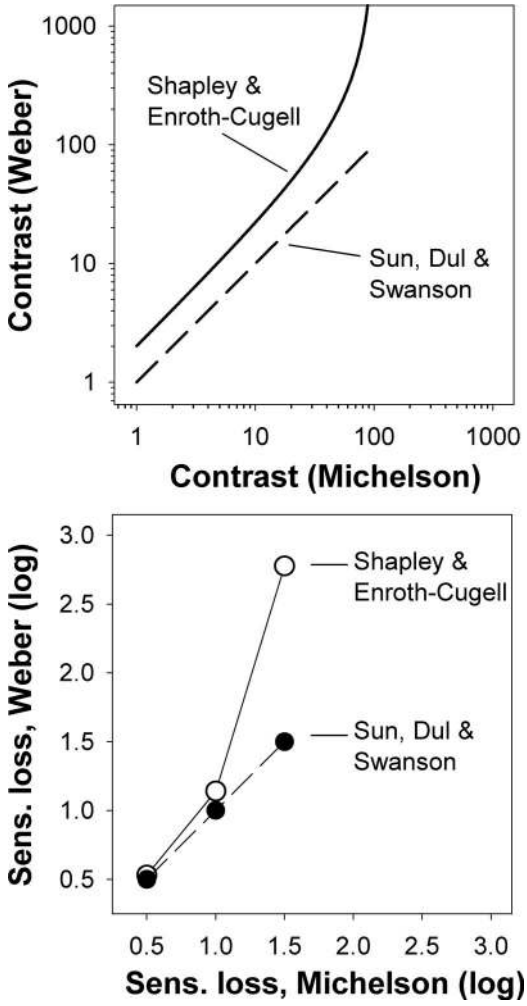

FIGURE 2.

Upper panel: relationship between the Michelson and the Weber contrast of a grating of the type used in the Matrix, using two different conversion techniques—being that described by Shapley and Enroth-Cugell[26] and that described by Sun et al.[25] Lower panel: relationship between sensitivity loss in Michelson contrast vs. Weber contrast, for a Matrix grating. A normal contrast threshold was assumed to be 3%, consistent with previous published normative values[2] for observers of the same average age as those investigated in this article.

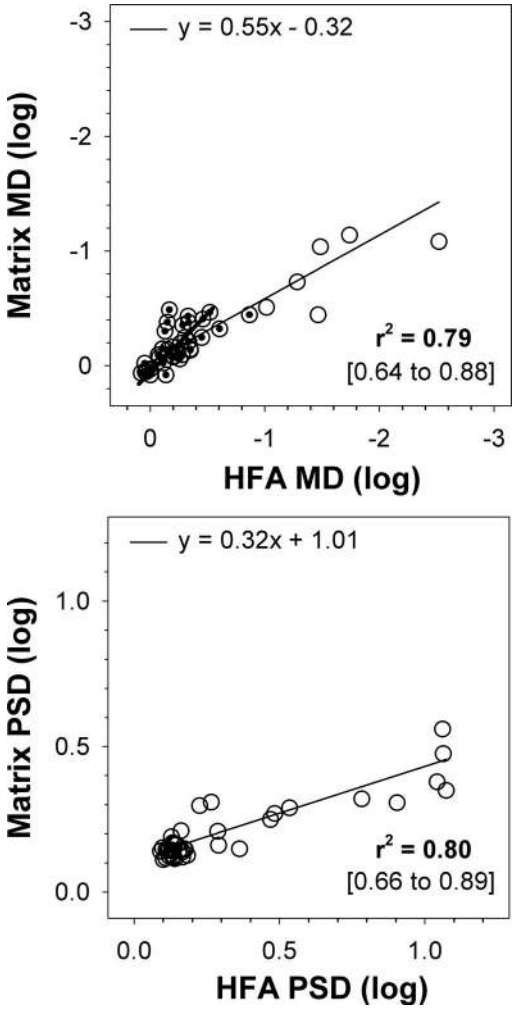

FIGURE 3.

Scattergrams comparing the HFA and Matrix perimeters, using MD and PSD indices. Pearson correlation coefficients (r^2) are given in the lower right corner of each panel, along with 95% CIs within brackets: p-values for both these regressions were <0.0001. 95% CIs for the Deming regression line parameters were upper panel, slope = 0.46 to 0.65, and intercept = −0.94 to 0.31; lower panel, slope = 0.27 to 0.37, and intercept = 0.80 to 1.23. A runs test showed no significant deviation from linearity (p = 0.25 and 0.15, upper and lower panels, respectively). Assuming unequal variability in the x and y data made little difference to the Deming slopes: for MD, slopes were 0.59 or 0.51 when either the x or y axis error, respectively, was assumed to be twice that of the other axis: for PSD, slopes were 0.35 and 0.31, respectively, using the same assumptions. Deming regression (thick line) for a subset of the data with MD values better than −10 dB in machine units (data with central dots) returned a slope of 1.02 (95% CI: 0.67 to 1.37; r^2 = 0.51): slopes were 1.14 or 0.80 for these data when either the x or y axis error, respectively, was assumed to be twice that of the other axis.

example, a depression in Weber contrast sensitivity of 1.5 $\log_{10}$ units using the method of Sun et al.[25] may be closer to 3 $\log_{10}$ units when the method of Shapley and Enroth-Cugell[26] is used.

In this article, we plot contrast values in $\log_{10}$ units, using Weber contrasts for gratings derived from the conversion technique of Sun et al.[25] Our selection of this conversion technique has no theoretical significance, although it does create a simple relationship between $\log_{10}$ units and the dB values returned from each machine for the indices MD and PSD. One dB on the HFA corresponds to a 0.1 $\log_{10}$ unit change (consistent with dB calculations based on power), and so our $\log_{10}$ values can be multiplied by 10 to give the equivalent machine dB values for MD and PSD on the HFA. One dB on the Matrix corresponds to a 0.05 $\log_{10}$ unit change (consistent with dB calculations based on amplitude)[2] and so our $\log_{10}$ values can be multiplied by 20 to give the equivalent Matrix machine dB values for MD and PSD.

RESULTS

Fig. 3 shows the comparison of the principle summary indices, MD and PSD, between the two tests. Considering the plot of MD (upper panel) first, the values are highly correlated. A repeated-measures t test did show a small (0.15 $\log_{10}$ units) but significant (p = 0.003) difference between MD values from each instrument. Although our regression failed to show any significant departures from linearity (runs test, p = 0.25), previous work has suggested that losses on the Matrix and HFA may not be linearly related, at least in glaucoma.[5,27] We therefore performed a regression on

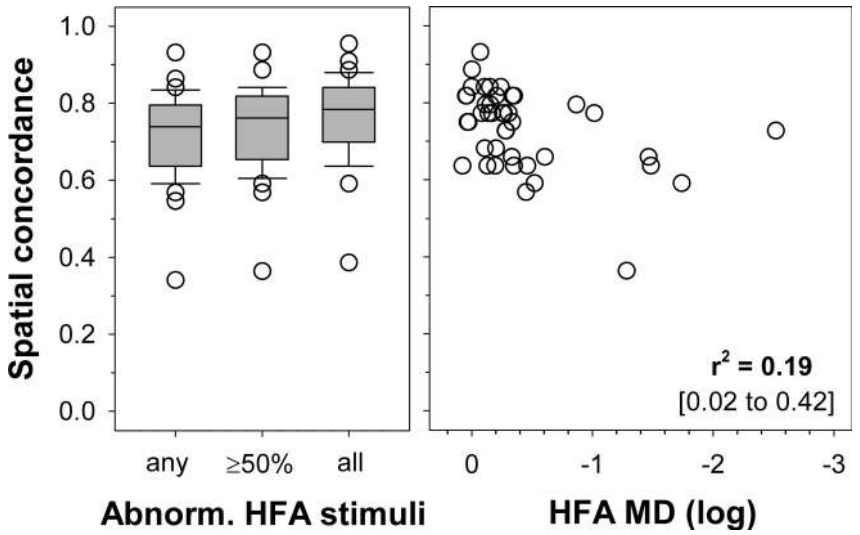

FIGURE 4.

Spatial concordance of visual fields assessed on the Matrix and HFA perimeters. Left panel: box plot of the concordance results using three different criteria for an abnormal location on HFA [any points abnormal ("any": liberal criterion), at least one-half points abnormal ["≥50%"; standard criterion], or all points abnormal ("all"; strict criterion)], where the limits of the box gives the 25th and 75th percentiles, the line within the box gives the median, error bars give the 10th and 90th percentiles, and data points show points below the 10th or greater than the 90th percentile. Right panel: concordance as a function of the MD on the HFA, using a criterion of ≥50% abnormal HFA points for a location to be judged abnormal. Pearson correlation coefficient (r^2) for these data was 0.19 ($p = 0.004$).

those data where MD for both HFA and Matrix was better than −10 dB in machine units (Fig. 3, thick black line): the regression slope was 1.0 over this range. For the PSD results (lower panel), values are again highly correlated although the slope of the regression line is significantly different from one.

Fig. 4 shows spatial concordance for the tests. A box plot of data obtained using our standard criterion (middle plot, left panel) shows that the median spatial concordance is high at 0.76, i.e., classification of locations into normal and abnormal agrees between the tests for 76% of locations. Applying different criteria altered the level of concordance significantly [repeated-measures analysis of variance $F_{(2,82)} = 37.0$, $p < 0.001$; all pairs different ($p < 0.05$) using a Tukey Multiple Comparison Test], although the changes in median concordance were small in magnitude (median = 0.74 and 0.78, for liberal and strict criteria, respectively). Using our standard criterion, concordance is greater than or equal to 0.59 save for a few outliers. The right panel shows that there is only a very weak association between the depth of the defect, as given by the HFA MD, and the degree of spatial concordance, suggesting that Matrix and HFA perimetry show similar spatial concordance for both low and high degrees of visual field loss. In addition, there was only a weak correlation between visual acuity in logarithm of the minimum angle of resolution and concordance {Pearson $r^2 = 0.18$ [95% confidence intervals (CIs) = 0.02 to 0.42], $p = 0.005$} and no significant correlation between age and concordance ($r^2 = 0.02$, $p = 0.43$). A Wilcoxon signed rank test showed no significant difference in the number of locations classified as abnormal on each test using the standard ($p < 0.06$) or strict ($p < 0.58$) criteria; however, a significant difference was found using the liberal criterion ($p = 0.005$). The median numbers of abnormal points for the HFA were 5 (strict), 7 (standard), and 8.5 (liberal), compared with 8 for the Matrix. There was no significant difference between the percentage of test stimuli (rather than locations) returning abnormal thresholds (Matrix = 18%, HFA = 14%, Wilcoxon signed rank test, $p = 0.19$), however.

Fig. 5 shows that there is only moderate correlation between visual acuity and the depth of a visual field defect (MD, upper panel), and the CIs for this correlation are lower than, and do not overlap with, those obtained for the correlation between MD determined for two different tests (Fig. 3, upper panel). This suggests that the poor correlation with visual acuity is not because the measure of MD is inherently variable, but rather that visual acuity and MD provide largely independent measures of visual function. The correlation between visual acuity and the size of a visual field defect—as quantified by the number of abnormal points on the HFA 10-2—is also modest.

Median fixation loss percentages were 7 and 0% for the HFA and Matrix and differed significantly (Wilcoxon signed rank test, $p = 0.03$), irrespective of the inclusion or exclusion of the subject tested using different fixation targets on each test (see Methods). Table 1 shows the distribution of these fixation loss percentages in comparison to published data from Johnson et al.[28]

Fig. 6 shows two examples of visual fields, one showing spatial concordance close to the median for the group (left panel) and one showing the lowest spatial concordance for the group (right panel). Considering the left panel first, both the Matrix and HFA results show abnormal sensitivities extending from the superior part of the field down past the center of the field, with the spatial extent of this defect being a few degrees larger for the HFA. Both tests show good agreement in classifying the most inferior portion of the visual field as normal. In contrast, the result on the right panel shows poor agreement, with the central area of the 10-2 result being abnormal on HFA but normal on the Matrix. There is also only limited agreement in how the two tests classify those locations outside this central region.

Fig. 7 shows the distribution of test durations for each test. Matrix perimetry was significantly faster than the HFA (Wilcoxon

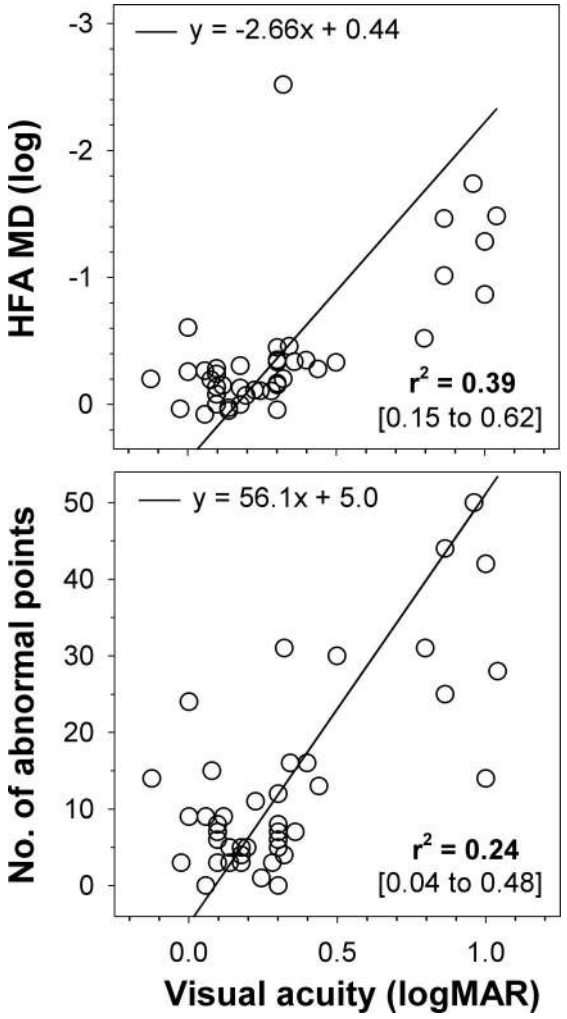

FIGURE 5.

Scattergrams showing the relationship between visual acuity and either MD (upper panel) or the number of abnormal points ($p < 5\%$; lower panel) in the HFA 10-2 visual field. Pearson correlation coefficients (r^2) are given in the lower right corner of each panel, along with 95% CIs within brackets: p values for both these regressions were <0.0001. 95% CIs for the Deming regression line parameters were upper panel, slope = −3.60 to −1.72, and intercept = 0.02 to 0.85; lower panel, slope = 38.8 to 73.3, and intercept = −12.6 to 2.6. A runs test showed a significant deviation from linearity ($p < 0.0001$ and $p = 0.01$, upper and lower panels, respectively).

signed rank test, $p < 0.0001$), showed less variability in test times, and had a median test duration of 4 min 21 s. There was no significant difference between tests times when expressed as a time to test each point (Wilcoxon signed rank test, $p = 0.41$). Test times ranged from 5 min 03 s to 10 min 51 s (HFA) and from 4 min 08 s to 6 min 10 s (Matrix).

DISCUSSION

Our results show a high correlation between the MD indices from the Matrix and HFA (Fig. 3, upper panel). In addition, spatial concordance between the two tests was high and was significantly improved by applying the strictest criterion to the HFA data. Using this criterion, the absolute size of the visual field defects, as quantified by the number of abnormal locations on the PD plot, was not significantly different between tests. That both tests identified similar sized defects was further supported by our finding that there was no significant difference in the percentage of test stimuli returning abnormal thresholds. Although the spatial concordance between our visual field tests was good, the depth and size of visual field loss was only moderately related to visual acuity (Fig. 5), suggesting that visual field assessment in AMD provides information that is not readily predictable from a patient's visual acuity. Previous work also suggests that visual field defects are only moderately correlated with the area of visible retinal pigment epithelial atrophy in the macula, and show no significant correlation with the area of visible drusen,[29] suggesting that the nature of visual field loss is also not readily predicted from ophthalmoscopic examination. Visual field assessment therefore appears to be an important tool in fully assessing a patient's visual function in AMD, which is consistent with recent work showing that both visual acuity and scotoma area were the two independent variables that could best explain reading speed in AMD.[30]

Our results show that the MD indices from the Matrix and HFA (Fig. 3, upper panel) were highly correlated, as were the PSD values (Fig. 3, lower panel). Correlation across the our entire range of MD values, although acceptably linear, hides the finding that at low MD values the slope relating MD on the Matrix to MD on the HFA had a slope of ~1 in $\log_{10}$ units, whereas for higher MD values the slope was significantly less than 1. This result indicates that when the average depression of the vision field is small, MD values returned from the Matrix will be approximately twofold larger than those on the HFA when each is expressed in its respective machine dB unit (see Methods). A similar non-linear relationship has also been shown before in a different disease (glaucoma)

TABLE 1.
Distribution of fixation loss percentages, as determined by the Heijl-Krakau blind spot method (see Methods)

	Proportion of subjects (p = comparison with Johnson et al.[28])		
	Fixation loss percentages ≥10%	Fixation loss percentages ≥20%	Fixation loss percentages ≥33%
HFA 10-2	40% (p = 0.13)	29% (p = 0.003)	10% (p = 0.06)
Matrix 10-2	33% (p = 0.45)	19% (p = 0.09)	12% (p = 0.02)
Johnson et al.[28]	28%	9%	3%

Data were compared (Fisher's exact test) to that of Johnson et al. (final row) obtained from 169 subjects performing a C30-2 test on the Humphrey Field Analyzer.

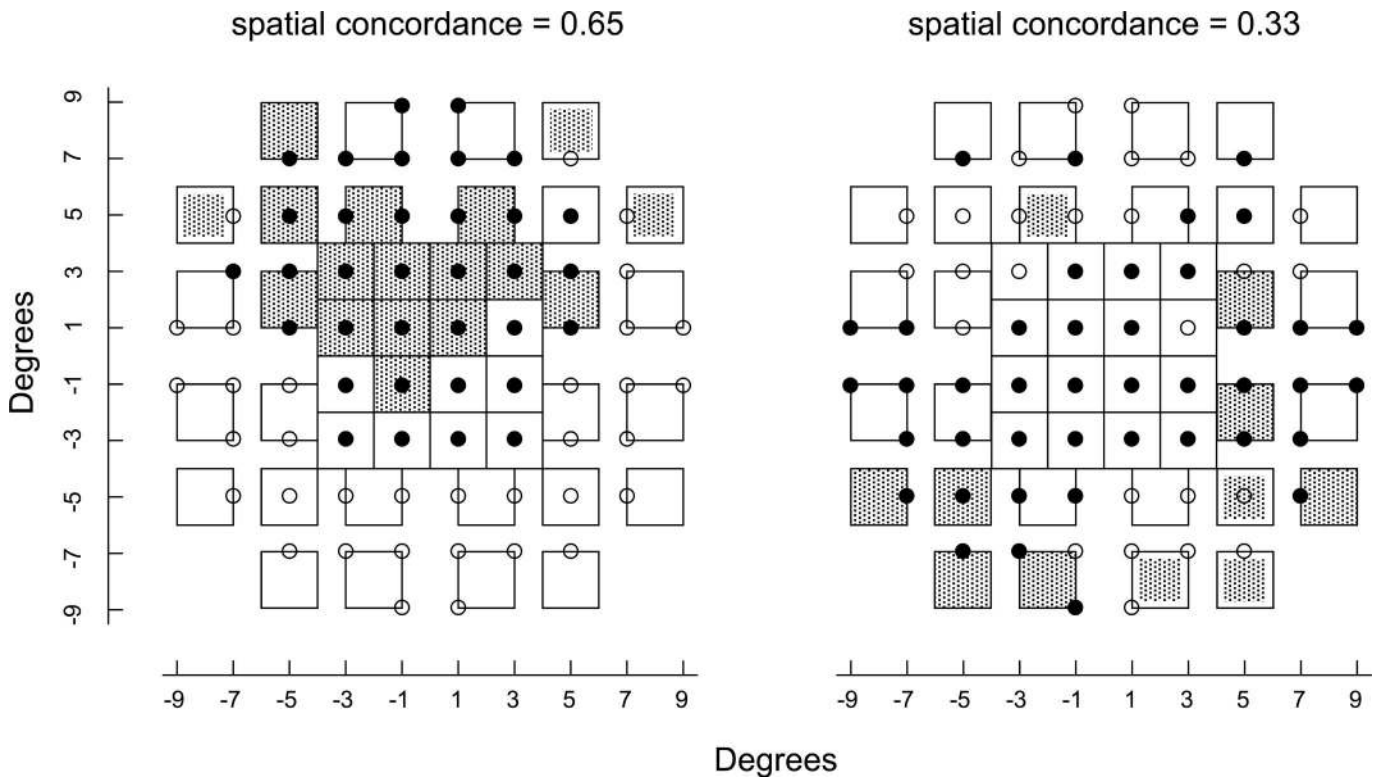

FIGURE 6.

Visual field results from two subjects with dry AMD changes and subretinal neovascular membranes, showing good (left) and poor (right) agreement between HFA and Matrix results. Left panel: right-eye results from a 75-year-old subject with visual acuity of 6/48. Right panel: left-eye results from a 72-year-old subject with a visual acuity of 6/60. Both panels: circles show the location of test points in the HFA 10-2 test, with filled points having abnormal PD values at the <5% level. Squares show locations from the Matrix 10-2 test, with shaded squares having abnormal PD values at the <5% level: complete shading shows locations that were also abnormal on the HFA, using the criteria shown in Fig. 1. The HFA MD indices were −10.13 and −12.82 dB (left and right panels, respectively).

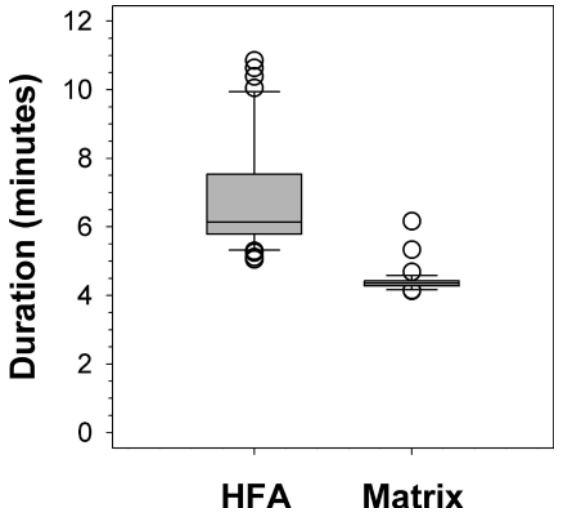

FIGURE 7.

Box plot of test durations for the HFA 10-2 and Matrix 10-2. Box-plot details are as given in Fig. 3.

for data analyzed in different ways (sectorially determine MD values[27] and average thresholds at a single location[5]), suggesting that our results reflect a general finding for how visual thresholds in disease are non-linearly related on the Matrix and the HFA. The significance of the relationship between the HFA and Matrix MD values for the diagnostic performance of each perimeter can only be assessed by simultaneously considering the noise characteristics of each instrument, however, which is complicated somewhat by the fact that frequency doubling perimetry and increment threshold perimetry have different variability characteristics as a function of defect depth.[5,31] The signal-to-noise ratio of the Matrix and the HFA has recently been examined in glaucoma, with the signal-to-noise ratio of the Matrix being only moderately greater than for the HFA. This is consistent with clinical investigations that show the diagnostic performance of the Matrix is similar to that of the HFA.[32–34]

Evidence for Flicker Sensitivity Losses in AMD

Our finding that visual field defects have similar spatial extent in both the HFA and Matrix contrasts with the results of other authors who have found larger defects are identified using flickering targets in exudative maculopathies[35] and AMD.[9] One source of variation between studies is that some use flickering targets whose time-averaged luminance simultaneously increases, and it is known that such targets tap different mechanisms than those targets whose average luminance remains the same as the background.[36,37] Phipps et al.[38] found similar losses in sensitivity to both low-spatial frequency static targets and targets flickering about a mean background in AMD but found significantly greater losses in flicker sensitivity in a subsequent study[10] when flickering targets were accompanied by an increase in time-averaged lumi-

nance (i.e., a luminance pedestal). It is possible, therefore, that the presence of a luminance pedestal may be important in exposing flicker defects in AMD, possibly because the pedestal perturbs adaptation mechanisms that are known to be altered in the disease.[38] Unfortunately, no study to date has concurrently measured flicker with and without a luminance-pedestal while keeping other stimulus parameters (e.g., stimulus size, color, flicker rate, etc) constant, and so the role of the luminance pedestal is still unclear. Another source of potential variability involves our calculation of visual field defect size, which was based on probability limits determined separately for each instrument using different subjects and inclusion criteria.[2,39] Probability limits for the PSD plot that are nominally the same will likely exclude slightly different proportions of the general population, therefore; we have reviewed some of these differences elsewhere.[40]

Limits on Spatial Agreement between Tests

Visual sensitivity measured by perimetry is subject to test-retest variability,[5] which necessarily means that a visual field measured on one occasion will usually not precisely match the field produced on retest. Spatial agreement between two instruments can therefore not be any better than the test-retest agreement of each individual instrument. Unfortunately, we do not have test-retest data from our subjects with AMD that would allow us to calculate intratest spatial concordance values for the Matrix or the HFA, and so the theoretical limit to which any test can agree with the HFA is currently unknown. It should be noted that our metric of spatial concordance—as described in the equation in the Methods—is not limited to assessing agreement across different instruments but can also be used to calculate intratest spatial concordance on a single instrument type. Another factor that might limit cross-sectionally determined agreement between tests is if flicker sensitivity is longitudinally predictive of impending wet AMD, as proposed by Mayer et al.,[41] and so different static- and flicker-perimetry results would be expected in the group of subjects in whom conversion to wet AMD was imminent. The good spatial agreement found between the HFA and Matrix 10-2 tests in our study in AMD is consistent with the previous calculations of spatial agreement for the same tests in glaucomatous observers[25]: this previous analysis was limited to agreement among quadrants with the lowest average sensitivity, however, and so had only gross spatial resolution.

Test Duration

We found the Matrix perimeter to be significantly faster than the HFA for assessing central visual function (Fig. 7). This time saving appears to be due to the reduced number of points tested by the Matrix, as no significant difference was found between the two tests when test duration was divided by the number of stimuli tested (44 in the Matrix, vs. 68 in the HFA). There is a reduced spatial resolution of the Matrix 10-2 outside 5° eccentricity, where stimuli are no longer spaced 2° but 3° apart, although this increase in stimulus spacing with eccentricity is probably sensible given that the spatial resolution of the visual system similarly decreases with increasing retinal eccentricity: by 5° eccentricity, the minimum angle of resolution is at least doubled, with hyperacuity performance dropping off at an even more rapid rate.[42] The predictability of tests times was much higher with the Matrix and is likely due to the employment of a fixed-duration ZEST procedure to determine sensitivities.[43] It should be remembered that the times reported in Fig. 7 constitute the duration of the test procedure in isolation, and other factors such as entry of patient data, patient set-up, and test instruction will contribute to the total time required to perform the test in a clinical setting.

Fixation Ability of Observers with AMD

We found that most of our observers could maintain acceptable fixation while performing perimetry, as they returned fixation loss indices not dramatically higher than those from a clinical population of predominantly normal and early glaucomatous observers in whom foveal vision would be largely unaffected.[28] The majority of people with AMD would be expected to have visual acuities equal to or better than the limit (6/90) used in our study,[44] and so we believe the fixation ability shown by our patient group does not represent that of a small subgroup of AMD subjects with unusually good central vision (as indicated by visual acuity) but rather should reflect the majority of people with AMD. Of the four of our subjects who returned fixation loss percentages of ≥50%, two were judged to have good fixation by the clinician administering the test, using visual inspection of the anterior eye via the video-monitoring system built in to the Matrix perimeter. Although the Heijl-Krakau blind spot method of monitoring fixation in the Matrix may episodically fail in observers without AMD,[3] the possibility of eccentric fixation[45] in AMD raises another possibility as to why fixation loss percentages in perimetry may be high despite stable gaze, as the physiological blind spot—relative to fixation—would no longer be in the position predicted by the normal anatomical relationship between the fovea and the optic nerve head. The preferred retinal locus for fixation was found to be on average 6° away from the fovea in a group of AMD patients with a mean visual acuity of 6/43,[46] a shift that would be sufficient to move the high-contrast target, used to check fixation, outside of the 3.5° radius of the blind spot.[3] Unfortunately, we do not have data on whether or not participants in our study used eccentric viewing, and so we cannot directly test this possibility in our study. It should be noted that any eccentric fixation might be expected to influence both the HFA and Matrix in similar ways, and so the calculation of the spatial concordance between tests—our principle analysis—should not be substantially affected.

CONCLUSIONS

We find that the Humphrey Matrix 10-2 visual field test characterizes the spatial extent of central visual field losses in AMD in a manner similar to the HFA 10-2 test, and that information about the depth and size of visual loss is not well predicted by visual acuity. The Matrix provides a significant reduction in test duration, as well as reduced variability in the time to perform the test. When tests need to be compared across instruments—either in a research or clinical setting—spatial agreement can be quantified using a simple metric and can be maximized by applying a strict criterion for determining abnormal locations on the HFA.

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