Elsevier Editorial System(tm) for American

Journal of Ophthalmology

Manuscript Draft

Manuscript Number: AJO-18-85R1

Title: Six-month longitudinal comparison of a portable tablet perimeter with the Humphrey Field Analyser

Article Type: Original Article

Keywords: perimetry; visual field; iPad (MRF); Humphrey field analyser (HFA); SITA; glaucoma; repeatability

Corresponding Author: Professor Algis J Vingrys, PhD

Corresponding Author's Institution: University of Melbourne

First Author: Selwyn M Prea, BOptom, MPhil

Order of Authors: Selwyn M Prea, BOptom, MPhil; Yu Xiang (George) Kong, MB BS, BMed Sci, PhD; Aditi Mehta; Mingguang He, MD, PhD; Jonathan G Crowston, BSc, MB BS, PhD; Viney Gupta, MB BS, MD; Keith R Martin, MA DM; Algis J Vingrys, PhD

Abstract

Purpose: To establish the medium-term repeatability of the iPad perimetry app Melbourne Rapid Fields (MRF) compared to Humphrey Field Analyzer (HFA) 24-2 SITA-standard and SITA-fast programs.

Design: Multicentre longitudinal observational clinical study.

Participants: 60 patients (stable glaucoma/ocular hypertension/glaucoma suspects) were recruited into a 6-month longitudinal clinical study with visits planned at baseline, 2-, 4- and 6-months.

Methods: At each visit patients undertook visual field assessment using the MRF perimetry application and either HFA SITA-fast (n=21) or SITA-standard (n=39).

Main outcome measures: The primary measure was the association and repeatability of mean defect (MD) for the MRF and HFA tests. Secondary measures were the point-wise threshold and repeatability for each test as well as test time.

Results: MRF was similar to SITA-fast in speed and significantly faster than SITA-standard (MRF 4.6±0.1 mins vs. SITA-fast 4.3±0.2 mins vs. SITA-standard 6.2±0.1 mins, P<0.001). Intra-class correlation coefficients (ICC) between MRF and SITA-fast for Mean Deviation (MD) at the four visits ranged from 0.71 to 0.88. ICC values between MRF and SITA-standard for MD ranged from 0.81 to 0.90. Repeatability of MRF MD outcomes was excellent, with ICC for baseline and the 6-month visit being 0.98 [95%: 0.96-0.99]. In comparison, ICC at 6-month retest for SITA-fast was 0.95 and SITA-standard 0.93. Fewer points changed with the MRF although for those that did, the MRF gave greater point-wise variability than did the SITA tests.

Conclusions: MRF correlated strongly with HFA across 4 visits over a 6-month period, and has good test-retest reliability. MRF is suitable for monitoring visual fields in settings where conventional perimetry is not readily accessible.

1 2 3	Six-month longitudinal comparison of a portable tablet perimeter with the Humphrey Field Analyser.
4 5 6 7 8	Selwyn Marc Prea ¹ , Yu Xiang George Kong ⁴ , Aditi Mehta ⁵ , Mingguang He ³ , Jonathan G Crowston ^{2,3} , Viney Gupta ⁵ , Keith R. Martin ⁴ , Algis J Vingrys ¹
9 10 11 12 13 14 15 16 17 18 19 20	 Department of Optometry & Vision Sciences, The University of Melbourne, Australia Royal Victorian Eye and Ear Hospital, East Melbourne, Australia Centre for Eye Research Australia, Department of Ophthalmology, The University Melbourne, Melbourne, Australia Department of Ophthalmology, Cambridge University Hospitals NHS Foundation Trust, Cambridgeshire, United Kingdom Dr RP Centre for Ophthalmic Sciences, All India Institute of Medical Sciences, New Delhi, India
21 22 23 24 25 26 27 28 29 30 31 32	Corresponding Author: Professor Algis J Vingrys Department of Optometry and Vision Sciences Level 4, Alice Hoy Building, Monash Rd The University of Melbourne, Parkville, Victoria, Australia, 3010 Ph: +61 3 8433 7001 Email: algis@unimelb.edu.au
33 34 35 36 37 38	Footnote: Dr YX George Kong is now located at Royal Victorian Eye and Ear Hospital, East Melbourne, Australia.
39 40 41 42 43 44 45 46 47 48 49 50 51 52 53 54 55 56 57 58 59 60 61	Short title: "Clinical application of a tablet perimeter"
62 63 64	1

Abstract

Purpose: To establish the medium-term repeatability of the iPad perimetry app Melbourne Rapid Fields (MRF) compared to Humphrey Field Analyzer (HFA) 24-2 SITA-standard and SITA-fast programs.

Design: Multicentre longitudinal observational clinical study.

Participants: 60 patients (stable glaucoma/ocular hypertension/glaucoma suspects) were recruited into a 6-month longitudinal clinical study with visits planned at baseline, 2-, 4- and 6-months.

Methods: At each visit patients undertook visual field assessment using the MRF perimetry application and either HFA SITA-fast (n=21) or SITA-standard (n=39).

Main outcome measures: The primary measure was the association and repeatability of mean defect (MD) for the MRF and HFA tests. Secondary measures were the point-wise threshold and repeatability for each test as well as test time.

Results: MRF was similar to SITA-fast in speed and significantly faster than SITA-standard (MRF 4.6±0.1 mins vs. SITA-fast 4.3±0.2 mins vs. SITA-standard 6.2±0.1 mins, P<0.001). Intra-class correlation coefficients (ICC) between MRF and SITA-fast for Mean Deviation (MD) at the four visits ranged from 0.71 to 0.88. ICC values between MRF and SITA-standard for MD ranged from 0.81 to 0.90. Repeatability of MRF MD outcomes was excellent, with ICC for baseline and the 6-month visit being 0.98 [95%: 0.96-0.99]. In comparison, ICC at 6-month retest for SITA-fast was 0.95 and SITA-standard 0.93. Fewer points changed with the MRF although for those that did, the MRF gave greater point-wise variability than did the SITA tests.

Conclusions: MRF correlated strongly with HFA across 4 visits over a 6-month period, and has good test-retest reliability. MRF is suitable for monitoring visual fields in settings where conventional perimetry is not readily accessible.

Introduction

The Humphrey Field Analyser (HFA) is the clinical standard for reliable and reproducible visual field outcomes in patients with glaucoma ¹, however the cost of the device and its lack of portability limit its accessibility to patients from impoverished places and those in rural and remote locations. There are some who have used hardcopy charts, tablets, virtual reality goggles and other devices as portable visual field screeners or threshold devices ²⁻⁷. In comparison, the Melbourne Rapid Fields (MRF) is an iPad tablet application (iPad3 or later) that allows in office or remote visual field testing due to its low cost and portability. MRF has been shown to produce comparable results to the HFA and have good intra-session test-retest repeatability ^{8,9},however, the longer-term repeatability of this device is unknown. Detection of visual field testing procedure ^{10,11}, therefore, knowing the longer-term repeatability of the device is important in determining whether MRF is suitable for clinical use.

The MRF has been validated as a tangent perimeter which can perform efficient and reliable thresholding comparable to HFA 24-2 SITA-standard protocol⁹. It has been shown to be robust to variations in ambient light, blur and viewing distance ⁸. When retest was undertaken after a 5-minute break in 78 cases with glaucoma (intrasession test-retest repeatability), patients classified as mild (MD \geq -6 dB, n=41) gave a coefficient of repeatability (std. dev./mean) of 7.8% for their MD whereas 37 cases with moderate to severe defect (MD < -6 dB) returned a coefficient of repeatability of 24.2% in their MD⁹. Retest variability for the Medmont M700 automated perimeter has been reported as 2.9 dB (11.6%), whereas abnormal locations have a larger coefficient of repeatability (33%; SD ~8.0 dB)⁸. Hence, test-retest repeatability depends upon the threshold of the location, and for the MRF, it appears comparable to that reported for other perimeters ^{8,12}.

Despite the similarity to the literature and high intra-test repeatability, it is not known whether this good performance of the MRF will be returned over longer retest periods. This is because the MRF differs from the HFA in many ways ⁸ and it is not clear how these differences may impact on long term reliability. The main differences in the MRF rests in test spot location, test spot size (which increases into the periphery) and its thresholding logic. Threshold variability is known to increase with eccentricity in normals ¹³. As the MRF spot size increases in the periphery of MRF test patterns⁸ it could be expected that the MRF will have reduced variability due to the larger spot sizes¹³. Another factor to influence variability is the MRF thresholding logic which is achieved using a3-step Bayes predictor^{8,14}. Although similar procedures have been shown to return reliable outcomes with 6 to 12 steps^{14,15} it is not clear that this will hold for a 3-step prediction. In particular, it is not apparent how this approach will compare to the SITA algorithms which utilise a post-hoc Bayes prediction returned from 4/2dB (SITA-standard) or 4dB step (SITA-fast) procedures.

Given these differences in test logic, the repeatability of both the MRF and HFA are in need of comparison especially when applied in a review schedule common to clinical settings. This 6-month longitudinal study was undertaken to investigate the medium-term repeatability of the MRF compared to that found for HFA SITA-fast and SITA-standard outcomes derived from a common cohort of patients who undertook repeated testing on these devices.

Method

The clinical trials reported in this manuscript were undertaken with approval of the local ethics committees (Integrated Research Application System IRAS ID: 204698: West of Scotland Research Ethics Service REC No: 16/WS/0130: and AIIMS IEC-564/03.11.2017) and were conducted in accordance with the tenets of the Declaration of Helsinki with all subjects giving informed consent prior to participation. This clinical trial has been registered as ISRCTN77744218 at https://doi.org/10.1186/ISRCTN77744218.

Melbourne Rapid Fields app

The MRF app (GLANCE Optical Pty Ltd, Melbourne, Australia) produces efficient and reliable thresholds using an iPad (Apple, Cupertino, CA) tablet device viewed at 33 cm with the patient wearing their normal reading glasses. The radial test pattern comprises 66 test locations (Figure 1) with more details of the test procedures found elsewhere^{8,9}. The 9.7-inch iPad subtends 30° x 24° (H x V) at a viewing distance of 33 cm (13 inches: eccentricity 15° x 12° with central fixation). Regions having greater eccentricity than 15° x 12° can be tested by having the patient shift fixation to one of the four corners of the iPad, allowing one quadrant 30° x 24° (H x V) to be tested at a time. Voice commands generated by the tablet instruct the patient on how to perform the test and when to alter fixation during the test to permit evaluation of the peripheral visual field. Apart from the need to alter fixation, some of the other procedural or test differences in the application have been detailed before ^{8,9}. Our previous study found that despite these differences the MRF returns outcomes that were strongly correlated to HFA thresholds ⁹ and the purpose of this study is to consider whether medium-term variability is similar to that of the HFA.

Figure 1 about here

Participants

Sixty patients were recruited at two clinical sites (Table 1) namely: Cambridge UK (n = 39, age: 37–89, mean: 70.1) and New Delhi, India (n = 21, age: 15–59, mean: 35.3). Study participants had either: stable ocular hypertension (n = 3: IOP>21 mmHg with normal VF and optic nerve), stable treated glaucoma (n = 51: optic nerve and/or VF changes consistent with glaucoma and diagnosis confirmed by fellowship trained glaucoma subspecialists), or are glaucoma suspects (n = 6:IOP<=21, with subtle changes in optic nerve and/or VF that do not meet definitive diagnosis of glaucoma). Patients were asked to return every 2-months during a 6-month cycle of normal reviews (3 follow up visits). Table 1 shows that 25 participants (42%) had a mild visual field defect (HFA MD \geq -6dB), 20(33%) exhibited a moderate loss (HFA MD -6 to -12dB) and 15 (25%) exhibited an advanced loss (HFA MD < - 12dB). Exclusion criteria were: the presence of a systemic condition or use of systemic drugs that could affect vision, a need to change glaucoma medications or undergo eye surgery over the review period or in the preceding 6-months, inability to understand or comply with

the English voice commands of the MRF, visual acuity worse than 6/12 (20/40) and, poor reliability indices on HFA at baseline (FL >30%, FP >15%, FN >20%).

Table 1 about here

Testing Procedures

Study participants were recruited at baseline, being one of their normal review dates, and were requested to come again at 2-, 4-, and 6-months; the 6-month visit was part of their review schedule. At each visit, they performed the MRF and either 24-2 SITA-fast or SITA-standard (but not both, see Table 1) on the worse eye having the lower Mean Defect on HFA. At baseline, patients performed HFA first followed by MRF to determine if they met inclusion criteria. The order of the tests was randomised at subsequent visits. Not all patients complied with the scheduled 2-monthly visits and attendance rates for the respective time points are listed in Table 2 (range 70-97%).The average interval between tests was 2.6-months.

MRF testing was performed using a 9.7-inch iPad generation 3 tablet (Apple, Cupertino, CA) in a dimly lit room with screen brightness automatically adjusted to maximal hardware brightness by the app at the start of the testing procedure. The iPad was turned on for a minimum of 10 minutes prior to testing to allow for stability of luminous output.

Table 2 about here

Data Analysis

Elsewhere we have found the correlation between MRF MD and HFA SITA-standard MD values follow a linear relationship $(MD_{HFA} = 1.25 * MD_{MRF} - 0.51)^9$. In the present study we have corrected the raw MD values from MRF using this relationship without altering the raw dB thresholds. Later when we analyse the variability in the pointwise data, this analysis has been derived from the raw values and not the scaled data.

To allow comparison of point-wise retinal thresholds, all left eye data were reflected in the vertical to produce equivalent right eye fields. Correlation analysis was conducted using a Deming regression that allows for error in both the x- and y-axes. For this study, we performed two analyses: one that included repeated testing on individuals and the other derived from the average outcome for individual patients over multiple time points (average of at least 3 tests). All data are shown as mean ±SEM unless stated otherwise.

Bland-Altman analysis quantified bias (average difference) and the 95% limits of agreement (LoA) by comparing baseline to the 6-month test. A coefficient of repeatability(CoR %) was determined as the standard deviation of the Bland-Altman difference data divided by the mean threshold¹¹. To quantify the accuracy of the tests we adopted Lin's Coefficient of Accuracy (Ca) which indicates concordance between two tests measuring a common attribute¹⁶. Other coefficients (eg. Pearson) consider association

between data to a line of any slope whereas the Coefficient of Accuracy determines the degree to which pairs of observations derived from two continuous variables fall on the diagonal line that passes through the origin; perfect concordance to the diagonal is a Ca of 1.0.Ca values between 0.65 and 0.79 indicate 'moderate' concordance, between 0.8 and 0.89'substantial' concordance and between 0.9 and 1.0 indicate 'almost perfect' concordance¹⁶.We have also calculated the Intra-class correlation (ICC) for our data, as this is a commonly used statistic for such comparisons. ICCs and many other statistics were calculated using Microsoft Excel for Windows (Microsoft, Redmond, WA, USA) spreadsheets.

As the mean defect statistic (MD) is a global measure it may act to mask changes at a local or regional level, so we consider repeatability in the 8 regions defined in Figure 1 as well as on a point-wise basis.

Group comparisons were performed using a repeated measure analysis of variance (ANOVA) and t-tests were used to identify significant departures when the ANOVA indicated a significant main effect. An alpha of 0.05 was used for all analysis.

Results

Figure 2 shows representative field results for two patients measured with the MRF and HFA SITA-standard test. The left panels are MRF outcomes for a patient having mild (Figure 2, upper-left) and moderate (Figure 2, lower-left) visual field loss whereas the right panels show the corresponding HFA outcomes for the same patients with key statistics indicated beside each panel.

Figure 2 about here

The average test times for MRF, SITA-fast and SITA-standard are shown in Figure 3. The MRF required 4.6 \pm 0.1 mins (mean \pm SEM) for testing which is significantly faster than the average for SITA-standard,6.2 \pm 0.1 mins (p<0.001) but marginally slower than SITA-fast, 4.3 \pm 0.2mins (p=0.05, Figure 3).

Figure 3 about here

Figure 4 and Table 3 show the concordance between the corrected MD of the MRF and SITA-fast and SITA-standard outcomes. Figure 4 shows the data averaged over all time points whereas Table 3 lists these outcomes for each retest period. As can be seen from the regression lines of Figure 4, the data show strong associations for MRF and SITA-standard and SITA-fast (dashed and solid lines in Figure 4) with the average Coefficient of Accuracy being substantial (0.83) between MRF and SITA-standard and moderate (0.77) between MRF and SITA-fast. This concordance in the average MD statistic is further evidenced in Table 3 where moderate to substantial Coefficients of Accuracy are returned between the MRF MDs and those of the HFA tests. The negative bias (-1.2 to -3.4 dB) present at all time points in Table 3 indicates that on average the MRF returns marginally smaller MDs than does the HFA although the average difference (-1.32 dB) may not be clinically significant.

Figure 4 about here

Table 3 about here

One important consideration from a clinic context, is how the tests perform between two successive visits for the same patient. For this analysis we compare MRF and SITA outcomes as a difference from baseline and at 6-months for each patient. This comparison is shown as Bland-Altman plots in Figure 6 and the strength of association at retest is listed in Table 4. Figure 6 shows that the corrected MRF values have little bias and a similar level of test-retest repeatability as both the HFA SITA-fast or SITA-standard tests (Table 4). Overall, the concordance in MRF outcomes between baseline and the 6-month visit are almost perfect (Ca=0.95; ICC =0.98, Table 4) and was greater than either version of SITA test (p<0.05, Table 4). The average bias for both versions of SITA at retest is significantly removed from zero (SITA-standard: 0.8 dB, SITA-fast: 1.0, p<0.05) indicating a small improvement or 'learning effect'. The MRF shows lower variability in its MD at retest, as evident by the 95% LoA in Table 4 (4.0 vs 5.6, SITA-standard, p=0.19and 7.5, SITA-fast, p=0.04). These return a better Coefficient of Repeatability for MRF (8.1%) compared with SITA-fast (17.9%, p=0.001) or SITA-standard (12.2%, p=0.02).

Table 4 about here

Given that the global MD of the MRF compares well to the equivalent index in both SITA tests, this does not mean that the tests have concordance on a regional or point-wise basis. Figure 5 considers the point-wise retest variability across the three tests as a function of average threshold. These data were pooled and binned across all observers to yield Figure 5, left panel, which shows that variability increases with a decrease in threshold, peaking at about 8 dB for the HFA tests over a threshold range of 10-20 dB. The peak for the MRF was about 10 dB (average 35% greater) over a similar threshold range. Of note, SITAfast is marginally more variable compared to SITA-standard at intermediate threshold values (14-22 dB) consistent with a similar observation made by Saunders et al¹⁷.

These point-wise findings expose a paradox, in that, how do we reconcile the better global performance of MRF (Table 4) given this 35% greater variability? The answer lies in Figure 5, right panel, which shows that majority of points (~60%) do not change at retest with the MRF (0-3.9 dB standard deviation) compared with 10% for the HFA (both SITA tests were similar). The outcomes in Figure 5 indicate that the 3-step Bayes used by the MRF returns more stable outcomes than either SITA logic, but that when thresholds change, they do so with greater variability. This likely arises from the larger 'steps' used by the 3-step procedure. Figure 5, left-panel, also indicates that large changes are more likely at intermediate threshold values.

Figure 5 about here

Figure 6 about here

Given that the point-wise analysis for the MRF shows more stability yet greater variability in outcomes, we consider whether the regional analysis defined in Figure 1 does likewise. Table 5 shows that the MRF returns similar thresholds to the HFA tests in all zones with Coefficient of Accuracy (Ca) ranging from 0.61 to 0.92. Of note, the best Ca's are found in the arcuate/nasal step zones (MRF vs SITA-fast 0.76 to 0.90: MRF vs SITA-standard 0.81 to 0.92) which are areas more commonly affected by glaucoma. However, the central zones 1, 2 yield moderate Ca's (0.61 to 0.74) which might reflect the lower number of points that the HFA grid has in this region. Indeed, the positive bias in Table 5 indicates that the MRF has lower thresholds (up to 2.7dB) in these locations, implying that its more densely arranged grid might be detecting early macula defects in some glaucoma patients.

Table 5 about here

Discussion

In this study, we demonstrate that, over a 6-month period, the MRF provides a reliable and repeatable estimate of HFA MD (SITA-standard and SITA-fast) within a test time that approximates that of the SITA-fast logic. This is despite: the greater number of test spots (with more spots in the macular region), the different test spot locations, the variable size of the spot, the different procedures used to determine threshold and the need for fixation changes during the test. We find the test time of the MRF is some 0.3 min/eye slower than is SITA-fast but approximately 1.6 min/eye faster than SITA-standard when testing is conducted on the 9.7-inch iPad. In a separate and unpublished study, test times were derived from 28 patients for the large screen (12.9-inch) iPad Pro and found a 1.2 ±0.8 mins shorter test time than with for the standard 9.7-inch screen version (data not shown). The faster time arises from the fewer fixational movements needed with the 12.9-inch screen which means tests will be about 1 minute/eye faster than SITA-fast. Faster test times are important where there is limited time and resources available to care for large patient loads and they also facilitate home monitoring by patients.

The corrected MRF MD provides a reliable estimate of HFA MD returned from both the SITA-standard and SITA-fast testing procedures (Figure 4). Moreover, the MRF shows similar or better repeatability (Figures 6) in the MD than do either HFA procedures. We find the coefficient of repeatability (CoR) for MD to be 17.9% for SITA-fast, 12.2% for SITAstandard and 8.1% for MRF. For the MRF, this CoR was similar to the 7.8% reported elsewhere for patients having mild defects [3] and is significantly smaller than the CoR returned for both HFA tests. The retest variability found for the SITA tests in this study is similar to that reported for the Medmont perimeter (11.6%)¹² although past work has noted that this can increase substantially in areas of scotoma; therefore the CoR value returned for any study will in part, reflect the severity of visual field defects in those patients included in that study. For that reason, we do not believe that the absolute level of variability should be considered in such comparisons but rather the relative level for both HFA tests should be compared to the MRF, as these were obtained from a common cohort of patients tested at the same visit. This comparison indicates that the MRF has about 30-50% less variability in the global index MD than does either HFA test protocol.

In what appears to be a paradox, we find that the quantisation used by the 3-step test strategy leads to greater stability in most test points but larger variability on a point-wise basis when change occurs (Figure 5). This finding implies that the test might be limited in detecting early progression especially in regions having some loss of threshold already (10-22 dB) as it will require a larger change in order to be found by the MRF. This possibility has not been supported by recent simulation which finds frequent retesting (weekly or monthly) will minimise this effect¹¹.

In conclusion, we find that the MRF provides a reliable and repeatable index of visual field defect comparable to that seen with HFA in either SITA-standard or SITA-fast test modes. It does so in about the same time as it takes for a SITA-fast test using a standard iPad (9.7-inch) screen. Together with the portability and relative low cost of tablet devices, tablet-based visual field tests have great potential in the delivery of quality vision care for glaucoma patients in situations where access to standard perimetry machines is difficult (eg. in rural/remote locations, developing countries, indigent outreach, domiciliary service etc.). The fact that the MRF compares well to the HFA for the detection of glaucoma has been confirmed by an independent clinical trial where correlations similar to those found in this manuscript have been reported¹⁸.

Acknowledgements

a. Funding support:

Cambridge Eye Trust

Jukes Glaucoma Research Fund

Glance Optical Pty. Ltd.

b. Financial disclosures:

Prof Algis J Vingrys and Dr George YX Kong are founding directors of Glance Optical Pty. Ltd., the manufacturer of the MRF software.

References

1. Bosworth CF, Sample PA, Johnson CA, Weinreb RN. Current practice with standard automated perimetry. *Semin Ophthalmol.* 2000;15(4):172-181.

Interface for Objective Assessment of Visual Function Loss. JAMA Ophthalmol. 2017;135(6):550-557. 3. Johnson CA, Thapa S, George Kong YX, Robin AL. Performance of an iPad Application to Detect Moderate and Advanced Visual Field Loss in Nepal. Am J Ophthalmol. 2017;182:147-154. 4. Matsumoto C, Yamao S, Nomoto H, et al. Visual Field Testing with Head-Mounted Perimeter 'imo'. PLoS One. 2016;11(8):e0161974. Rosen PN, Boer ER, Gracitelli CP, et al. A Portable Platform for Evaluation of Visual 5. Performance in Glaucoma Patients. PLoS One. 2015;10(10):e0139426. 6. Rowe FJ, Sueke H, Gawley SD. Comparison of Damato campimetry and Humphrey automated perimetry results in a clinical population. Br J Ophthalmol. 2010;94(6):757-762. 7. Bruckmann A, Volpe NJ, Paetzold J, Vonthein R, Schiefer U. Comparison of advanced visual field defects measured with the Tubingen Mobile Campimeter and the Octopus 101 perimeter. Eur J Ophthalmol. 2010;20(1):149-157. 8. Vingrys AJ, Healey JK, Liew S, et al. Validation of a Tablet as a Tangent Perimeter. Transl Vis Sci Technol. 2016;5(4):3. 9. Kong YX, He M, Crowston JG, Vingrys AJ. A Comparison of Perimetric Results from a Tablet Perimeter and Humphrey Field Analyzer in Glaucoma Patients. Transl Vis Sci Technol. 2016;5(6):2. 10. Chauhan BC, Garway-Heath DF, Goni FJ, et al. Practical recommendations for measuring rates of visual field change in glaucoma. Br J Ophthalmol. 2008;92(4):569-573. 11. Anderson AJ, Bedggood PA, Kong YXG, Martin KR, Vingrys AJ. Can Home Monitoring Allow Earlier Detection of Rapid Visual Field Progression in Glaucoma? Ophthalmology. 2017. 12. Pearce JG. Maddess T. Retest Variability in the Medmont M700 Automated Perimeter. Optom Vis Sci. 2016;93(3):272-280. Wall M, Kutzko KE, Chauhan BC. Variability in patients with glaucomatous visual field 13. damage is reduced using size V stimuli. Invest Ophthalmol Vis Sci. 1997;38(2):426-435. 14. King-Smith PE, Grigsby SS, Vingrys AJ, Benes SC, Supowit A. Efficient and unbiased modifications of the QUEST threshold method: theory, simulations, experimental evaluation and practical implementation. Vision Res. 1994;34(7):885-912. 15. Turpin A, McKendrick AM, Johnson CA, Vingrys AJ. Properties of perimetric threshold estimates from full threshold, ZEST, and SITA-like strategies, as determined by computer simulation. Invest Ophthalmol Vis Sci. 2003:44(11):4787-4795. 16. Lawrence I, Lin K. A concordance correlation coefficient to evaluate reproducibility. Biometrics. 1989:255-268. 17. Saunders LJ, Russell RA, Crabb DP. Measurement precision in a series of visual fields acquired by the standard and fast versions of the Swedish interactive thresholding algorithm: analysis of large-scale data from clinics. JAMA Ophthalmol. 2015;133(1):74-80. 18. Schulz AM, Graham EC, You Y, Klistorner A, Graham SL. Performance of iPad-based threshold perimetry in glaucoma and controls. Clin Exp Ophthalmol. 2017 doi: 10.1111/ceo.13082. **Figure Legends** Figure 1. Location of test spots for the MRF (left, 66 spots) and HFA (right, 54 spots) and definition of eight zones used for regional analysis. The grey zone includes the blind spot and was excluded from analysis. All results are considered as right eye equivalent. Figure 2. Representative visual field outcomes in two eyes having mild (upper-left and upper-right) and moderate (lower-left and lower-right) visual field defects. MRF outcomes

Nakanishi M, Wang YT, Jung TP, et al. Detecting Glaucoma With a Portable Brain-Computer

10

65

2.

1

2

3

4

5

6 7

8

9

10

11

12

13 14

15

16

17

18

19 20

21

22

23

24

25 26

27

28

29

30

31 32

33

34

35

36

37

38 39

40

41

42

43

44 45

are shown in A and C. HFA SITA-standard thresholds and total deviation plots are shown in Band D. Note, all normal locations for the MRF return 30 dB.

Figure 3. Box plots of test time for SITA-fast (n=73), MRF (n=212) and SITA-standard (n=139) across all visits. Whiskers identify the maximum and minimum values.

Figure 4. Association between the HFA MD and the corrected MRF MD averaged over all tests that the patient attended. Unfilled circles (dotted line) show SITA-fast data and filled circles (solid line) show SITA-standard. Regression lines are: SITA-fast, $y = 0.92\pm0.11*x - 3.4\pm1.0$: SITA-standard: $y = 1.00\pm0.07*x - 1.6\pm0.5$.

Figure 5. Point-wise variability of HFA and MRF over the entire trial in observers who undertook 3 or more retests. **Left panel.** Point-wise standard deviation (dB) plotted against average threshold (dB). Black circles show SITA-fast, grey circles indicate MRF outcomes, and unfilled circles represent SITA-standard. **Right panel.** The relative number of points that return the standard deviation (dB) on the x-axis for both HFA (black bars) and MRF (grey bars) tests.

Figure 6. Bland-Altman plot of outcomes comparing the MD of MRF and HFA at baseline and 6 months. **Left panel.** SITA-Fast vs MRF-Radial (n = 17). **Right panel.** SITA-standard vs MRF (n = 34). Black filled circles are SITA-fast, and grey filled circles are MRF and unfilled circles are SITA-standard. Solid horizontal line is the bias and dotted lines show 95% Limits of Agreement for HFA.

Table Legends

Table 1. Patient demographics for groups recruited at the 2 sites. Patients at the Cambridge site performed MRF and SITA-standard whereas those at the India site performed MRF and SITA-fast. **POAG:** Primary open angle glaucoma. **JOAG:** Juvenile open angle glaucoma. **OHT:** Ocular hypertension. Other Glaucoma includes: Psuedoexfoliative glaucoma (1), Normal tension glaucoma (4), Neovascular glaucoma (1), Primary angle closure glaucoma (2) Inflammatory glaucoma (1).

Table 2. Patient compliance for testing at baseline, 2-, 4- and 6-month review periods.Figures in brackets indicate numbers (or %) who attended in Cambridge and India,respectively.

Table 3. Comparison of MD for SITA-fast vs MRF and SITA-standard vs MRF at each time point. Negative values indicate lower average MD values on the HFA. Ca: coefficient of accuracy (0.65<Ca<0.79, moderate; 0.8<Ca<0.89, substantial; 0.9<Ca<1.0, almost perfect).
ICC: Intra-class coefficient. 95% CI: 95% confidence interval for ICC. Bland-Altman, Bias and 95% LoA: 95% limits of agreement for retest data.

Table 4. Correlation statistics for baseline vs next visit for the MRF, SITA-fast and SITAstandard. **Ca:** Lin's concordance coefficient (0.8<Ca<0.89, substantial; 0.9<Ca<1.0, almost perfect). **ICC:** Intra-class coefficient. **95% CI:** 95% confidence interval for ICC. Bland-Altman, **Bias** and **95% LoA:** 95% limits of agreement for retest data. * significantly removed from zero, p<0.05.

Table 5. Average zone threshold for SITA-fast vs MRF and SITA-standard vs MRF. Negative values indicate lower average zone thresholds on the HFA in that region. **Ca:** Lim's concordance coefficient (0.8<Ca<0.9; substantial; 0.9<Ca<1.0, almost perfect). **ICC:** Intra-class coefficient. **95% CI:** 95% confidence interval for ICC. Bland-Altman, **Bias** and **95% LoA:** 95% limits of agreement for retest data.

		Cambridge	India	All
Test Subjects		39	21	60
Age [min-max]		70.1 [37-89]	35.3 [15-59]	57.9 [15-89]
Gender	% Female	51	14	38
Diagnosis	Glaucoma Suspect	6	0	6
	POAG	22	2	24
	JOAG	0	18	18
	ОНТ	3	0	3
	Other Glaucoma	8	1	9
HFA Protocol	SITA-standard	34	1	35
	SITA-fast	5	20	25
Severity (HFA MD)	Mild (≥ -6 dB)	20	5	25
	Moderate (-6 to -12 dB)	11	9	20
	Severe (< -12 dB)	8	7	15

Table 1

Table 1. Patient demographics for groups recruited at the 2 sites. Patients at the Cambridge site performed MRF and SITA-standard whereas those at the India site performed MRF and SITA-fast. **POAG:** Primary open angle glaucoma. **JOAG:** Juvenile open angle glaucoma. **OHT:** Ocular hypertension. Other Glaucoma includes: Psuedoexfoliative glaucoma (1), Normal tension glaucoma (4), Neovascular glaucoma (1), Primary angle closure glaucoma (2) Inflammatory glaucoma (1).

Table 2

	Baseline 2-months		4-months	6-months	
No. of patients	50 (39, 21)	52 (33 <i>,</i> 19)	42 (28,14)	58 (39, 19)	
% Compliance	100	87 (85 <i>,</i> 90)	70 (72, 67)	97 (100, 90)	

Table 2. Patient compliance for testing at baseline, 2-, 4- and 6-month review periods. Figures in brackets indicate numbers (or %) who attended in Cambridge and India, respectively.

	SITA-fast vs MRF across all visits, MD comparison								
Zone	Са	ICC	(95% CI)	Bias, dB	95% LoA, dB				
Baseline	0.67	0.71	(0.53 <i>,</i> 0.83)	-2.9	-5.5, -0.5				
2-months	0.78	0.82	(0.68 <i>,</i> 0.89)	-3.4	-4.6, -2.2				
4-months	0.81	0.88	(0.78 <i>,</i> 0.92)	-3.1	-4.7, -1.5				
6-months	0.82	0.87	(0.77, 0.92)	-2.9	-4.5, -1.3				

Table 3

SITA-standard vs MRF across all visit, MD comparison

Zone	Са	ICC	(95% CI)	Bias, dB	95% LoA, dB
Baseline	0.79	0.81	(0.67, 0.89)	-2.2	-3.2, -1.3
2-months	0.85	0.88	(0.78, 0.93)	-1.3	-2.1, -0.4
4-months	0.86	0.90	(0.82, 0.94)	-1.2	-2.0, -0.4
6-months	0.83	0.86	(0.74, 0.91)	-1.9	-2.7, -1.1

Table 3. Comparison of MD for SITA-fast vs MRF and SITA-standard vs MRF at each timepoint. Negative values indicate lower average MD values on the HFA.

Ca: coefficient of accuracy (0.65<Ca<0.79, moderate; 0.8<Ca<0.89, substantial; 0.9<Ca<1.0, almost perfect). **ICC:** Intra-class coefficient. **95% CI:** 95% confidence interval for ICC. Bland-Altman, **Bias** and **95% LoA:** 95% limits of agreement for retest data.

Table	4
-------	---

Table 4							
	Baseline vs 6-monthvisit, MD						
	n	Са	ICC	(95% CI)	Bias, dB	95% LoA, dB	
SITA-fast	18	0.89	0.95	(0.91, 0.97)	1.0*	-2.7, 4.8	
SITA-standard	35	0.90	0.93	(0.87 <i>,</i> 0.96)	0.8*	-2.0, 3.6	
MRF	50	0.95	0.98	(0.96, 0.99)	0.0	-2.0, 2.0	

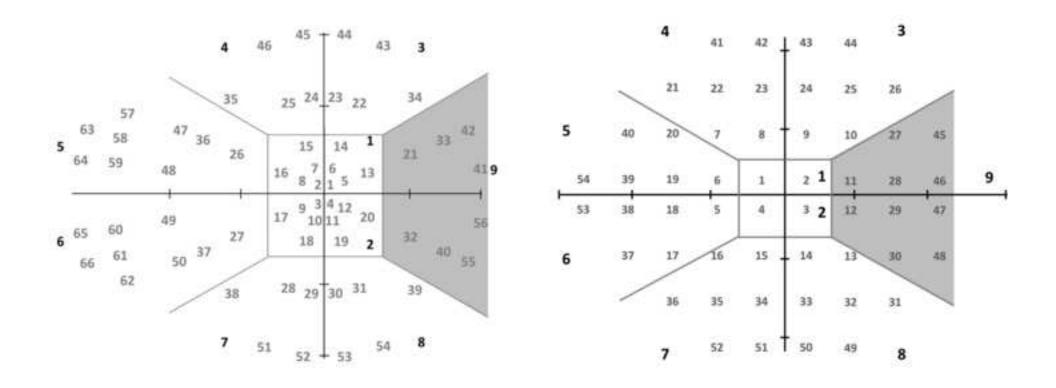
Table 4. Correlation statistics for baseline vs next visit for the MRF, SITA-fast and SITA-standard.

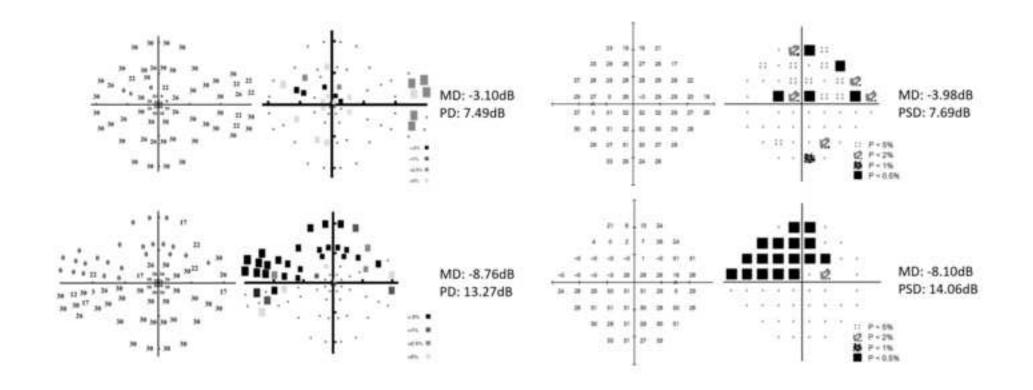
Ca: Lin's concordance coefficient (0.8<Ca<0.89, substantial; 0.9<Ca<1.0, almost perfect). **ICC:** Intra-class coefficient. **95% CI:** 95% confidence interval for ICC. Bland-Altman, **Bias** and **95% LoA:** 95% limits of agreement for retest data. * significantly removed from zero, p<0.05.

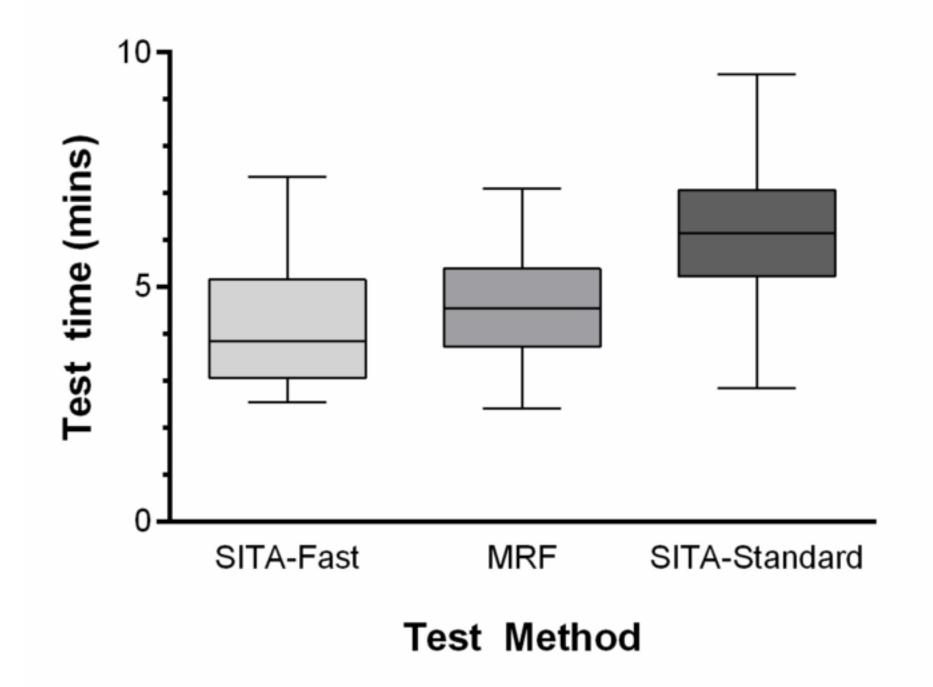
Table 5								
	SITA-fast vs MRF mean zone threshold							
Zone	Са	ICC	(95% CI)	Bias, dB	95% LoA, dB			
1	0.61	0.62	(0.40, 0.78)	2.7	1.3, 4.2			
2	0.65	0.67	(0.47, 0.81)	1.3	0.2, 2.4			
3	0.79	0.82	(0.70 <i>,</i> 0.90)	1.0	-0.6, 2.6			
4	0.88	0.91	(0.84 <i>,</i> 0.95)	0.6	-0.7, 2.0			
5	0.90	0.92	(0.86, 0.96)	-0.3	-1.6, 1.1			
6	0.76	0.80	(0.66, 0.88)	0.1	-2.0, 2.1			
7	0.80	0.83	(0.70 <i>,</i> 0.90)	-0.3	-2.0, 1.3			
8	0.83	0.86	(0.76, 0.92)	1.3	0.0, 2.5			
	SITA-s	tandard	l vs MRF mean	zone thresh	old			
Zone	Са	ICC	(95% CI)	Bias, dB	95% LoA, dB			
1	0.74	0.78	(0.62, 0.87)	0.0	-1.8, 1.8			
2	0.67	0.68	(0.48, 0.81)	2.3	1.4, 3.2			
3	0.88	0.91	(0.85 <i>,</i> 0.95)	0.7	-0.5, 1.9			
4	0.92	0.95	(0.92 <i>,</i> 0.97)	1.0	0.1, 2.0			
5	0.85	0.88	(0.80 <i>,</i> 0.93)	-0.7	-2.1, 0.8			
6	0.83	0.86	(0.76, 0.92)	-0.1	-1.3, 1.0			
7	0.81	0.84	(0.73 <i>,</i> 0.91)	1.2	0.0, 2.3			
8	0.84	0.87	(0.77, 0.92)	2.1	1.1, 3.1			

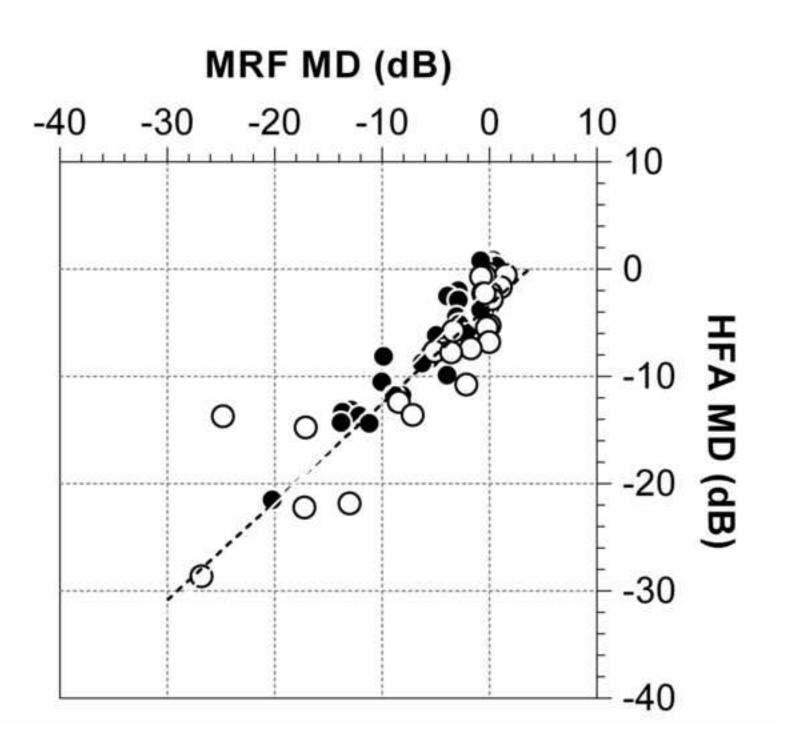
Table 5. Average zone threshold for SITA-fast vs MRF and SITA-standard vs MRF. Negative values indicate lower average zone thresholds on the HFA in that region.

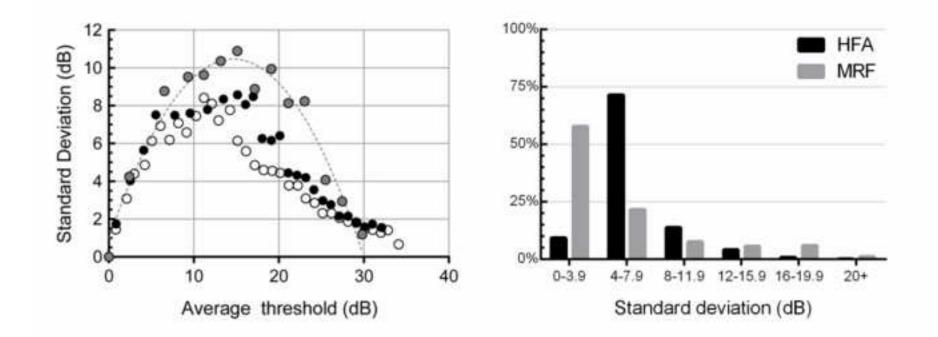
Ca: Lim's concordance coefficient (0.8<Ca<0.9; substantial; 0.9<Ca<1.0, almost perfect). **ICC:** Intra-class coefficient. **95% CI:** 95% confidence interval for ICC. Bland-Altman, **Bias** and **95% LoA:** 95% limits of agreement for retest data.

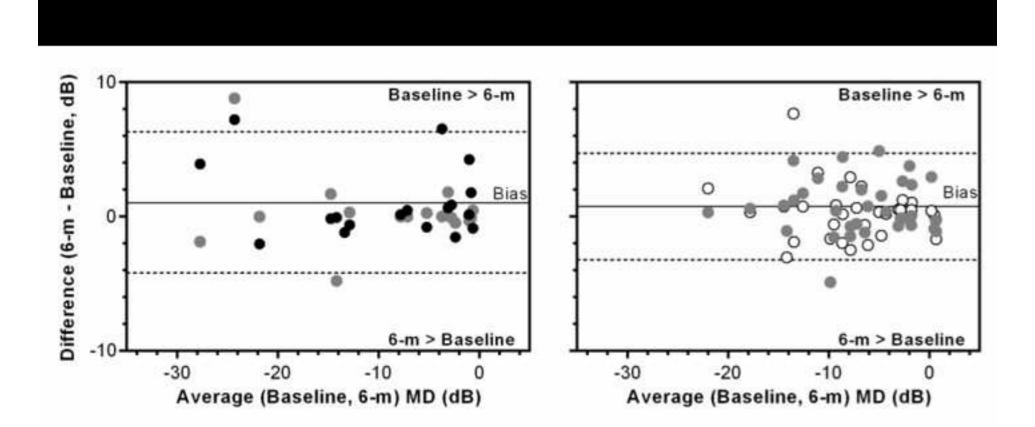












TOC statement

In this multicentre longitudinal study we establish the medium-term repeatability of an iPad perimetry app Melbourne Rapid Fields (MRF) and compare this to the Humphrey Field Analyzer (HFA) 24-2 SITA-standard and SITA-fast programs. MRF was similar to SITA-fast in test speed. MRF correlated strongly with HFA across 4 visits over a 6-month period and has good test-retest reliability. MRF is suitable for monitoring visual fields in settings where conventional perimetry is not readily accessible.