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Measuring Visual Fields in Children With Glaucoma Using a Portable Tablet

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Purpose: To compare perimetric outcomes of an iPad perimetry app (Melbourne Rapid Fields [MRF]) with those of the Humphrey Field Analyser (HFA) testing children with glaucoma.

Methods: Sixteen children diagnosed and treated for glaucoma were recruited to evaluate their perimetric performance over two visits. At each visit, they undertook visual field assessment using the MRF application as well as the HFA. The HFA test was part of their usual clinical work up and a clinical assistant judged which test format (24-2 SITA standard or SITA fast) might be suited to the testing of that child. The primary outcome measure was the association and repeatability of mean deviation (MD) for the MRF and HFA tests, by way of regression, intraclass correlation coefficient and Bland–Altman analysis. Secondary measures were comparisons of pattern deviation indices, test times as well as an indication of participant test preference. Summary data show means ± standard deviation.

Results: The age for our cohort was 7 to 15 years of age (mean, 10.0 ± 2.4 years of age). The MRF MD was in close concordance to HFA MD with an intraclass correlation coefficient of 0.91 (95% confidence interval, 0.82–0.95). Bland–Altman analysis found little bias (−0.6 dB) and a 95% coefficient of repeatability of 2.1 dB in eyes having a normal HFA MD. In eyes with glaucomatous visual field defects the 95% coefficient of repeatability at retest was much larger for both the MRF (10.5 dB) as well as for the HFA (10.0 dB). Average MRF test times (5.6 ± 1.2 minutes) were similar to SITA Fast (5.4 ± 1.9 minutes) with both being significantly faster than SITA standard (8.6 ± 1.4 minutes; $P < 0.001$). All children chose testing with the MRF as their preference.

Conclusions: MRF correlated strongly with HFA and was preferred by the children over the HFA. MRF is suitable for perimetric evaluation of children with glaucoma.

Translational Relevance: This study finds that an iPad based visual field test can be used with children having glaucoma to yield outcomes similar to SITA-fast. Children indicate a preference for such testing.

Introduction

Perimetry is a useful and desirable test for pediatric clinics, because it provides important information regarding the integrity of the eye, the optic nerve and the visual pathways.[1] It has been reported that standard automated perimetry (static perimetry) is the most common form of visual field test used to evaluate children in UK hospitals.[1,2] However, standard automated perimetry has been designed from knowledge gained on adults and might not apply to the perimetric testing of children who return poorer reliability and give greater fixational instability owing to their reduced attentiveness.[2–6]

The development of smart technology (phones and tablets) has produced engaging experiences across the educational and entertainment industries. These

interactions are enjoyed by adults and children alike and we believe that a commercial tablet device can provide an easy-to-use visual field test (Melbourne Rapid Fields [MRF]) to determine standard automated perimetry thresholds in children. We aim to test this possibility in a cohort of children with glaucoma by comparing visual field outcomes from the MRF device to an industry standard bowl perimeter (Humphrey field analyzer [HFA], Zeiss Meditech, Inc, Dublin, CA).

Methods

This study was undertaken at the Dr Rajendra Prasad Centre for Ophthalmic Sciences, AIIMS New Delhi after approval from the local ethics committee (AIIMS 564/03.11.2017) and conducted in accordance with the tenets of the Declaration of Helsinki with all children and their parents giving informed consent before participation. To determine the accuracy and acceptability of the MRF tablet visual field test in a pediatric clinic, we sequentially recruited children who had been diagnosed with pediatric glaucoma and who were in need of visual field testing. Glaucoma was established when the child first presented to our clinic, with an intraocular pressure of greater than 21 mm Hg in the presence of any one of the following: (1) corneal diameter of more than 11mm at 1 year of age or more than 12 mm at any age, (2) axial length greater than that for age, or (3) a cup disc ratio of more than 0.6 or an asymmetry of more than 0.2 when the optic disc was of similar size in the presence of focal rim thinning.

The children had never performed perimetry before and were recruited to be tested during routine clinical visits, once on the HFA as needed for the clinical management of the child, and once on the MRF. The presentation order was counterbalanced randomly so that the HFA was administered first in one-half of the cases, followed by the MRF on that same eye. All children completed testing in a sequential manner and all performed a second MRF and HFA test at their next clinical visit. At retest, the order of testing was kept the same as for the initial visit. The clinical protocol for HFA testing required the clinical assistant to explain the test to the child and try to have the child complete a 24-2 SITA-Standard test (the preferred option in this clinic). Based on the assistant's feeling for how the child might cope with this longer test, and the clinical presentation, the assistant could choose a 24-2 SITA Fast test for that particular child.

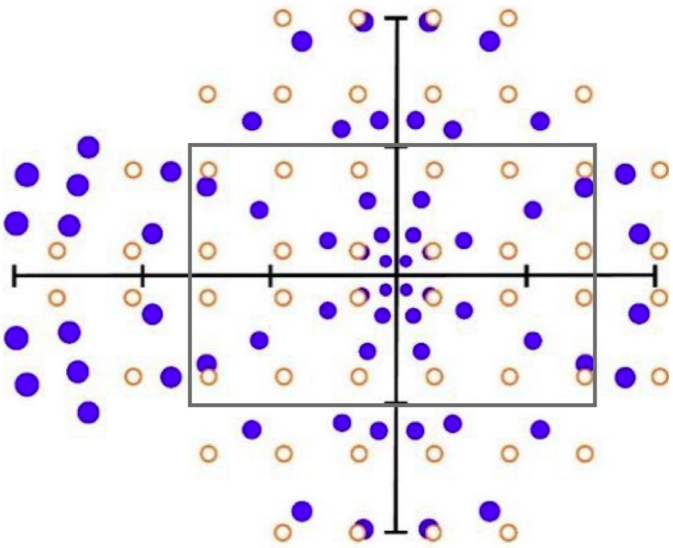

Figure 1. Location of MRF-glaucoma spots (*blue-filled circles*) compared with the 24-2 Humphrey Grid (*unfilled circles*). Note that the MRF spots become larger with eccentricity (shown here as a schematic) from about Goldman size 2.6 in fovea to about Goldman Size 5 at 30°. A 9.7-inch iPad subtends abut 15 × 10° (*gray outline*) indicating that the spots outside of this region need to be tested by moving the point of fixation to the corners of the tablet (see text for details).

The MRF

The MRF app (GLANCE Optical Pty Ltd, Melbourne, Australia) is a stand-alone application available for the iPad tablet (Apple, Cupertino, CA) for the testing of vision. The tests available on the MRF include visual acuity and visual field tests. This application has been optimized for different eye diseases: MRF–glaucoma, MRF–macula, MRF–neural, and MRF–diabetes. In this study, we report on the visual field testing of children with the iPad application: MRF–glaucoma. For our study, we compare the machine specific mean deviation (MD) returned by both devices from age-specific normative databases.

MRF–glaucoma has a radial test pattern that comprises 66 test locations (Fig. 1). A 9.7-inch iPad was used to test the central visual field at a viewing distance of 33 cm in free space (no chin or forehead constraint) with children requested to keep their heads still during testing. Audio instructions are given by the tablet during the test procedure and these reinforce the instructions provided by the clinical assistant. All participants wore their normal reading glasses (if needed). Viewing distance was set at the start of testing with a ruler and the clinical assistant visually monitored for stability in the child's head or face during testing. If viewing distance was not maintained, our protocol was to pause the test, reinstruct the child

and recommence testing. This protocol was not implemented in our study, because all children complied with the request to maintain a stable head position. Details of the use of the MRF for perimetry and its concordance with HFA thresholds in adults are reported elsewhere.[7,8]

Participants

We included children with glaucoma of age 16 years or younger at the initial visit and who needed perimetric testing for their eye care. All children were retested on both HFA and MRF at a subsequent clinical visit (within 2 years) as needed for their condition and these data were analyzed for test–retest reliability.

Our inclusion criterion for perimetry testing was to recruit children who were judged by the clinical assistant as cooperative at a visual acuity test. Only those who had undergone surgery at least 6 months earlier and having a stable intraocular pressure, with or without topical medication, were included.

Exclusion criteria were the presence of a systemic condition or the use of systemic drugs that could affect vision, a need to change glaucoma medications or undergo eye surgery 6 months before or during the observation period, inability to understand or comply with the voice commands of the MRF, children having a visual acuity of worse than 6/36 (20/120) or nystagmus.

At the end of the first session of testing, all children were surveyed about their preferred test format and which they would like to use in the future: MRF tablet perimeter or HFA bowl perimeter.

Statistics

We used an analysis of variance or Student *t* tests (paired) where appropriate, Deming regressions, intraclass correlation coefficient, and Bland–Altman methods. As the two devices have different numbers of points sited at different locations and which vary in size, direct point-wise comparisons are difficult. We compare HFA and MRF in terms of the device MD and pattern standard deviation (PSD or PD) and where needed, give the average threshold found in each quadrant.

Results

The mean age for our cohort was 10.3 ± 2.4 years (range, 7–15 years). The diagnostic categories for the children included: primary congenital glaucoma, steroid-induced glaucoma, and juvenile open-angle glaucoma. Since the correlation between the MDs of right and left eyes from the HFA was low 0.31 (range, −0.07 to 0.61) consistent with differential monocular eye disease, we used each eye ($n = 32$) as an independent observation for analysis. All children were retested (aged 11.0 ± 2.4 years) at a subsequent visit on average some 11.0 ± 6.4 months (range, 2–21 months) after their first visit as needed for their clinical management (Fig. 2). The data from both tests contributed to the test–retest analysis except as indicated in the following.

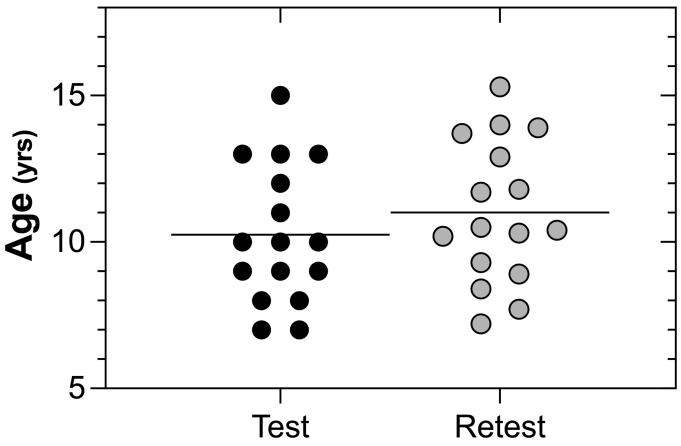

Figure 2. Age profile of the 16 children participating in our trial (*black symbols* first test), children were retested (*gray symbols* age at retest) at a later date (range, 2–21 months later; see text for details) as indicated for clinical management. Horizontal bar indicates group mean ages (test 10.1 ± 2.5 years; retest 10.8 ± 2.5 years).

Three children (five eyes [15.6%] of all eyes; ages 8, 9, and 13 years) could not complete the HFA SITA standard test at the first visit, but could do so in their fellow eye after having performed the MRF, which possibly provided them some familiarity and learning to perimetry testing. Over both the test and retest 11% (7 eyes) of eyes could not be tested on the HFA and 3.1% (2 eyes) could not be tested on the MRF. Possibly the more concerning prospect was that three eyes (9.4%) of three children, aged 13, 13, and 15 years, could not be tested at the retest visit despite a successful first test, indicating that a successful outcome does not guarantee future perimetric success in a child.

We determined the glaucoma severity score for the 32 eyes of the children based on the HFA MD index (normal, −2 dB < MD; mild −2.1 > MD >−6 dB; moderate −6.1 > MD > 12 dB; advanced −12.1 > MD > −20 dB; severe −20 dB > MD).[9] Here we used the HFA MD from the first successful test visit, which in most cases (27/32) was the first visit. Figure 3 shows the distribution of the severity of visual field loss in our test cohort.

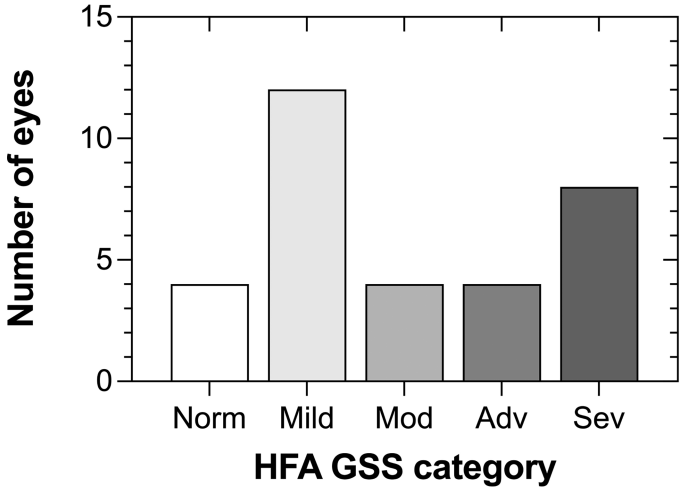

Figure 3. Glaucoma Severity Score (GSS) derived from the MD of the HFA in 32 eyes of 16 participating children as detailed in the text.

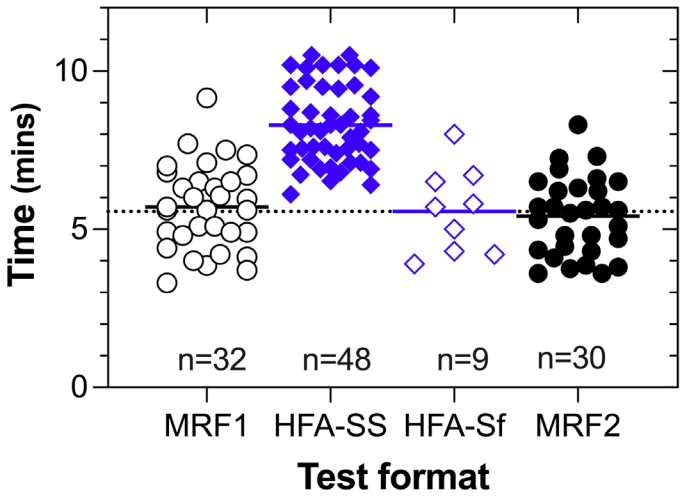

Figure 4. Test time for MRF performed on two occasions (*circles*; MRF1 and MRF2) and HFA SITA standard (*SS*; *filled diamonds*) or SITA-Fast (*SF*; *unfilled diamonds*) tests. The horizontal bars identify group mean times and the dotted horizontal identifies the average test time for MRF over all tests.

Including both test and retest, we achieved 57 results (89%) with HFA testing and 62 results (97%) with MRF. Figure 4 shows the test times for 32 eyes on the MRF at the initial visit and for the 30 eyes that were able to be retested. It also shows the test times for the same children on HFA SITA standard ($n = 48$) or SITA fast ($n = 9$) over both the test and retest visits. Average MRF test times across both test sessions (5.6 ± 1.2 minutes) were similar to SITA Fast (5.6 ± 1.4 minutes) and both were significantly faster (approximately 3 minutes per eye) than SITA standard (8.3 ± 1.2 minutes; $P < 0.001$).

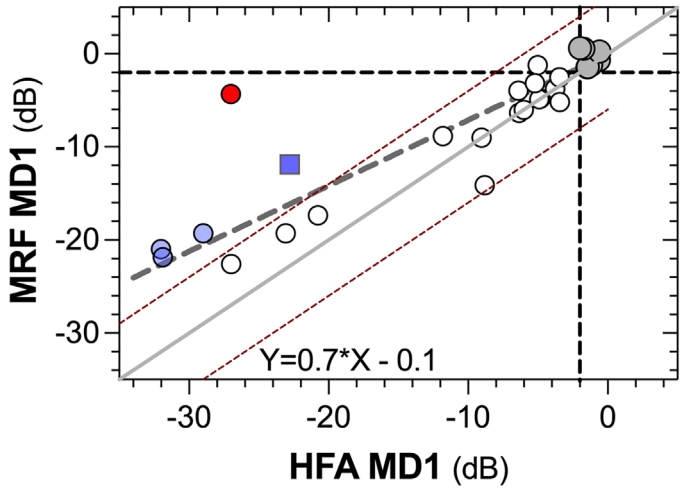

Figure 5. MRF MD vs. HFA MD for $n = 27$ initial tests from 16 participants (5 could not perform HFA testing). These data have a slope of 0.70 (*gray dashed line*); the *gray solid line* is the line of identity (slope = 1); red dotted lines are ±6 dB from the identity line. Five MRF data (*blue*) lie outside the ±6 dB locus. One child is an outlier (*red spot*), and the other four (*blue*) reflect the lower threshold returned by the larger MRF spots (see text for details). The gray data identify children who gave normal HFA MD. The square symbol is the child shown in Figures 6, 7, and 8.

We analyzed the concordance between the MD obtained with the first MRF test and the first HFA test for those 28 eyes for which we had data (Fig. 5). These show excellent correlation (intraclass correlation coefficient = 0.91; 95% confidence interval, 0.82–0.96) with one outlier identified by an outlier test ($P < 0.05$, GraphPad Prism: https://www.graphpad.com/quickcalcs/Grubbs1.cfm) and indicated by the red-colored symbol in Figure 5. Without this outlier, most of the data (86%) was within ±6 dB (dashed red diagonals) of the unity line (gray diagonal in Fig. 5) and returned a Deming regression of $Y = 0.70*X - 0.08$ (thick dashed gray line). The gray symbols in the top right of Figure 5 identify seven eyes that returned HFA MD values of greater than −2 dB and were considered as having normal visual fields. Of note, our data do not approximate the unity line in Figure 5, but has a slope of 0.7. We believe that this shallower slope results from the larger test spot used in peripheral locations of the MRF as shown in Figure 1. The four blue symbols identify children who lie more than 6 dB from the unity line: these all are found at high MD values consistent with the slope of 0.7. The raw data for the child shown as a blue square in Figure 5 is presented in Figure 6. Here it is evident that the MRF has higher thresholds (by approximately 5–7 dB) in the periphery owing to its larger spots particularly in the nasal region, even though the patterns of defect shown by the gray scales look similar.

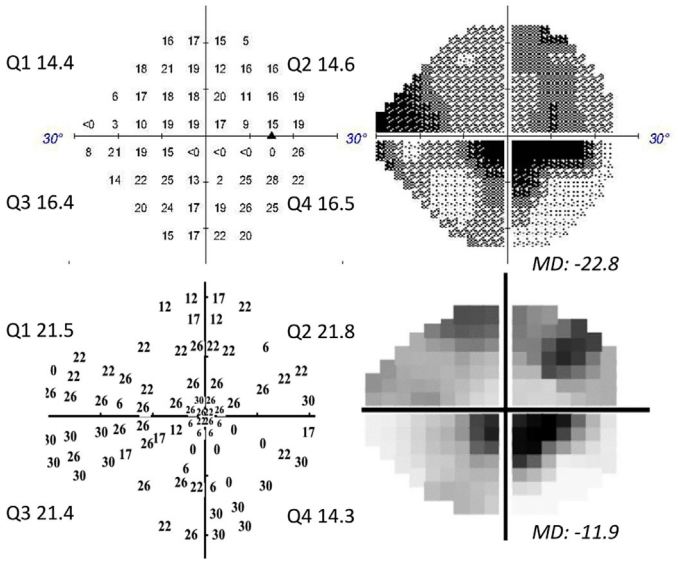

Figure 6. Representative HFA (*top*) and MRF (*bottom*) data for one 13-year-old child who is identified in Figures 5, 7, and 8 by the *blue square symbol*. Although the gray scales look similar, thresholds across the four quadrants (Q1, Q2, Q3, and Q4) show that MRF returns higher average quadrant thresholds than does the HFA by approximately 5 to 7 dB owing to the larger test spot. This finding is particularly apparent in the nasal region of this child's visual field where many MRF test locations return 26 to 30 dB, but the HFA outcomes over this region are much lower.

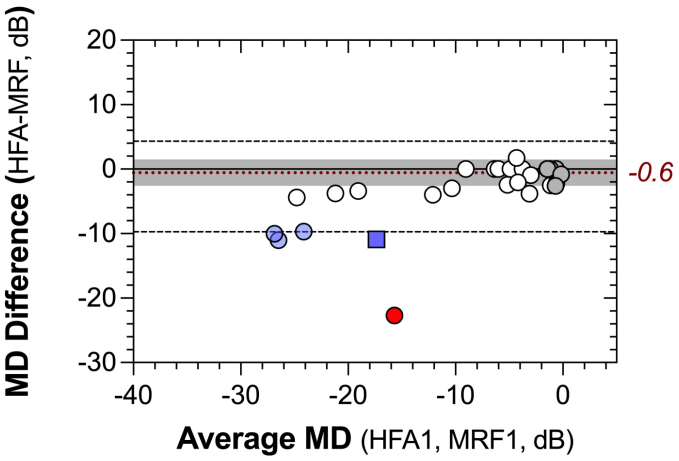

Figure 7. Bland–Altman plot comparing the MD of the MRF and HFA found at the initial test (HFA1, MRF1). The red horizontal line dotted identifies the bias (−0.6 dB) of participants having normal HFA MD values (>−2 dB; *gray filled circles*) and the gray zone indicates their 95% limits of agreement (1.6 to −2.7). The *dashed horizontal lines* indicate the 95% limits of agreement for the entire group, excluding the *red outlier*. Note how some children with advanced defects (average MD of <−12 dB) show greater departure from HFA outcomes (more negative values), as evident in Figure 5.

Figure 7 shows the Bland–Altman analysis for the data of Figure 5. The gray zone identifies the 95% limits of agreement for the seven eyes with normal MD and the bias is shown on the right. We undertook this analysis in eyes having normal MD because variability is known to increase as threshold decreases and we wanted to find out how children with normal visual fields would perform. The bias for these eyes was −0.6 dB with a 95% coefficient of repeatability (COR) of 2.2 dB (shaded region). These findings suggest that the MRF will return reliable estimates of HFA MD in children with normal thresholds. The small 95% COR (2.2 dB) is a useful measure of precision for clinicians as it defines the limit which will contain 95% of repeat test results, such as when testing a child over several visits. Figure 7 also shows the 95% limits of agreement for the total group of eyes, excluding the outlier (dash horizontals). This has a bias of −2.7 dB confirming that the HFA returns a larger MD (more negative) and that there is a large range for 95% limits of agreement (4.3 to −9.7 dB) with 4 of 28 eyes (14%) of children producing outcomes that deviate beyond 6 dB of the HFA MD. Such deviation is most evident in children having advanced glaucoma (MD <−12 dB).

This lack of association may reflect high variability in MRF outcomes in advanced disease. Figure 8 considers this prospect by showing the Bland–Altman analysis for test–retest made on the same device. Figure 8A shows HFA test–retest data where little bias (1.8 dB) is evident and a 95% COR of 10.0 dB, these calculations exclude the outlier. In contrast, Figure 8B shows that the MRF has a bias of 1.1 dB between test and retest and a 95% COR of 10.5 dB. Thus, the MRF data were repeatable, as were the data from the HFA in this cohort of children.

The pattern deviation from the first test of the MRF was found to have a nonlinear relationship with HFA PSD (Fig. 9). What was evident was that the MRF has a larger pattern index than does the HFA particularly in some children having low PSD values for HFA (shaded region, <5 dB). In fact, 10 eyes (28%) had an abnormal pattern deviation on MRF in the presence of a normal or borderline PSD in the HFA (shaded region in Fig. 9). Possibly early losses of visual threshold in children have a pattern in their loss and clinicians should look for the patterns and consider this index to identify them.

We checked the reliability of children in performing visual field tests on the two devices. Over the test and retest of 16 children (16 × 2 eyes × 2 tests), we achieved 62 viable tests for the MRF and 57 for the HFA. The HFA device flagged 19 of 57 outcomes (33%) as unreliable: 8 (14%) were flagged for high false-positive (FP) rates (>15%) and all 19 (33%) had excessive (>25%) fixation loss. The MRF flagged 23 of the 62 tests (37%) as unreliable: 13 (21%) with high FP rates and 16 (26%) with poor fixation using a criterion of 33% as unreli-

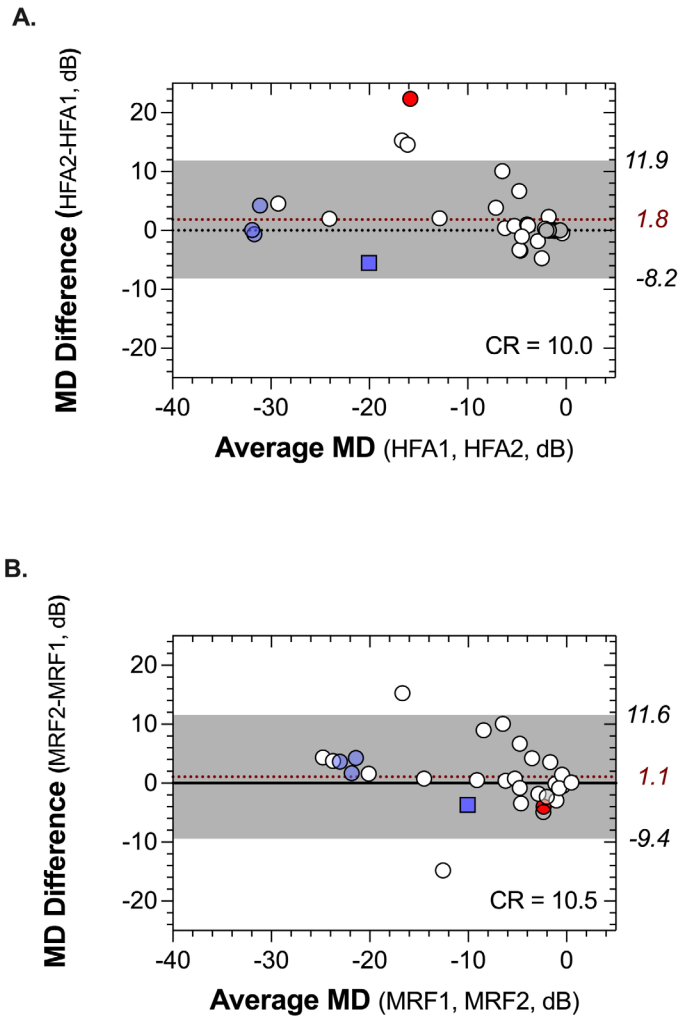

Figure 8. Bland–Altman plots comparing test and retest outcomes for each device in children who returned two tests: (**A**) HFA and (**B**) MRF. The symbols and color codes are as defined in Figure 5. The *dotted red horizontal* identifies the bias from test to retest (typically <2 dB) and the gray zone shows the 95% limits of agreement for each device with the 95% coefficient of repeatability (CR) given at the *bottom* of each panel.

able (Fig. 10). We found that test reliability is a function of age with unreliable outcomes more likely in children under the age of 12.5 years (Fig. 8, vertical line). We also find that FPs have a significant downward slope (−2.9; $P = 0.01$) for the linear regression against age, compared with fixation loss (FL), where the age-related slope was not significantly (−1.60; $P = 0.17$) removed from zero.

The outcome of our survey after the second test session found that all children preferred the test experience on the MRF, reporting it easier and more agreeable than for the HFA. One 9-year-old child was uncooperative and refused to do the HFA test on their first exposure, resulting in a typical cauliflower defect (Supplementary Fig. S1). This child successfully

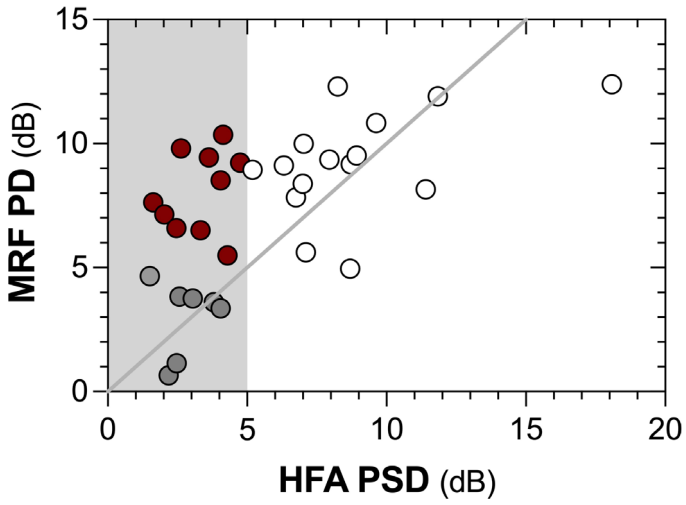

Figure 9. The relationship between MRF pattern defect (PD) and HFA PSD index found at the initial test. The *gray diagonal* identifies the identity line. The fact that most data lie above the identity line indicates that MRF PD is larger than the HFA PSD, particularly for early loss on HFA (gray zone PSD <5 dB). The *filled gray circles* define children who return normal thresholds and the *filled red symbols* identify children who have a large PD, but near normal PSD. Retest data show a similar outcome and have not been plotted for clarity.

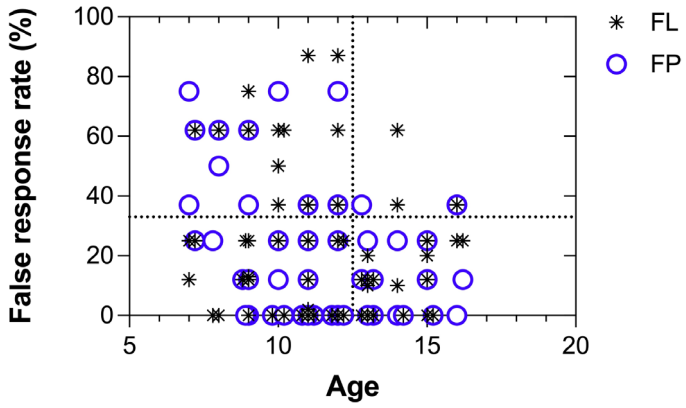

Figure 10. Reliability indices for the first MRF and HFA test outcomes as a function of age. Fixation loss (FL) and false-positive (FP) response rate is shown as a percent of the number of catch trials. The *horizontal dotted line* identifies one criterion (33%) for reliable performance. There is a marked age dependency in the FP and FL responses. Some children under the age of 12.5 years (*dotted vertical*) give high levels of poor reliability.

completed MRF testing at that same visit and likewise successfully completed HFA testing on their fellow eye after the MRF exposure.

Discussion

Our study set out to consider whether a tangent iPad perimeter (MRF) can provide reliable and accurate

thresholds when compared with the HFA in young children. We found that the MRF produces reliable and accurate estimates of HFA MD in all pediatric cases of glaucoma. We also found that the accuracy of MRF estimates is within 1 dB (bias) and the 95% COR is 2.2 dB in eyes having normal HFA thresholds (Fig. 7). However, as glaucoma progresses to advanced stages (MD < -12 dB) both the accuracy (bias $= -2.7$ dB) and repeatability suffer (95% COR $= 10$ dB). This result is so for both the MRF and HFA. In our cohort, 14% of children had MRF thresholds that were displaced from the HFA value by more than 6 dB, especially if they had advanced loss (MD < -12 dB) (Fig. 7), which likely occurs owing to the larger test spot, as will be detailed in the following.

We also considered whether this lack of concordance between HFA and MRF is a characteristic of the MRF given its different spot configurations (spots scaled to get larger in periphery) (Fig. 1) and the Bayes thresholding approach. The spot scaling should yield higher thresholds in the periphery,[10] which we show to be the case in one participant and indeed is a general characteristic of the entire group once thresholds reach an advanced level of loss (MD < -12 dB). This produces a regression between MRF and HFA threshold outcomes with a slope of 0.7 and not 1.0, similar to that reported by others when using test spots larger than Goldman Size III.[11–13] We have also found in a previous study that the larger spots will decrease threshold variability, making early changes easier to detect.[10] In case these attributes manifest negatively on threshold outcomes for the MRF we considered the test–retest outcomes of both devices. If the larger spots or Bayes approach were to corrupt threshold estimates, especially in advanced cases of glaucoma, we could expect that the test–retest data would show this up when comparing HFA and MRF thresholds. That this is not the case, was evident in the Bland–Altman plots of Figure 8. It was also evident that both the MRF and HFA produce similar levels of repeatability from test to retest with the coefficients of repeatability being similar (10.5 vs. 10.0). So we believe that the major contributing element that explains why large magnitude MD losses are less profound in the MRF, would most likely be related to the size of the spot yielding a greater dynamic test range.

It is known that children are more variable in performing visual field tests than adults.[2,3] This was so in our study too, for both the MRF and HFA. MRF false response checks (FL and FP) identified similar numbers of FL and FP, as did the HFA although MRF outcomes reflect discretization from the smaller sampling rates, as is evident in the discrete outcomes seen with the MRF (Fig. 8). For example, the MRF monitor usually shows eight false response checks resulting in 12.5% steps for its outcomes. So absolute comparisons of reliability index are complicated by this different testing strategy, as well as the different method used by the HFA to estimate FP. Nevertheless, we found that children return higher fixation losses and false response errors at younger ages. Others have noted a similar lack of reliability that is age related[2] and showed that retinal stabilized perimetry with the macular integrity assessment device finds decreased fixational stability in 9- to 12-year-old children.[3] This finding suggests that fixational instability is a physiological component of younger age.

When surveyed, children stated that they preferred being tested with the MRF compared with the HFA. Because the test times of HFA SITA-Fast are about the same as the MRF (Fig. 4), this preference does not seem to arise from a difference in test time. Likewise, because the tasks are similar, we felt that this preference is task independent. One parsimonious explanation underlying such preference could be the free space test environment of the MRF and the moving fixation. However, this test approach requires that the clinical assistant monitor head position during the test to be sure of stability in head position. Changing fixation during testing makes the MRF test procedure less tedious. Nevertheless, these suggestions remain speculative, because we did not set out to test for such a possibility and we accept that they are in need of experiments that test this prospect directly.

High variability is evident in children. We found a 95% COR for children having normal MD values of 2.2 dB, similar to those found in adults.[7] However in more advanced visual field loss the COR was 10.5 dB. So how should a clinician deal with abnormal outcomes, given this high variability? One option is to average multiple test outcomes, because averaging decreases the effect of variability. A similar suggestion for using multiple tests and allowing one test for learning has also been made by Jones et al.[3] For example, taking the average of four test outcomes will reduce COR of children by one-half (sqrt[4]) to approximately 5.2 dB, close to adult values. Achieving multiple test outcomes, however, is not an easy option with children. One alternative would be for the child and/or parent to be taught how to administer the test at home, guided by the audio of the MRF software, and be asked to perform daily self-testing for the week (7 days) either after or before a clinical visit. We find such requests of adults yield five to seven tests over that week and decease variability in MD by about 60%. This type of frequent testing is similar to

the cluster testing approach, which was successfully applied to stabilize the MD in the UK Glaucoma Treatment Study.[14] However, the prospect of testing children at home remains speculative in need of a clinical trial to show that children can undertake home monitoring and return useful outcomes.

One interesting observation in our data was that the pattern deviation from the MRF was affected early in children, much more so than the PSD of the HFA perimeter. The cause for this difference likely rests in the fact that the PSD of HFA is calculated after weighting of data which allows for the increase in variability found with locations at higher eccentricities. But this is exactly where glaucoma expresses in the early stages so weighting in this manner will decrease the scope to expose early loss. Weighting is not needed with the MRF because thresholds and variability across the visual field are reasonably constant, which is achieved by scaling test points,[10] with larger spots being used at locations further removed from fixation.[15]

One of the limitations of the study was the small sample size owing to the uncommon disease as well as the fact that it was imperative to include children with relatively good vision to perform perimetry. This precluded larger numbers in different age groups to establish age-related comparisons. Also having the children perform a specific test on HFA (e.g., 24-2 SITA-fast) would have provided a better platform for device comparison although, at the same time, it would have decreased the clinical translation of the findings. Given that our test method was regulated by the clinical milieu, we feel it will provide a reasonable representation of real-world application. Also because we only selected our test cohort by only including children who were cooperative, our results may not represent the entire gamut of children with pediatric glaucoma who may be less cooperative with visual field testing.

In conclusion, we found that children can undergo perimetry with a MRF tablet perimeter. Because children return high levels of fixation instability and FP response, we recommend that visual field outcomes of children need to be considered by averaging over multiple tests, something that could be achieved by adopting a self-testing program at home under the supervision of the parents, although this latter aspect needs verification by a clinical trial.

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VG and AV designed the study protocol. SG, AP, AS designed data collection tools, monitored data collection. AV, VG, and SP drafted the paper. GK, VG, SP, AV revised the paper. AV, as guarantor, is responsible for the overall content.

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Data Availability Statement: Data may be obtained from a third party and are not publicly available.

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