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Title

The short-term compliance and concordance to in clinic testing for tablet-based home monitoring in age-related macular degeneration.

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Short title

Home monitoring in age-related macular degeneration.

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Abstract

Purpose

This study determines the short-term compliance to regular home monitoring of macular retinal sensitivity (RS) in intermediate age-related macular degeneration (iAMD). We also compare home-based outcomes with in-clinic outcomes determined using 1. the same tablet device under supervision and 2. the Macular Integrity Assessment (MaIA) microperimeter.

Design

Single-centre longitudinal compliance and reliability study.

Methods

Seventy-three participants with iAMD were trained to perform macular field testing with the Melbourne Rapid Fields-macular (MRF-m) iPad application. Volunteers were asked to retur 6 weekly tests from home, guided by audio instructions. We determined compliance to weekly testing and surveyed for factors that limited compliance. Test reliability (false positive, false negative) and retinal sensitivity (RS) were compared to in-clinic assays (MaIA). Data are shown as mean ▯[standard deviation] or median[quartile 1-3 range]. Group comparisons were achieved with bootstrap to define the 95% confidence limits.

Results

Fifty-nine participants submitted 6 home exams with a median inter-test interval of 8.0 [7.0–17] days. Compliance to weekly testing (7 days ±24 hours) was 55%. The main barrier to compliance was IT logistic reasons. Of 694 home exams submitted, 96% were reliable (FP<25%). The mean RS returned by the tablet was significantly higher (+3.2 dB, $p<0.05$) compared to the MaIA.

Conclusions

Home monitoring produces reliable results that differ from in-clinic tests due to test design. This should not impact self-monitoring once an at-home baseline is established, but these differences will affect comparisons to in-clinic outcomes. Reasonable compliance to weekly testing was achieved. Improved IT support might lead to better compliance.

Introduction

Age-related macular degeneration (AMD) is a chronic eye disease affecting approximately 196 million people worldwide.[1] The neovascular form of the disease (nAMD) can produce a sudden, irreversible loss of vision. Intravitreal injections of anti-vascular endothelial growth factor (anti-VEGF) can improve visual acuity (VA) by ≥3 lines in some cases and stabilise vision in 95% of eyes.[2-6] Presenting VA, at the time treatment commences, has a major impact on long term outcomes, hence early detection of nAMD is key to commencing treatment in the presence of relatively good vision, and thus achieving a better visual outcome with anti -VEGF treatment. However, despite knowing the importance of early detection and the commencement of treatment, in many instances, patients are still presenting with significant loss of central vision before treatment is initiated.[7,8]

Standard care for individuals at high risk of progression to late-stage AMD is routine clinical reviews (typically 6 monthly) and home monitoring with the Amsler grid. This method, used since 1945,[9] increases the likelihood of detecting early visual changes, such as metamorphopsia, suggestive of progression to neovascular complications. However, the sensitivity for detection of early neovascular change with Amsler grid is low, at 30%.[10,11] Compliance to regular home-monitoring of vision with the Amsler grid is also poor and has been reported by one study to be 55% over a 12 month period.[12]

There are several smart device tools available for home monitoring by patients with AMD. These tests implement either Amsler grid (OdySight, Tilak Healthcare, France),[13,14] hyperacuity principles (myVisionTrack, Vital Art and Science, U.S.A.; ForeseeHome, Notal Vision, Ltd., Israel),[15,16] or visual acuity (OdySight),[13,14] but no home monitoring tool to date offers a test of retinal sensitivity (RS), as employed by clinical microperimetry methods.

We propose RS, as measured by Differential Light Sensitivity (DLS), provides a sound method for assay in iAMD cases that has been shown to correlate with spectral domain optical coherence tomography (SD-OCT) defined pathology.[17,18] Such correlations have been established by image stabilised methods[17] as well as testing using a tablet perimeter.[18] One study of high-risk AMD patients who undertook home monitoring of retinal function with a smart device found reasonable short-term compliance (55% over 2 months) and returned results comparable to in-clinic microperimetry testing with the Macular Integrity Assessment device (MaIA, CenterVue, Padova, Italy).[19,20] These findings imply that tablet devices are suitable platforms for home-monitoring AMD and can yield similar outcomes with greater regularity than would be feasible for clinic-based tests. In particular, the high frequency that can be achieved with home testing might reduce testing noise thereby exposing real changes in RS earlier.[16,21]

The iPad (Apple, Cupertino, U.S.A.) is an inexpensive, portable tablet device that can be used for testing vision. The Melbourne Rapid Fields-macular (MRF-m) iPad app is capable of measuring thresholds across the central visual field[22,23] and is an appealing test for home monitoring applications due to its ubiquitous availability and audio feature which allows audible guides for patients in completing the test. Our group recently investigated the application of MRF in the home monitoring of glaucoma patients where we found a weekly compliance of 72% over a 6-week period.[24] Given this promising result, we wished to evaluate the application of home monitoring on a weekly basis to patients with high-risk early stages of AMD. AMD typically affects people aged 50 and over, thus there could be technological challenges in operating the application. Although daily testing might achieve high compliance rates,[15] a weekly schedule was adopted as it is the recommended test frequency for the Amsler grid. Furthermore, the demands of contemporary daily living

might impede compliance to undertake regular testing or, distractions in the home could yield poorer outcomes than those found in clinical settings. Both aspects would challenge the capacity of home monitoring to detect early changes in macular function in people with AMD.

In this study we investigated the use of a home monitoring tool, the MRF-macular (MRF-m) iPad application, which permits the testing of RS across the macula visual field. We aimed to consider whether participants with iAMD were compliant to weekly testing in the short term, and to understand possible barriers to compliance. We also investigated the concordance of the home monitoring results with the same test performed in clinic and to the standard in clinic test of RS, the MaIA microperimeter.

Methods

This single-centre, longitudinal, observational clinical study was approval by the Royal Victorian Eye and Ear Hospital (RVEEH) ethics committee (AMD: HREC 95/238H/15). All experiments were conducted in accordance with the tenets of the Declaration of Helsinki and informed consent was obtained from all participants prior to participation.

Inclusion criteria

Participants diagnosed with iAMD were recruited from the Macular Research Unit (MRU) at the Centre for Eye Research Australia. Inclusion criteria were diagnosis of intermediate AMD (bilateral large drusen), visual acuity better than 20/40 (6/12), the ability to understand English instructions as provided by the iPad audio prompt, and access to their own iPad 3 or newer with broadband connection. Patients with any evidence of late AMD (geographic atrophy or neovascular AMD) were excluded as were those who had undergone

eye surgery within the past 6 months. All participants had extensive experience with past microperimetry testing on the MaIA due to participation in other Macular Research Unit (MRU) AMD research studies (at least 6 exposures).

Melbourne Rapid Fields iPad application

The MRF-macular (MRF-m) application requires an iPad (version 3 or newer) with retina display running iOS 8 or newer. (Note: the software has been modified to work on an iPad mini given the several participants had these devices). The visual field (VF) test uses a 33-point, size-scaled, radial grid in the central 9.5 degrees with spot-size increasing with eccentricity to maintain constant threshold and variability (Figures 1B, 1C). MRF-m implements a 3-step Bayes predictor for threshold coupled with a neighbourhood logic that identifies unexpected values and adds extra points in adjacent regions to confirm a defect.[23] The test pattern in the MRF-m test (eccentricity and radial angulations of stimuli) was designed to test over a similar pattern as does the MaIA microperimeter which was used during the clinical visits, however, the MRF-m adopts a brighter background luminance (5 cd/m^2) compared to the MaIA (~1.3 cd/m^2) . Luminance control was standardised by using a common gamma correction, as outlined previously.[22,23,25] In fact, our calculations and, the screen calibrations of others,[26] find that as variations in screen luminance affect both the background and target, they have minor impact on target contrast and should not impact clinical application. Participants were guided through the test by tablet generated audio commands wearing their habitual near correction at 33cm. Reliability indices were determined throughout the test using false positive (FP) and false negative (FN) checks (≤25% considered reliable). The MRF-m uses a volley method with high intensity sampling for false response monitoring compared with the MaIA where a more regular sampling pattern is adopted. This test did not implement fixation monitoring. The fixation target is

automatically made larger in cases with reduced acuity (< 20/60 or 6/18) to facilitate fixational stability, although the inclusion criterion meant that this option was never utilised.

Test protocol

The schematic in Figure 2 details the timeline for this study. Because the MRF-m had never been used for testing AMD cases, our experimental design compared the MRF-m in-clinic (MRF_c) against standard clinical assays (MaIA) where both were administered by a clinical assistant. We also compare the results from home monitoring (MRF_h) which were obtained monocularly with audio guidance alone, to the clinical assays. At the first clinical visit (Clinic 1, Figure 3), patients were introduced to the MRF-m tests with the supervision and guidance of a clinical assistant. Note that all clinical MRF-m tests were performed with the participant's own iPad after the clinical assistant had downloaded the app. These were used as learning trials with opportunity given for the participant to ask questions about logging on, conducting, and saving test results. The participant was then asked to obtain baseline VF tests on both eyes (MRF_C) in the presence of audio and minimal input from the clinical assistant, although any questions were answered again on completion. Baseline retinal sensitivity assessment was also conducted with a MaIA microperimeter. A second clinical visit (Clinic 2, Figure 2) took place at the participant's next scheduled review (6 months later), where MaIA and MRF-m were repeated with supervision. In between clinic visits, participants were asked to home monitor their macular function on a weekly basis (every 7 days ±24 hours) using MRF-m (MRF_h). A missed test reminder was sent to any participant who had not submitted a home-based test 14 days after the expected time or after a missed final test (Home 6).

Reasons for withdrawal or exclusion

Participants who did not return a single test from home were considered to have withdrawn from the study and those who did not achieve 6 tests from home within a 6-month study window were excluded from analysis. At their next clinical visit (Clinic 2) these subjects were asked to identify why they withdrew or did not comply to the request for 6 home tests using one of the following options as the main cause:

- MRF-m device too difficult to use
- Participation in the trial to be too much effort
- IT logistical reasons
- Deterioration in other health status and/or competing medical care
- Not interested/lack of motivation
- Competing life demands

IT logistical issues included internet connectivity issues, difficulty updating the iPad operating system or MRF-m application when required, testing the wrong eye and failure to save test results online.

Data analysis

VF indices obtained from home monitoring were compared to standard in-clinic results by T-test and bootstrap.[27,28] Ninety-five percent confidence limits of group data were established by performing 1000 bootstrap samples. Data are shown as mean ±standard deviation.

MRF-m did not track the participant's fixation thus reliability was estimated from the false positive (FP) outcome (FP <25% were considered reliable given the volley sampling).

Results

73 participants and one-hundred-and-forty-six eyes that met the inclusion criteria were enrolled into the study. The mean age was 70.7 ±7.0 years and 81% were female (Table 1). All eyes exhibited evidence of large drusen (>125µm) given the iAMD stage, confirmed by a retinal specialist.

All participants were requested to undertake 6 at-home vision examinations using the MRF-m application at regular 1-week (7 days +24 hours) intervals and in cases where a test result was not received after 2 weeks a 'missed-test' reminder was sent by email. In the analysed group, only 55% of all test results were conducted within a 1-week interval and 74% within 2 weeks, before a reminder was sent (Table 2). Approximately one quarter (26%) of all tests were performed after the reminder. The median inter-test duration over the entire period was 8 days [IQR: 7 to 17 days].

Fourteen participants were not analysed (Figure 3) comprising n=9 (18 eyes) who withdrew from the study and n=5 (10 eyes) who performed only one test at home. Reasons given for withdrawal were information technology (IT) logistical reasons (3 people, 33%), the perception that too much effort was required for participation in the study (3 people, 33%) and competing life demands (3 people, 33%) (Figure 4A). The main reasons frustrating regular compliance, in those who did perform some tests, but did not perform the 6 home exams, were a lack of motivation (2 people, 40%) and IT logistical issues (2 people, 40%) (Figure 4B).

Representative visual field results performed at home on the MRF-m from two iAMD participants are shown in Figure 5.

Home monitoring vs MaIA

The average test time for the full threshold MaIA protocol of 37 test locations in-clinic was 5.3 ±0.3 minutes per eye. The MRF-m (33 test locations) was significantly faster compared to the MaIA at 1.7 ±0.4 minutes at home (t=91.07, df=117, p<0.05, Figure 6).

MRF_h exhibited a significantly higher RS than MaIA (MRF_h: 28.9 [1.6] dB, MaIA: 25.7 [2.2] dB, t=19.3, df=117, p<0.05, Figure 7A, Table 4). When considering the pattern standard deviation (PSD) which allows for differences in RS, no significant difference was found between the MRF-m at home and the MaIA (MRF_h: 2.2[2.1] dB, MaIA: 2.5[0.9] dB, t=1.87, df=117, p>0.05, Figure 7B, Table 4).

At home (voice guided) vs in clinic (supervised) outcomes

In the absence of clinical supervision, there was no significant difference in test times at home to time in the clinic (MRF_h: 1.7 ±0.4 minutes, MRF_c: 1.8 ±0.4, t=0.97, df=209, p>0.05, Figure 8).

There was no significant difference between the RS recorded at home compared to in-clinic with the MRF-m (MRF_h: 28.9 [1.6] dB, MRF_c: 28.9 [1.4] dB, t=0.21, df=209, respectively p>0.05, Figure 9A, Table 4). PD recorded from unsupervised MRF-m testing at home was not different to supervised clinical testing in-clinic (MRF_h: 2.2[2.1] dB, MRF_c: 2.3[1.5] dB, t=0.41, df=209, p>0.05, Figure 9B, Table 4). The FP rate (3.2%), FN rate (1.0%) and Reliability (94%) of MRF_c was not significantly different from that found at home (t=2.31, df=6, p>0.05, Table 3).

Discussion

Home monitoring of visual field in high-risk AMD individuals allows for more frequent testing which has the potential to expose changes in function earlier than waiting for a routine clinic appointment, or by individuals noticing a change in their vision serendipitously, if not regularly checking with other methods. The MRF-m iPad application facilitates VF testing of the macula region at home on a device, which is becoming more and more familiar to individuals over the age of 50. In doing so, it affords an opportunity to improve home monitoring.

This study set out to establish compliance to a request for weekly home monitoring with the MRF-m in patients with iAMD. Although we requested participants to perform the test every 7 days, this only occurred in just over 50% of tests, with 75% of tests performed by 14.3 days (third quartile) and most (90.4% of tests) performed 2 weeks after a reminder (Table 2). These findings are comparable to those reported from a 2-month trial (55% compliance to weekly testing) where participants were asked to perform weekly home monitoring of their macula VF with weekly reminders sent in that study. Given the similarity in outcomes, and despite the different reminder timings, exact timing of reminders appears to have little impact on compliance to weekly testing but does appear to increase overall test returns (from 50% to 90%). Although weekly compliance was less than optimal, home monitoring with automated reminders could still be beneficial for the detection of change in macular function that would prompt an unscheduled clinical review.

A pilot trial using a hand-held, smart phone device (myVisionTrack) over 4 months reported 84% compliance to daily testing and 98% to weekly testing in 147 patients with AMD (>75 years old).[15] On the other hand, patients using the Notal Foresee Home device over a longer term (1.4 years) found a modest compliance of 48%,[9] similar to that found in

our trial. These past works indicate that patient compliance to regular and frequent self-monitoring of visual function at home is similar over an assortment of devices and testing approaches. Having noted the limitation in compliance and irregular test result submissions, it needs to be recognised that home monitoring has the capacity to return a greater number of test results, compared with 6-monthly clinical reviews. The higher frequency of results should serve to identify the time of any change earlier, if the tests are as sensitive as the in-clinic tools and reduce the coefficient to repeatability (see Table 5, MRF_c (2 tests, CoR=3.0 dB) vs MRF_h (6 tests, CoR=1.8 dB)), thereby improving the prospect of detecting early change with home testing, even in cases with less-than-optimal testing frequency.

Given the finding of a modest level of compliance in our study it is informative to learn what impact this might have on health outcomes. A study that considered "Home monitoring of chronic disease for aged care" explored the benefits of self-monitoring in 100 participants with high-risk cardiovascular disease, diabetes, or respiratory disease. User compliance to daily home monitoring of these serious systemic conditions using a purpose-built device was 63%.[29] Despite this modest compliance rate in the presence of serious disease, it was found that there was a 46% reduction in healthcare costs, 53% reduction in hospital admissions, and a 40% reduction in mortality over the 16-month self-monitoring period compared to standard clinical reviews.[29] We feel that similar health benefits will flow in the case of AMD home monitoring of RS but need a long term study to consider this issue fully.

In our current study we find IT logistic issues had a major role in restricting compliance to the requested testing frequency. This was despite the participant being able to use their own device, already having an internet connection at home, and having the study coordinator, able to be contacted by phone during business hours, to help resolve

issues. Specifically, the main IT issue that we identified involved inability to update the operating system (iOS). Compliance might be increased by improving training on the use of tablet devices and by designing a user experience where participants do not find it 'difficult to use' or to 'lose motivation' during the trial. Deterioration in health and competing life demands also hampered compliance, with both factors beyond the control of study coordinators, implying that ongoing, long term home monitoring will prove challenging for some people.

An important factor to consider with home monitoring is the reliability of at-home examinations made in an environment prone to distraction. In the absence of a clinical assistant, the participant must rely on programmed audio commands at home for encouragement to finish the test and for feedback on fixation whilst performing a test. A study that compared patient preference to the presence of; a human clinical assistant, a humanoid robot, audio instructions from a computer speaker and no feedback during vision testing, found that older test subjects preferred having a human assistant present but there was no greater preference for a humanoid robot over an audio instruction set from computer speakers.[30] In our implementation, despite the reliability being better in the presence of a clinician (FP: MRF_c 3.2% vs MRF_h 4.3%, $p<0.05$ Table 3) we find excellent reliability in the at-home AMD group who return average FP rate of 4.3%, a FN rate of 2.5%, and 96% of all results as reliable (Table 3). The lower FP rate found with the MaIA likely reflects the different methods used to sample these indices in the two devices; the MRF-m uses a volley method with high intensity sampling whereas the MaIA employs a more regular sampling pattern. In our trial, reliability remained similar over the 6 study weeks, implying that learning and familiarity to the test with successive home monitoring trials, had little or no impact on reliability. Even though the MRF-m lacks eye tracking and fixation

monitoring, its concordance to MaIA data, which is achieved with eye tracking and retinal stabilisation, and the MRF-m indicates that subjects can be reliable fixators for the test period (90-120s) needed for MRF-m.

Visual field results obtained from weekly home monitoring were compared to the MaIA microperimeter which is the current clinical standard. The RS returned from the home monitoring was approximately 3 dB greater than that found with the MaIA (Table 4). The PSD which allows for differences in RS, showed no significant difference between at home from the MRF-m versus in clinic with MaIA. This observation provides indirect evidence that the two tests are measuring similar attributes, albeit at different levels of RS. These findings are consistent with those of others [19,20] who have previously found that a tablet perimeter returns comparable outcomes to routine microperimetry when a common background luminance is adopted. The difference of our study from these earlier trials is that the early trials replicated the MaIA test environment and used a low background luminance (~1.3 cd/m^2) whereas we adopted a brighter background (5 cd/m^2) which should yield better outcomes in elderly patients as they develop age-related cataract or miosis. Our brighter background also likely explains the 3 dB difference in sensitivity that we find between the two devices.

The absence of a clinical assistant did not affect visual field outcomes or testing times obtained from home in our cohort of iAMD participants. The volume of tests that can potentially be acquired via home monitoring in between clinical reviews means that isolated instances, where distraction results in reduced RS, can be filtered out. Testing algorithms can identify outliers and confirm change with repeat testing before electronically alerting patients to arrange a clinical review.

Potential limitations of MRF-m are that the viewing distance (33 cm) was not ensured, that fixation was not monitored, and that unrestrained viewing was adopted by our participants. It should be noted that the tablet audio instructs the participant to set and maintain a viewing distance of 33cm prior to commencing an exam. Although patients were shown how to achieve and use the proper viewing distance it is possible that they erred at times. Likewise, accuracy of fixation was not monitored with the tablet device, but it was with MaIA as this test applied retinal stabilisation. Despite the presence of these factors that could make results less robust, the concordance that we found between at home testing with clinical outcomes (Table 4) implies that patients fixated and performed reliably over the short test times of the MRF-m, in the presence of the audio prompts. However, we believe that fixational instability or viewing distance errors can result in less accurate test outcomes and propose that any advice regarding action needing to be taken by the participant, should not be made based on a single test result.

Another limitation of this study is that our participants were well versed in clinical trials as they were patients of an active AMD research clinic. This may mean that 'real world' applications of home monitoring with MRF-m may yield less favourable outcomes. However, we do not believe that this will be the case as we have reported similar outcomes in a glaucoma cohort that did not have a history of clinical trial exposure.[24]

Several methods are presently available for monitoring iAMD patients and these include visual acuity, hyperacuity, Amsler grid and DLS with free-viewing perimetry. Loss of visual acuity has a poor correlation with anatomical changes observed in early AMD[17] and the Amsler grid has a reported sensitivity of 30% for detecting choroidal neovascularisation (CNV).[10,11] Hyperacuity has potential limitations for near viewing given that many past experiments have been conducted at viewing distances of 1-13m.[31-34] Thus it is unclear

whether threshold performance will transfer to the 33-40cm viewing distance required for smart devices at near. Furthermore, the relationship of hyperacuity loss to AMD pathology is unclear. On the other hand, DLS has been shown to correlate to AMD pathology as identified with SD-OCT.[17] Image stabilisation will not affect the detection of pathology but will reduce spatial uncertainty and possibly threshold variability. Free-viewing DLS (lack of head and chin stabilisation), as achieved with tablet methods, is correlted with AMD pathology and when done in the home gives outcomes similar to microperimetry even in the absence of fixation monitoring.[18] The benefits of retinal stabilisation are less evident in clinical implementations where a large number of outcomes can be averaged to reduce variability.[35]

Our study group comprised of iAMD participants with good vision (better than 6/12) and who did not have scotoma. There does not appear to be any difference in RS between image stabilised methods and free-viewing perimetry[20] in patients with iAMD. Our data confirms this association by finding a moderate correlation between the RS recorded at home compared with in-clinic MaIA (r=0.42) indicating reliable assays in the absence of fixation monitoring. It is worth mentioning that the MRF-m audio provides regular prompts for patients to fixate correctly and has a large fixation cross that becomes available to the patient to stablilise fixation once visual acuity drops below 6/15. The presence of a scotoma, however, may reduce the capacity of MRF-m to monitor patients, an issue in need of further research.

In this clinical trial, we show that VF results recorded using the MRF-m, at home by patients self-monitoring in the presence of audio prompts, produce results comparable to those returned from standard in-clinic tests achieved with the supervision of clinical assistants. Long-term clinical trials are needed to determine whether useful information on

disease progression can be detected by home monitoring with the MRF-m presented on a tablet device and these trials are presently underway.

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Figure captions

Figure 1. Details of the MRF-macular test used in this study. **1A.** The visual field test. Tablet generated instructions asked the participant to fixate centrally and respond by tapping the red touch zone each time they saw a spot of variable brightness. **1B.** The test pattern for MRF-m has 33 locations within the central 9.5° with spots scaled in size with eccentricity (cartoon of size scaling is shown in panel B).

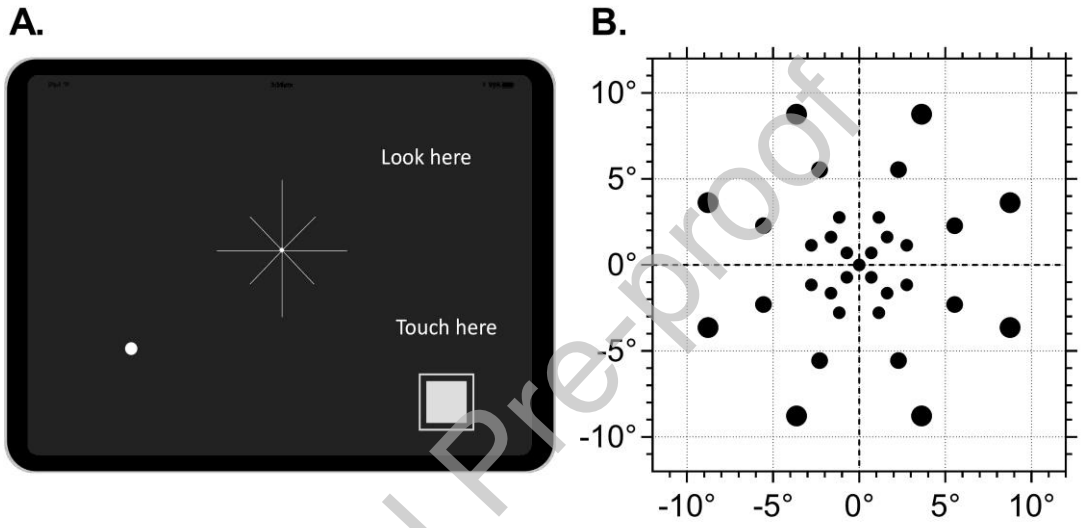

Figure 2. Test protocol. Participants attended a baseline clinic session (Clinic 1) where they were tested with BCVA and a MaIA microperimetry test and received an *in-clinic* MRF-m training session with a clinical assistant. A test was performed with audio guidance and any issues relating to operating the device or doing the test were clarified. Participants were then asked to perform weekly (every 7 days) testing for 6-weeks in the presence of audio instructions. The second clinic visit (clinic 2) was a routine review (6 months) and all clinical tests were repeated.

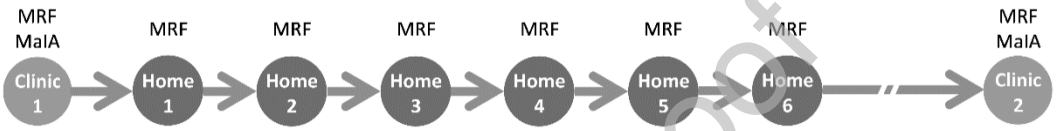

Figure 3. CONSORT diagram for short-term home monitoring trial detailed in the text. Results are expressed as participants[eyes]. Fifty-nine participants returned 6 home exams and were included in the analysis. Fourteen participants were not analysed (Figure 3) either because they withdrew from the study or returned fewer than 6 exams from home (excluded).

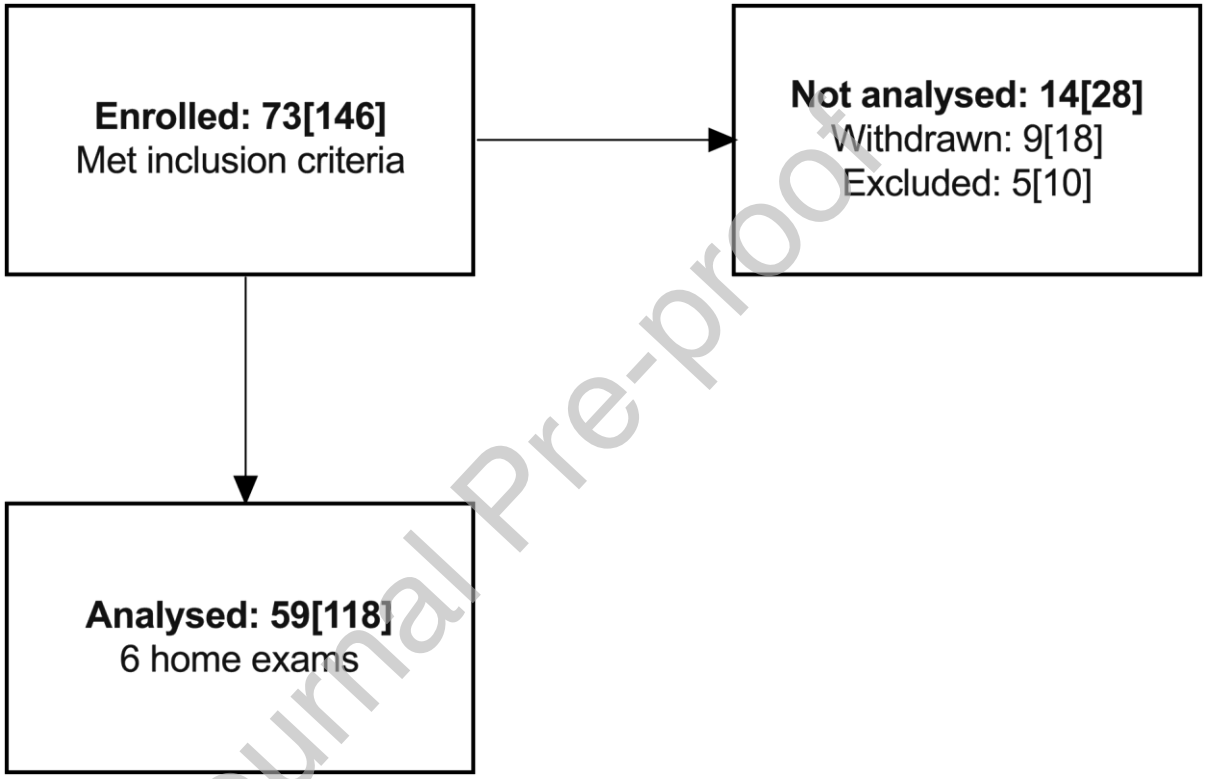

Figure 4. Reasons for withdrawal and non-compliance given by 14 participants. **A.** Reasons for withdrawal (n=9 participants). **B.** Reasons for non-compliance to 6 home exams (n=5 participants).

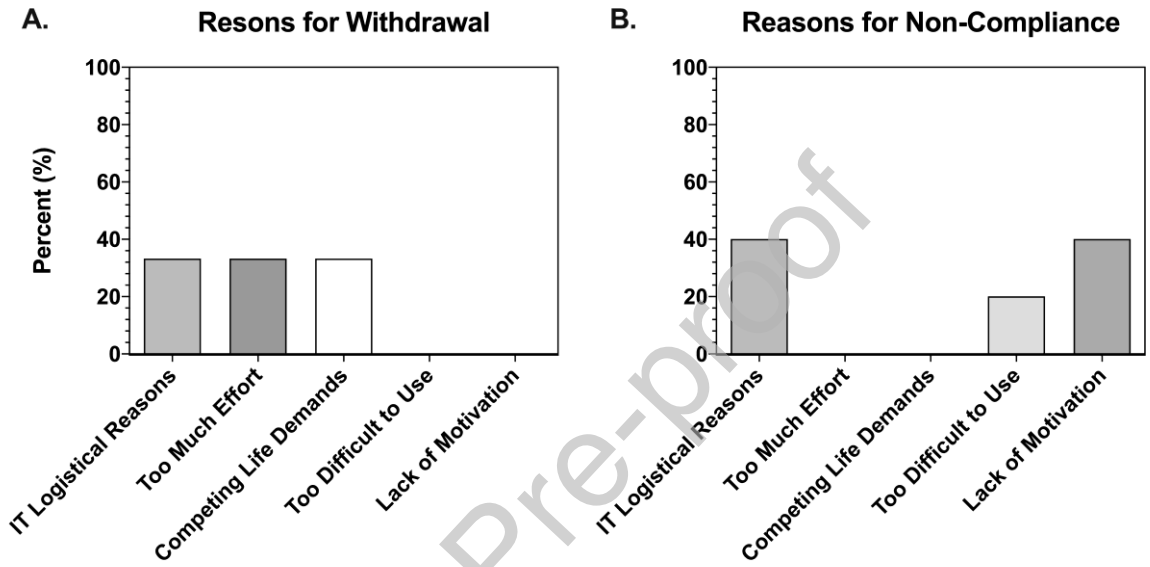

Figure 5. A. A 83-year-old male with iAMD. **B.** A 73-year-old female with iAMD showing outcomes returned by *at-home* testing (results on left are for test 6). **Numeric plot:** Left panel, shows raw point-wise sensitivities (dB) as returned by MRF-m. Note how the neighbourhood logic has added an extra test point along the lower vertical meridian (patient in A) and upper right quadrant (patient in B). **Grey scale:** A pictorial representation of the patient's retinal sensitivity. **Test details:** Reliability, test duration and global indices returned from MRF-m for test 6. **RS trend:** Average retinal sensitivity over study period. Left unfilled circle (C1) is first in-clinic MRF-m result. Right unfilled circle (C2) is second in-clinic MRF-m result (6-months later). Filled circles show the retinal sensitivity returned by self-monitoring at home. **FP:** False positives. **FN:** False negatives. **RS:** Retinal sensitivity. **PD:** Pattern defect.

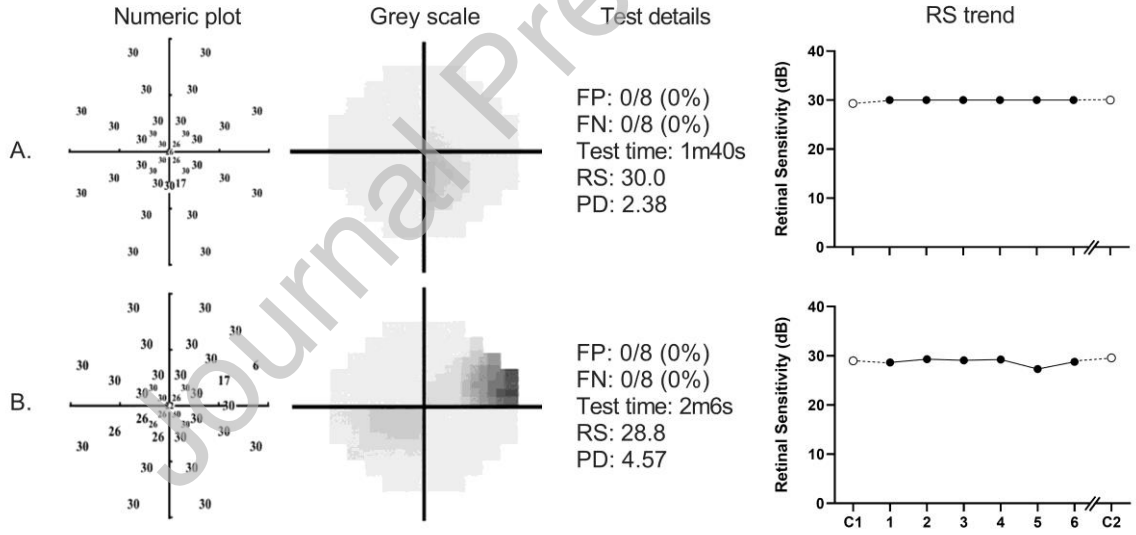

Figure 6. Time needed to complete the MRF-m at home (MRF_h) and MaIA in the clinic.

The reliability of MRF-m visual field results obtained from at-home, under the guidance of app-generated audio prompts was investigated by comparing global reliability indices from the MaIA and MRF-m. An exam was considered reliable if the FP rate was ≤25%. Of the 694 home results submitted, 4% were unreliable (Table 3). The rate of FP errors at-home was acceptable but double that of supervised MaIA testing (MRF_h: 4.3%, MaIA: 1.8%, t=5.24, df=6, p<0.05, Table 3).

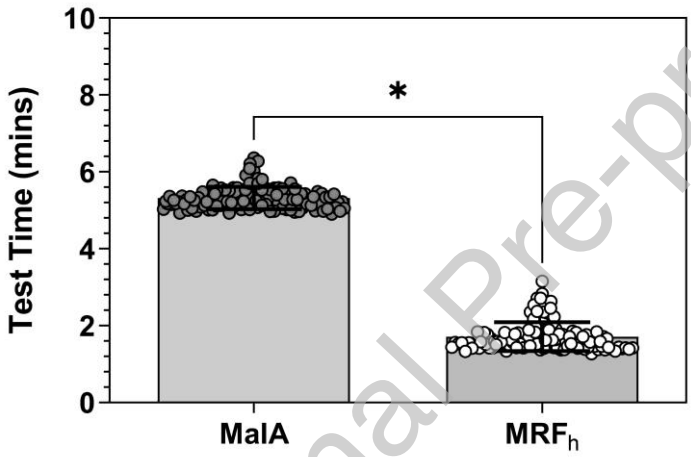

Figure 7. Comparison of visual field global indices in-clinic (MaIA) versus at-home (MRF_h) for AMD cases (n=118 eyes). Clinic mean is the average of 2 exams, home mean is the average of 6 exams. **A.** Mean sensitivity (dB). **B.** Pattern standard deviation (PSD, MaIA, dB)/Pattern Deviation (PD, MRF, dB)

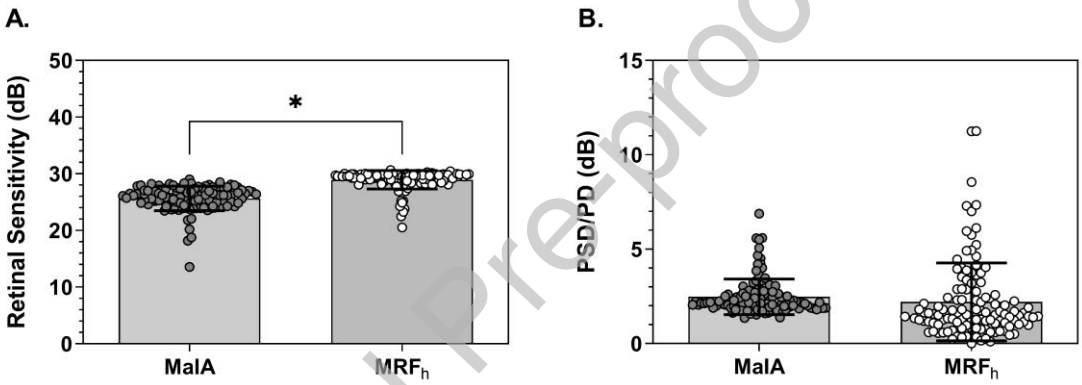

Figure 8. Time needed to complete the MRF-m at home with a virtual clinical assistant (MRF_h) and in the clinic under supervision (MRF_c).

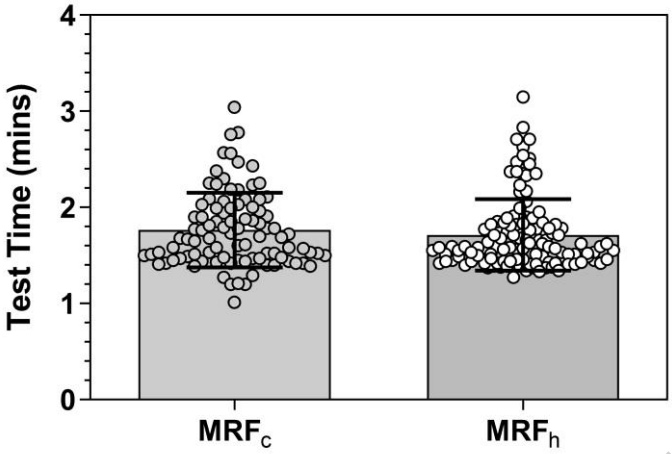

Figure 9. Comparison of visual field global indices when obtained with supervision in-clinic MRF-m (MRF_c) versus unsupervised at-home (MRF_h) for AMD cases (n=118 eyes). Clinic mean represents the average of 2 exams. Home mean represents the average of 6 exams. **A.** Mean sensitivity (dB). **B.** Pattern deviation (dB).

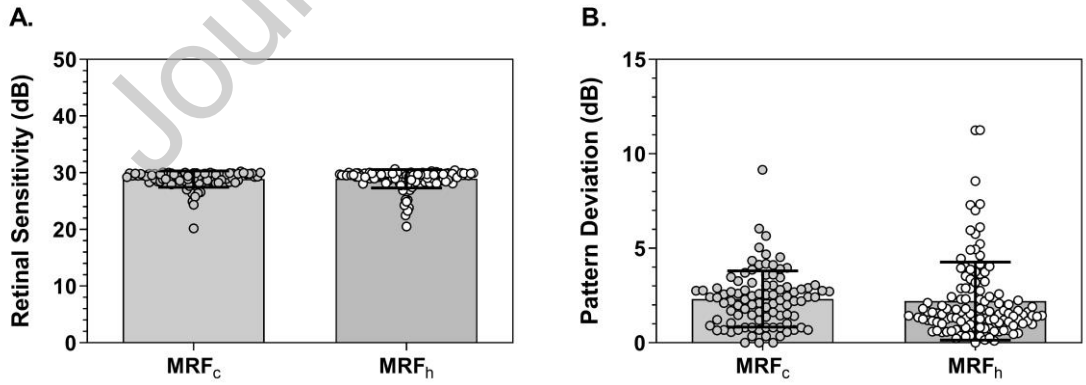

TABLE 1. Patient demographics

	Total group	Analysed group
Test subjects, y [eyes]	73 [146]	59 [118]
Age, y [min-max]	70.5 [55-84]	71.1 [55-84]
Sex (% female)	82	81

All AMD patients were diagnosed with bilateral intermediate AMD (drusen >125µm in both eyes).

TABLE 2. Frequency of home monitoring

Next test (days)	Test 2 (%)	Test 3 (%)	Test 4 (%)	Test 5 (%)	Test 6 (%)	All (%)
0-8	74.6	44.1	55.9	55.9	45.8	55.3
9-15	6.8	22.0	25.4	18.6	20.3	18.6
15-22[a]	1.7	18.6	8.5	6.8	11.9	9.5
22-29[a]	1.7	5.1	3.4	5.1	13.6	5.8
>29[a]	15.3	10.2	6.8	13.6	8.5	10.8

Frequency of home monitoring reports the percentage of participants performing exams after specific periods. Test 2 refers to the next test after the first baseline from home. [a] identifies period after a missed-test reminder was sent.

TABLE 3. Reliability of results obtained from home monitoring and the MaIA.

	Test	1	2	3	4	5	6	All
FP rate (%)	MRF_h	3.2	4.6	5.1	4.8	4.3	4.1	4.3
FN rate (%)	MRF_h	3.5	1.8	4.3	2.1	1.9	1.5	2.5
Reliable (%)	MRF_h	95	98	93	97	97	97	96
FP rate (%)	MaIA	1.7	1.8	--	--	--	--	1.8
FP rate (%)	MRF_c	3.1	3.3	--	--	--	--	3.2
FN rate (%)	MRF_c	0.9	1.1	--	--	--	--	1.0
Reliable (%)	MRF_c	98	89	--	--	--	--	94

FP = False positive. FN = False negative. %FP and %FN were calculated by dividing the respective number of FPs and FNs by the total number of tests returned. Reliability criteria: ≤25% FP and ≤25%. A test was deemed unreliable if one or both reliability indices were >25%.

TABLE 4. Repeatability for visual field testing in AMD

Test	Index	Mean [SD]	Bias (vs MRF_h)	CoR (dB)
MaIA	RS	25.7 [2.2]	3.3	5.9
MRF_h	RS	28.9 [1.6]		1.8
MRF_c	RS	28.9 [1.4]	0.4	3.0
MaIA	PSD	2.5 [0.9]	-0.3	2.8
MRF_h	PD	2.2 [2.1]		2.2
MRF_c	PD	2.3 [1.5]	-0.2	3.9

MRF_c = MRF-m in-clinic. MRF_h = MRF-m at-home. RS = retinal sensitivity. PSD = pattern standard deviation of MaIA visual field. PD: pattern deviation of MRF visual field. Bland-Altman bias = MRF-MaIA (dB). CoR = coefficient of repeatability. *bootstrap 95% confidence limit.