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Clinical evaluation of the MPS 9000 Macular Pigment Screener

Hannah Bartlett, Louise Stainer, Sandip Singh; Frank Eperjesi; Olivia Howells

Ophthalmic Research Group, School of Life and Health Sciences, Aston University, Birmingham B4 7ET,
UK

Corresponding author: Hannah Bartlett

H.E.Bartlett@aston.ac.uk

Tel: 0121 204 4182

Fax: 0121 204 4048

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ABSTRACT

Background/aims

The MPS 9000 uses a psychophysical technique known as heterochromatic flicker photometry to measure macular pigment optical density (MPOD). Our aim was to determine the measurement variability (noise) of the MPS 9000.

Methods

Forty normally sighted participants who ranged in age from 18 to 50 years (25.4 ± 8.2 years) were recruited from staff and students of Aston University. Data were collected by two operators, LS and SS, in two sessions separated by one week in order to assess test repeatability and reproducibility.

Results

The overall mean MPOD for the cohort was 0.35 ± 0.14 . There was no significant negative correlation between MPS 9000 MPOD readings and age ($r = -0.192$, $p = 0.236$). Coefficients were 0.33 and 0.28 for repeatability, and 0.25 and 0.26 for reproducibility. There was no significant correlation between mean and difference MPOD values for any of the four pairs of results.

Conclusions

If MPOD is being monitored over time then any change less than 0.33 units should not be considered clinically significant as it is very likely to be due to measurement noise. The size of the coefficient appears to be positively correlated with MPOD.

INTRODUCTION

Yellow pigmentation of the macular region was first documented in 1782, and was attributed to the xanthophyll group of carotenoids much later in 1945.¹ Two slightly different chemical structures have been found, and termed lutein (L) and zeaxanthin (Z).² It has been suggested that xanthophylls, in the form of macular pigment (MP) play a similar role in humans as in plants, as antioxidants and screeners of high-energy blue light.³ The presence of MP in the rod outer segments and retinal pigment epithelium (RPE)⁴ is suggestive of a reactive oxygen species-quenching function and the presence of MP in the inner retinal layers⁵ supports a photoprotective role. The absorbance spectrum of MP peaks at 460 nm and it is purported to act as a broadband filter, reducing the sensitivity of the macular region to short wavelength light which is most damaging in the 440 to 460 nm range.⁶

The human retina, and more specifically the macula, is the single richest site of carotenoid accumulation within the human body. Post-mortem retinal analysis has shown that the total L and Z concentration at the macula is 100 times greater than at the peripheral retina. The assumption that retinal L and Z is of dietary origin, is supported by fundus photographs of rhesus monkeys on carotenoid-depleted diets that demonstrate an absence of MP.⁷

Recently, instruments have been developed for the measurement of MP optical density (MPOD) in the clinical environment. These instruments employ a psychophysical technique called heterochromatic flicker photometry (HFP). The MPS 9000 (also known as the M:Pod and the QuantifEYE, Topcon, Topcon House, Kennet Side, Bone Lane, Newbury, Berkshire, RG14 5PX, UK), adopts a novel approach to measurement of MPOD by HFP. Instead of the subject responding to minimal or no flicker, as with the MacusScope™⁸, they respond to the appearance of flicker as the alternation rate is decreased at 6 Hz per sec from a starting level of 60 Hz⁹. This is above the critical flicker fusion frequency for the test conditions and therefore subjects do not perceive any flicker initially. Rather than the radiance of one wavelength being adjusted by the observer, a sequence of blue-green ratios is used and these are inverse-yoked to ensure that overall luminance remains constant. The device determines each observer's sensitivity to flicker prior to the main part of the test.

It is important to determine the measurement variability, or measurement noise, of the MPS 9000 in order to be able to identify what a clinically significant change in MPOD would be when using this instrument. This is of particular interest since the MPS 9000 might be used to monitor the longitudinal effect of nutritional supplementation or dietary modification on MPOD. There has been a significant rise in the use of nutritional supplements by people living in the UK, as well as other Western populations over the past ten years¹⁰, and it has been reported that 25 % of the UK population use complementary and alternative medicine¹¹. Macular pigment measurement devices are being marketed towards clinicians as a way of monitoring the effect of lutein supplements on MPOD. The aim of this study was to assess the repeatability and reproducibility of the MPS 9000 when used in a clinical setting.

MATERIALS AND METHODS

Setting

A clinical practice setting within the Ophthalmic Research Group, School of Life and Health Sciences at Aston University, Birmingham, UK.

Study Population

Forty normally sighted participants were recruited from staff and students of Aston University. All participants gave informed consent to take part in the study, which was approved by the Institutional Human Ethics Committee. Participants varied in age from 18 to 50 years (mean \pm SD: 25.4 \pm 8.2 years).

Exclusion criteria were; best corrected distance visual acuity (VA) of more than 0.2 log MAR (VA was measured under standard testing conditions using a log MAR chart; retinal disease detected through undilated pupils using a direct ophthalmoscope; abnormal Amsler grid test result; glaucoma; lenticular opacities; prescribed medication associated with changes in retinal function.

Observation procedures

The same room was used for each test for all data collection sessions. When both eyes met inclusion criteria, the right eye was tested; when only one eye was suitable for inclusion, this eye was tested. The test was carried out according to manufacturer instructions.

The eye not being tested was occluded and participants wore their habitual refractive correction (a trial frame and lenses were used when necessary) and were asked to place their forehead in position such that the test eye was centered on the appropriate target within the instrument. The central target is a 1° circular stimulus composed of blue (465 nm) and green (530 nm) LEDs. For the foveal (central) test, the observer looked directly at the stimulus whilst the alternation rate between the blue and green was ramped down from 60 Hz. At the point when they first detected flicker, the observer pressed a response button and this plotted a point on a graph that was visible to the operator on a computer screen. Once the flicker had been perceived, the process started again. The first five responses were used to ascertain the flicker sensitivity of the subject. Based on this, the main part of the test began and the observer responded to a series of green-blue ratios until a V-shaped curve was plotted on the computer screen. The minimum point on the curve corresponded to equiluminance of the blue and green lights. The whole process was then repeated for the peripheral test, where the subject's gaze was directed to a larger target, red in colour and 8° eccentric from the central spot. The difference between the central and peripheral minima determined the MPOD – the larger the difference, the higher the MPOD.

Data were collected by two operators, LS and SS, in two sessions separated by one week. Prior to the first session a trial run was completed, to allow each participant to practice the test. The manufacturers recommend that a short practice test is carried out to familiarise the participant with the technique. In session one, the first test was carried out by LS (LS1) and the second was carried out by SS (SS1). In session two the first test was carried out by SS (SS2) and the second was carried out by LS (LS2). This study design permitted assessment of the test repeatability (LS1 versus LS2 and SS1 versus SS2) and reproducibility (LS1 versus SS1 and LS2 versus SS2). SPSS for Microsoft Windows XP software was used for data analysis. Graphs were produced using SigmaPlot software (version 6) for Microsoft Windows XP.

RESULTS

The four sets of readings (the practice reading was excluded) were averaged for each subject. The overall mean MPOD for the cohort was 0.35 ± 0.14 . The mean individual standard deviation value (excluding the practice reading) for the whole cohort was $0.09 \pm .06$. The mean MPOD reading for females ($n = 32$) was 0.33 ± 0.12 and for males ($n = 8$) was 0.45 ± 0.19 . These mean values were significantly different ($t = -2.393$, $p = 0.0.22$).

Accurate analysis of test-retest data can be achieved using the coefficient of repeatability,^{12 13} which gives the 95% confidence limits for the amount of difference between two sets of results. It is calculated as 1.96 multiplied by the standard deviation of the mean differences between the two sets of data. Test-retest results for the four comparisons are shown in table 1.

	Repeatability		Reproducibility	
	LS1-LS2	SS1-SS2	LS1-SS1	LS2-SS2
Mean difference	-0.06	0.00	-0.04	0.02
Standard deviation of mean differences	0.17	0.14	0.13	0.13
Coefficient of repeatability/reproducibility	0.33	0.28	0.25	0.26

Table 1

The coefficient of repeatability and reproducibility values indicate the amount of change that can occur between readings and still be classed as measurement noise. In other words, using the highest value of the two for repeatability, our data suggests that when the same operator is taking repeated MPS 9000 readings over time, only increases or decreases in MPOD of more than 0.33 units can be classed as clinically significant (see figure 1). Using the highest value of the two for reproducibility, if two different operators are assessing MPOD with the MPS 9000 within the same session, only increases or decreases in MPOD of more than 0.26 units can be classed as clinically significant (see figure 2).

Insert figures 1 and 2 about here.

There is no correlation between mean and difference MPOD values for any of the four sets of results, and no significant negative correlation between MPS 9000 MPOD readings and age ($r = -0.192$, $p = 0.236$).

DISCUSSION

We consider our findings to be useful for eye care practitioners who use the MPS 9000 for monitoring of MPOD over time, or as an outcome measure to assess the longitudinal effect of dietary modification or nutritional supplementation on MPOD. Several large scale studies have used HFP techniques for assessment of MPOD.¹⁴⁻¹⁹ Our average MPOD value in this study was 0.35 ± 0.14 . Other studies have reported average values in normal cohorts of 0.211 ± 0.13 ($n = 280$, age range: 18-50 years),¹⁴ 0.28 ± 0.21 ($n = 280$, age range: 18-50 years),¹⁵ 0.289 ± 0.156 ($n = 46$, age range: 21-81 years),²⁰ 0.319 ($n = 100$, age range: 22-60 years),¹⁶ 0.43 ± 0.23 ($n = 1648$, age range: 53-86 years),²¹ and 0.47 ± 0.14 ($n = 38$, age range: 19-46 years)⁸.

Within our cohort there was no correlation between MPOD and age, although the age range of our cohort was limited and so this result should be treated with caution. This relationship has also been investigated using HFP in other studies; some have reported a positive correlation between the two variables,^{8,20,22} while others reported no relationship.^{15,23,24}

Our reliability results differ markedly from those found by Beatty *et al.*, who reported a coefficient of reproducibility of 0.08 and a coefficient of repeatability of 0.09 for an instrument employing the HFP technique to measure MPOD.²⁰ These differences might be explained by the fact that we used an instrument manufactured for a clinical setting rather than a laboratory based instrument designed for research purposes. The four sets of repeat data were not significantly different when analysed using ANOVA ($F = 1.463$, $p = 0.240$), suggesting no significant learning or fatigue effect. Our MPS 9000 coefficients of repeatability and reproducibility are lower (that is, there is less measurement noise) than those found using the same protocol with the MacuScope™ instrument (Macuvision Europe Ltd, 122 Station Lane, Solihull, B74 6JJ, United Kingdom).⁸ The MacuScope™ employs HFP but requires the

subject to observe flickering stimuli which are comprised of two alternating wavelengths of light, and to identify a 'minimum flicker' point as the luminance ratio of the two wavelengths is reduced. Our coefficients of repeatability for the MacuScope™ (obtained using the same design as for this study) were 0.45 and 0.58 for repeatability, and 0.49 and 0.36 for reproducibility⁸. We believe that the MacuScope™ task is more conceptually difficult than the identification of onset of flicker required with the MPS 9000 and that this explains the reduction in repeatability and reproducibility coefficients when using the MPS 9000 compared to the MacuScope™.

The repeatability of the MPS 9000 has been investigated previously⁹; the authors report a correlation coefficient of 0.97 ($p < 0.001$) for re-test data on 11 subjects. However, in this study, the measurement was repeated five times at the first data collection session, and so we believe that our study, in which participants were allowed just one practice run, provides a more realistic impression of repeatability of the MPS 9000 in a clinical, rather than research, setting.

There have been no large-scale studies looking at the effect of L and Z supplementation on MPOD. The results of several small studies suggest that MPOD can be modified by nutritional supplementation and dietary modification but only for some people. For example, MPOD increased by 4 % to 5 % in eight males supplementing with 10 mg L daily.²⁵ In another study an average increase in MPOD of 19 % was found in people supplementing with spinach (providing 10.8 mg L and 0.3 mg Z) or sweet corn (providing 0.4 mg L and 0.3 mg Z) for up to 15 weeks, although two out of the 13 participants were reported as non-responders because their serum lutein levels increased but their MPOD values did not appear to change, or at least the change was not picked up by the instrument. One participant did not demonstrate any increase in serum lutein or MPOD.²⁶

The MPS 9000 (also known as the M:Pod and QuantifEYE) Macular Pigment Screener is a MPOD measurement device designed for use in clinical practice on naïve subjects. In conclusion, our results suggest that if MPOD is being monitored over time to assess the effect of an intervention, then any

change less than 0.33 units should not be considered clinically significant as it is very likely to be due to measurement noise.

ACKNOWLEDGEMENTS

The authors declare no conflict of interest.

WHAT IS ALREADY KNOWN ABOUT THIS TOPIC

Heterochromatic flicker photometry (HFP) has been used in research environments to assess macular pigment optical density (MPOD). This psychophysical technique is considered to be the gold standard for macular pigment measurement and reported mean MPOD readings in normal eyes range from 0.211 ± 0.13 to 0.47 ± 0.14 . This study is the first to independently evaluate the MPS 9000, which is a commercially available MPOD measurement device that employs HFP and is marketed towards clinicians.

WHAT THIS STUDY ADDS

The mean MPOD value for our cohort was 0.35 ± 0.14 . The largest coefficients were 0.33 for repeatability, and 0.26 for reproducibility. These coefficients are essential for identifying clinically significant change when using the MPS 9000. They are of particular importance since practitioners may be using the MPS 9000 to assess the longitudinal effect of nutritional supplementation or dietary modification on MPOD.

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AUTHORSHIP

All named authors were involved in the conception and design of the study, analysis and interpretation of data, and revising it critically for important intellectual content. All named authors gave final approval of the version published. LS and SS collected the data. HB and OH drafted the article. FE provided training on data collection technique.

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COMPETING INTERESTS

None declared.

LEGENDS

Tables

Table 1: Coefficient of repeatability/reproducibility values for the four data sets.

Figures

Figure 1: Difference in MPS 9000 reading between LS1 and LS2, compared with the mean (n = 38). The mean bias is represented by the solid line, and the 95% confidence limits are represented by the dashed lines.

Figure 2: Difference in MPS 9000 reading between LS2 and SS2, compared with the mean (n = 38). The mean bias is represented by the solid line, and the 95% confidence limits are represented by the dashed lines.

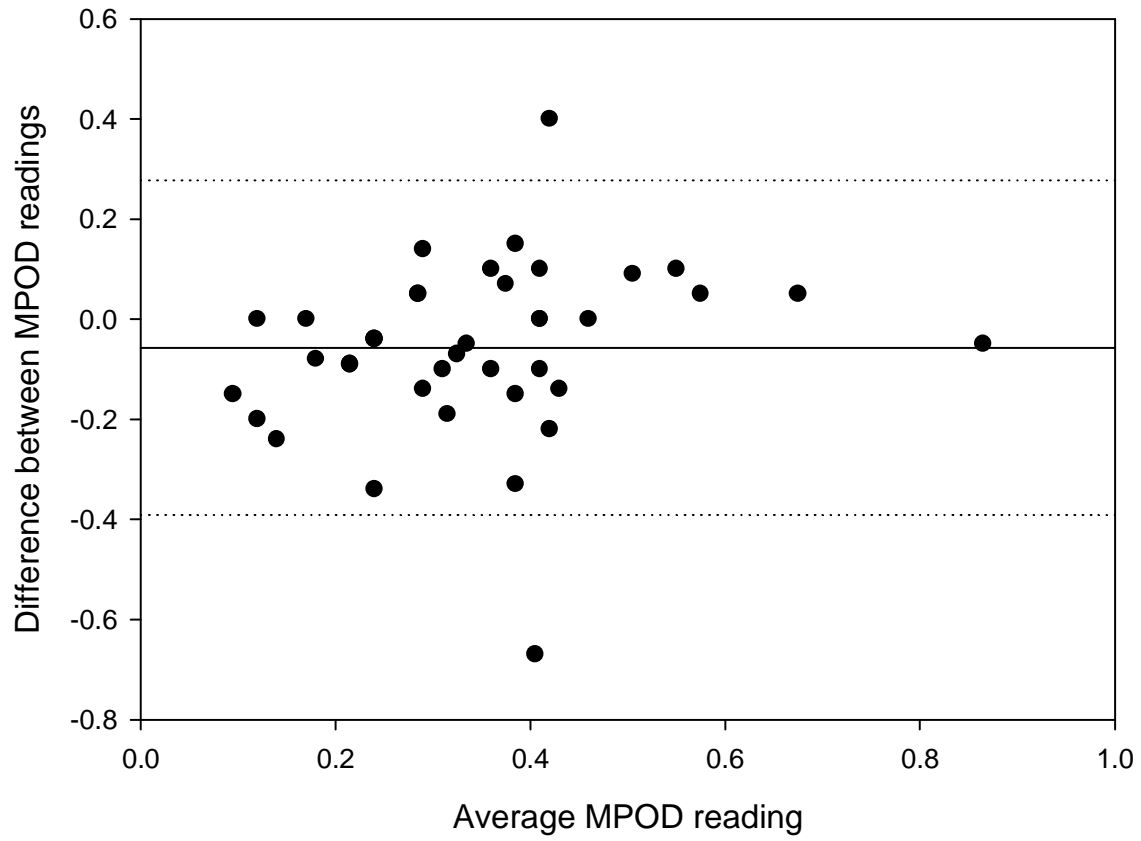


Figure 1

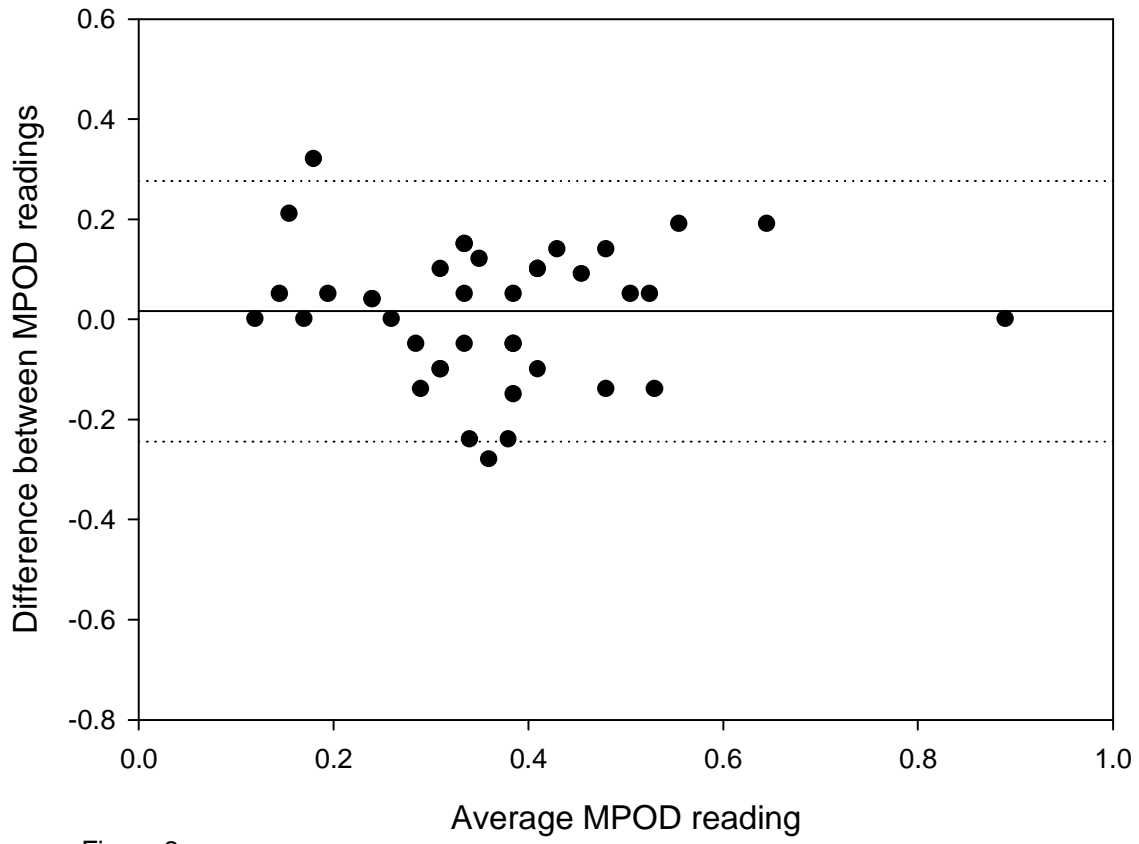


Figure 2