



# Measuring MP in practice

Dr Ian Murray, Dr Maria Makridaki and David Carden present evidence that changes in macular pigment levels with supplementation may be detected by the M-POD instrument

**M**acular pigment (MP) is composed of the retinal carotenoids lutein (L) and zeaxanthin (Z). These compounds are the main components of most ocular supplements now available in optometrists' practices. The justification for the use of supplements rests on the premise that L and Z help to maintain retinal health in old age and the assumption that additional L and Z will be deposited in the retina in response to the supplementation. However, there are persistent reports in the literature that a few patients are non-responders, that is, they may take ocular supplements for many years without increasing the levels of MP in the retina. It is therefore important to distinguish patients who are increasing their MP with supplements from those who, for some reason, do not increase their MP.

It has recently been suggested that commercially available techniques for measuring MP are not sufficiently sensitive to detect an increase in MP following supplementation. Here we present compelling empirical evidence to the contrary; it is clear that when used competently, the Macular Pigment Optical Densitometer (M-POD) is ideally suited to monitoring changes in the MP induced by taking ocular supplements. The data show that, regardless of whether the device is located in a laboratory environment or in private practice, it is easily capable of revealing increases in MP following supplementation.

## Macular pigment

The conspicuous yellow spot centred on the macula in humans and higher primates has now been identified to be composed mainly of the naturally occurring xanthophylls lutein (L) and zeaxanthin (Z).<sup>1</sup> Collectively L and Z are often referred to as the retinal carotenoids, but for many years the yellow spot was referred to simply as the macular pigment (MP). MP also contains an isomer of zeaxanthin, meso-zeaxanthin which is formed in retinal tissue from lutein.<sup>2</sup> The concentration

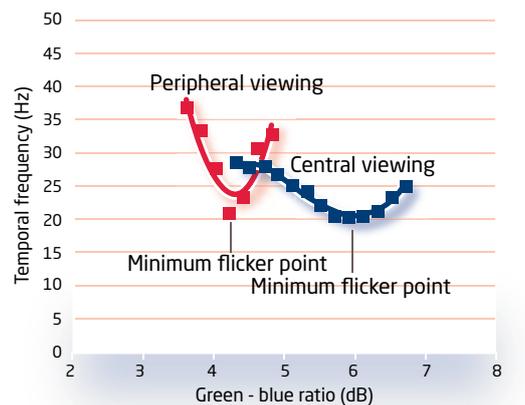


Figure 1 Example data from the M-POD

of L and Z reaches very high levels in the retina and it is thought by many, to help maintain the photoreceptors during the ageing process because of its ability to absorb damaging blue light and its anti-oxidant properties.<sup>3,4</sup> L and Z cannot be synthesised in the body and therefore their presence in the eye relies entirely on direct ingestion from the diet. Individuals who have a healthy lifestyle and follow a healthy diet including fruit, eggs and dark green vegetables have medium to high levels of MP. However it is well known that those who smoke, are obese, and/or have a poor diet have low levels of MP. It is interesting to note that these aspects of life-style are the so-called modifiable risk factors for AMD and that low MP in particular, is a major risk factor for the disease.

## AMD – a management strategy

AMD is set to become a major medical problem. It is extremely common in all the developed countries. Typically around 30 per cent of the over 65s will have some form of the disease. Due to demography it will increase markedly in the next decade.<sup>5</sup> At present the therapeutic options are extremely limited; when formulating a management strategy for AMD, there can be no doubt that prevention is better than cure.

When patients present with early-stage macular disease they are frequently advised that there are few prospects for

improvement and, for the most part, are told to expect a gradual deterioration in their vision. The hallmark of the more common, dry form of the disease is drusen, accumulations of lipoproteins in the macula, (central 25 degrees) of the retina. Drusen invariably appear before any visual symptoms, and of the many types, large, soft confluent drusen are regarded as pathognomic for AMD. By the time they experience reduced visual acuity, patients will have lost large numbers of photoreceptors and have had the disease for many years.<sup>6</sup>

There is a very substantial literature suggesting that high levels of MP may impede or even reverse the progress of AMD.<sup>7,8</sup> MP can readily be augmented by following an appropriate diet or by taking ocular supplements which are high in L or Z. There are now many studies showing a marked increase in MP with this approach. The fact that it is easy to increase MP raises the possibility of a management strategy based on risk reduction centred on enhancing MP, modifying diet and changing lifestyle.

Increasing the MP, especially if it is below normal, is the first step towards mitigating against AMD-related vision loss. Following the onset of supplements and/or a lutein-rich diet, an increase in MP is easily obtained in most observers. Blood plasma levels of L or Z increase within a few days, but the time course for deposition in the retina is much longer. Patience is required by both patient and practitioner, as detectable increases may take 2-6 months and sometimes longer. The subsequent steps in the vision-preservation strategy are equally important, but may be more difficult to implement. In appropriate cases the patient should be encouraged, perhaps with the help of the GP, to embark on a radical change in lifestyle. This will include advice on cessation of smoking, reducing weight, ensuring no cardiovascular abnormalities, controlling cholesterol levels and increasing exercise. These well-known modifiable risk factors will require long-term self discipline and application. Some may argue that discussion of these matters falls outside the remit of optometrists. But



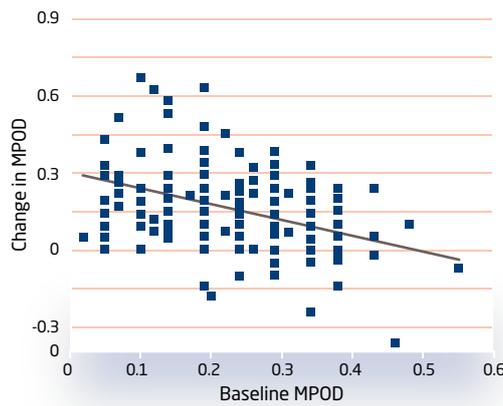
this ignores the powerful psychological impact of patients being able to see a steady increase in their MP. This is often of great importance to the individual concerned and provides encouragement in the other, more challenging strands of the strategy.

The aetiology of AMD is highly complex and it is not possible to predict with certainty that a particular patient will benefit from enhancing their MP. According to the epidemiology, high MP and changes in lifestyle will slow the progress of underlying disease and reduce the risk of extreme loss of sight.<sup>9</sup> It is important not to oversell the benefits of MP, but taking L and Z supplements can be thought of as analogous to a sun-blocker which reduces the risk of UV-related skin damage. Using sun-tan cream does not guarantee protection from the harmful effects of UV and short-wave light, but it does reduce risk. Exactly the same can be said of MP.

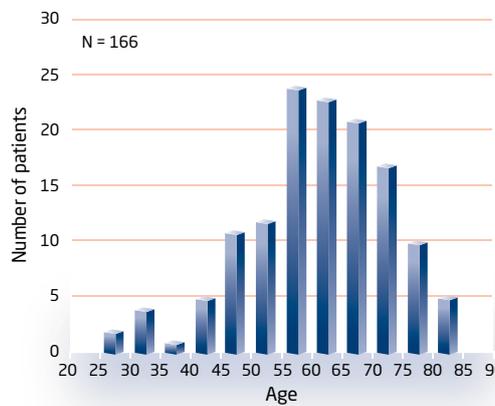
## Measuring MP in practice

There are many ways of determining MP optical density and most rely on the property that it selectively absorbs blue light. Psychophysical methods also exploit the fact that MP is concentrated in the central 1-6 degrees. The principle is simple. A minimum flicker technique is used to equalise the perceived luminance of a blue and green light and compare the ratio of these lights for central and peripheral viewing. When the minimum flicker setting is made for central viewing, extra blue light is needed to match the green light because some blue light is absorbed by the MP. It is assumed the MP is absent in the periphery, so this setting acts as a reference. MPOD is calculated simply by taking the ratio of the perceived luminance of the blue light for central viewing and the perceived luminance for peripheral viewing.

The M-POD uses exactly the same principle but employs a novel method for obtaining the minimum flicker point between the blue and green lights.<sup>10</sup> Instead of asking the observer to eliminate flicker by adjusting blue-green ratio, the observer presses a button when they detect flicker for a series of different blue-green ratios which are pre-set by the software. This flicker detection strategy makes the technique easy for naïve observers. It also means that a graph can be drawn as the measurement progresses so that the operator can monitor the quality of the data and ensure the observer is performing the task correctly. An example of the output is illustrated



**Figure 2a** M-POD data from 166 patients in a private practice illustrating that the majority increased their MP after 6-12 months supplementation with Restore. Note the tendency for those with low baseline MP to benefit the most



**Figure 2b** Age distribution for the patients in Figure 2a

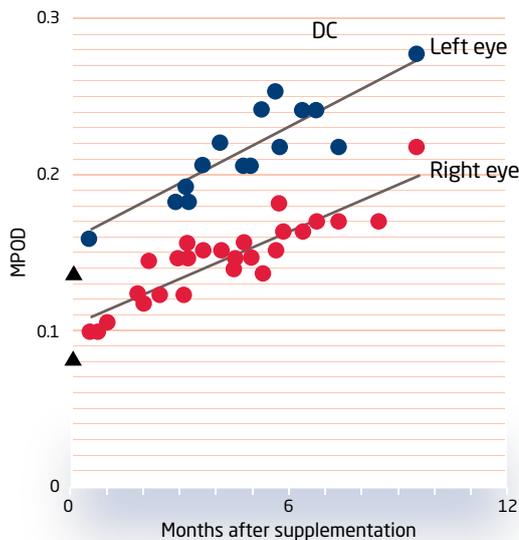
in Figure 1. Note the horizontal axis is blue-green ratio. A rightward shift of the minima along the x-axis means more blue is required in the blue green ratio. The MPOD is calculated from the difference between the two minima.

The M-POD has another unique feature, called the Age Estimate Technique.<sup>12</sup> Some patients encounter difficulty making the peripheral setting. This problem is easily avoided because the peripheral minima can be calculated from the degree of lens yellowing. It is well known that the crystalline lens absorbs blue light more or less linearly with age. As the eye becomes older the peripheral minimum is shifted to the right along the x-axis in Figure 1. It is therefore a simple matter to calculate the peripheral setting for a particular age. This means that the MP can be calculated from the central measurement only, thus dramatically reducing the time taken for the test. Using this approach many users report obtaining a measurement within three to four minutes with additional time being allowed for explaining the test. Apart from time and ease, the

age estimate technique is particularly useful if operators are interested only in the change in MP from visit to visit because the centre-only measurement is then compared with a fixed reference on each visit. Note that because there is a close correlation between right and left eye it is rarely necessary to measure both eyes.

In Figure 2a we present MP data, collected using the M-POD for 166 patients from an optometrist practice in the Midwest of the US. Figure 2b shows the age distribution of this population; the oldest was 86 years old and the youngest 27. There were 106 females. The x-axis indicates the MPOD at baseline and the y-axis represents the increase in MPOD following daily supplementation over an 18-month period with Eye Promise Restore (ZeaVision LLC, MO, USA) which contains 4mg L and 8mg Z. Two main points should be noted. First, there is a tendency for patients with lower baseline levels to increase their MP more than those who start at a higher level. Secondly, it is apparent that in 24 cases there was no increase in MP over the supplementation period and a handful of cases experienced a decrease in their MP. This is consistent with reports in the literature; most supplementation studies find a non-responder rate of around 20 per cent.<sup>13,14</sup> In accordance with the US HIPPA regulations covering data protection, these data were collected and are published on the understanding that details other than gender and date of birth would not be released. We therefore have no information about the clinical status of the patients, how well they complied with instructions for taking their supplements or whether they were smokers or were obese. Nor do we have access to blood plasma levels of L and Z. Nevertheless it is clear that the majority increased their MP. The average increase over the entire group was 76 per cent, but in some cases where baseline MP was low, there are cases in which MP increased dramatically. Almost all those with low MP increased by at least 0.3 optical density units. Because MPOD is a logarithmic scale this means that the intensity of blue light incident on their central macula would be halved as a result of the supplementation.

In order to provide a perspective on the data in Figure 2, we present MPOD measurements we have shown previously in this journal from a different study in which a single observer with initially low MP, took the



**Figure 3** M-POD data showing how MP increases in one individual with initial low MP. The black triangles indicate baseline measurements

same supplement as the patients in Figure 2. In this case, illustrated in Figure 3, we were able to make many measurements over the one-year supplementation period. The subject was experienced at doing psychophysical experiments. At first sight the data might appear rather noisy. However it is important to recognise that measurements of MP are based on the optical density of a passive filter which is located in retinal tissue. Even with a skilled individual, repeat measurements cannot be expected to be within less than 0.1 OD units. In terms of absorption of blue light, 0.1 OD is small.

The data in Figure 3 were collected with a psychophysical technique which relies on the observer setting flicker thresholds. Some have described this as a subjective technique. Although, the measurement relies on the observer making a particular setting, there is no escaping the veracity of the settings when they form a mathematically predictable function as shown in Figure 1. It is important to remember that so-called objective techniques have approximately the same inherent errors of measurement (at least  $\pm 0.1$ OD units) and this applies to any techniques for estimating MP, regardless of whether they use reflectometry, autofluorescence, Raman spectroscopy or any other imaging-based method.

Some would argue that optometry cannot afford to ignore AMD. The profession is well placed to make an impact on AMD. Practitioners are well educated and have an excellent grounding in ocular pathology. A large percentage of the population visit an optometrist at some time in their lives and increasingly, patients are seeking advice and guidance as well as new spectacles. In the US, optometrists are incorporating AMD management and measurement of MP in to the core of their clinical activities. It has become a bottom line contributor to the business, maintains regular contacts with patients and allows them to have a major impact on ocular health. ●

**References**

A list of references is available from [william.harvey@rbi.co.uk](mailto:william.harvey@rbi.co.uk)

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