The MPod – a new instrument for measuring macular pigment

Ian Murray and **David Carden** describe a new instrument aiming to make macular pigment assessment easy and reliable

Macular pigment (MP) is a yellow, oily substance located in the fibres of Henlé and the outer segment membranes of photoreceptors in the macular region of the human retina. Although the presence of MP has been known for many years, its precise composition was identified relatively recently by Bone *et al* as the carotenoids lutein (L) and zeaxanthin (Z).[1] MP has some remarkable characteristics; it is uniquely located to protect the photoreceptors from damaging short wave light, it aids visual resolution by reducing chromatic aberrations and, like many carotenoids, acts as a powerful anti-oxidant. This combination of properties has led to speculation that it may help protect the eye from macular disease. While the idea has its detractors, there is a substantial body of evidence supporting the notion.[1-3]

MP is available only through the diet, so individuals with poor diets have low levels of MP. This also means MP can be enhanced, not only by eating food rich in L, such as spinach, but also by taking one of the many commercially available food supplements containing L. The fact that MP can be enhanced has prompted interest in its measurement on a large scale.

There are many techniques for measuring MP and all have different advantages and disadvantages. The majority take advantage of the unique wavelength spectrum of MP. The least expensive and most convenient technique is based on heterochromatic flicker photometry. In the conventional form of the technique, observers view two alternating flickering lights of around 460nm (blue) and 570nm (green). They adjust the relative intensity of the two lights until the flicker is minimised and the lights are then defined as of equal luminance. Because the blue light is absorbed by MP and the green light is not, a relatively high intensity of blue light is required to obtain minimum flicker when the target is viewed centrally. The test is then repeated when viewing the target eccentrically, using a part of the retina where MP is known to be absent. Here, because MP is absent, the blue light effectively has higher luminance, meaning the intensity ratio at which minimum flicker is obtained is different from that in the fovea. MP is then defined as follows:

$MP = \log_{10} (Lc/Lp)$

where Lp = intensity of the blue light for peripheral viewing

and Lc = intensity of the blue light for central viewing.

Figure 1 The M/Pod measures 300mm x 230mm x 350mm (LxDxH) and weighs 4.4kg

Under laboratory conditions with trained operators and subjects, this method works satisfactorily. Observers become skilled at setting the minimum flicker point and repeated determinations ensure noise is minimised. The method has been used extensively in investigating the link between macular disease and MP, and the data compare favourably with the objective reflectometry-based techniques.[4]

There is a need, however, to understand the distribution of MP in the population at large and to do this, measurement of a large number of eyes is required. For example there are said to be differences between races due to iris colour and inevitably there are variations due to diet, which in turn reflect cultural differences.

Problems arise when naïve observers attempt the task using the conventional technique. These are due mainly to the difficulty of making a minimum flicker setting and particularly in the periphery where adaptation effects are more prevalent.

The new instrument described in this report is designed to reduce the difficulty of determining flicker thresholds. It is easy for non-clinical staff to operate and can be used under clinical conditions, enabling clinicians to quickly measure MP. The device has sufficient accuracy to enable clinicians to advise patients on whether their MP is too low and whether they should consider modifying their diet or taking supplements.

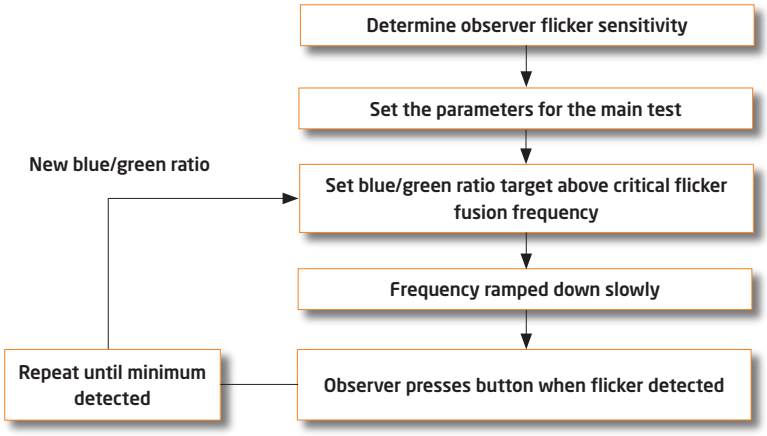

Figure 2a The algorithm used to obtain the V-shaped central and peripheral

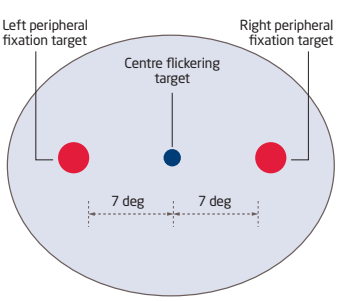

Figure 2b The observer's view of the target and fixation points

The MPod: a new approach

The new device is manufactured by Tinsley Instruments and is built into the same surround assembly as the Henson 9000 (Figure 1). In conventional methods, observers have control over the blue-green ratio, and are required to indicate when flicker disappears or is minimised. In the new, fully automatic technique the observer presses a series of buttons in response to the appearance of flicker at different blue-green ratios. Flicker sensitivity varies between individuals, so observer sensitivity to flicker is first determined by a built-in pre-test routine that enables the appropriate initial luminance contrast of the two lights to be established.

In the main test, the frequency of the blue (460nm) and green (540nm) lights is automatically ramped down from 55Hz for a series of luminance ratios of the two lights. The initial blue-green ratio is set, and the frequency gradually reduces. The observer views the targets centrally and presses a button when flicker is detected. The blue-green ratio is then changed and again the flicker rate is gradually reduced from 55Hz until the observer signals they detect a flicker. The operating sequence and the view of the target is illustrated in Figures 2a and 2b.

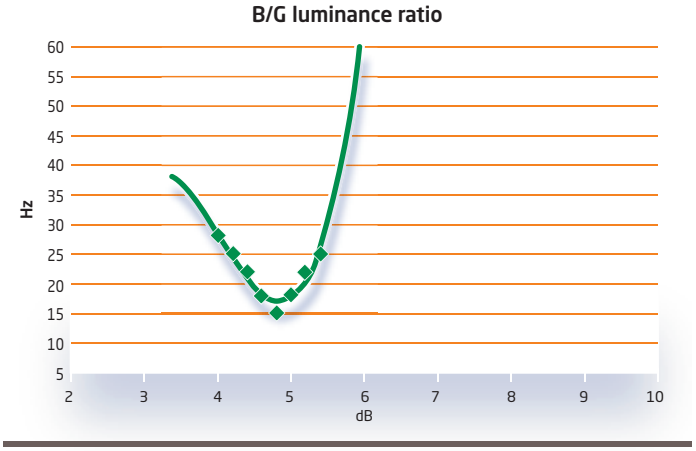

Figure 3 An example of the data obtained from a sequence of eight settings of blue green ratios and their corresponding temporal frequencies. Peripheral viewing

This sequence of obtaining a flicker threshold for each blue-green ratio is continued until a curve, as seen in Figure 3, is obtained. The minimum of the curve is the point where the two lights are of equal luminance. Effectively, this minimum tells us the luminance of the blue target for central viewing. Obtaining these data is quick, taking around one minute.

The procedure of obtaining the flicker detection for a series of blue-green ratios is repeated for peripheral viewing and a new minimum, corresponding to the luminance of the blue target for peripheral viewing is obtained. The difference between the two minima is a measure of the MP optical density. The total testing time for one eye takes around two to three minutes. Data for central and peripheral conditions are illustrated in Figure 4. The green data points are obtained for peripheral viewing. The blue data are for central viewing. Here we are illustrating three hypothetical observers with high, medium or low macular pigment optical density. A conspicuous minimum is obtained in each case. The difference between

the minimum for peripheral viewing and that for central viewing is the macular pigment in optical density units. An important advantage of the technique is that the operator can see that the observer is performing the task correctly from the way the curve develops during the procedure.

Measuring lutein during an MP enhancement regime

As shown in a recent BBC programme, *The Truth About Food*, developed with the collaboration of the Faculty of Life Sciences, University of Manchester,[5] it is possible to increase the levels of MP by following a spinach-rich diet. However, it is well known that the levels of L in the blood plasma are increased within a week by regular supplementation with lutein tablets and that within a month or so, the MP also increases. The amount of L deposited in the eye, as MP, takes much longer to respond to the supplementation. Also, individuals differ in how well their retina deposits the L and so the time period over which a measurable increase in MP occurs can vary dramatically.

Figure 5 illustrates the time course of MP increase measured with the new instrument, during the course of a daily supplementation with L and Z. The supplementation was two capsules per day of Eye Promise Restore (ZeaVision Inc, St Lewis MO). Each capsule is composed of 8mg of Z and 4mg of L. This individual had very low MP optical density at the start of the supplementation period (right eye = 0.1 and left eye = 0.14). The current MPod values are R = 0.22 and L = 0.28. In terms of optical density, which is in log units, there has been more than a 100 per cent increase in MP. The MP is continuing to increase at the time of writing this paper. The supplementation has enabled the subject to increase his MP levels substantially, thereby possibly reducing his risk of developing macular disease in later life.

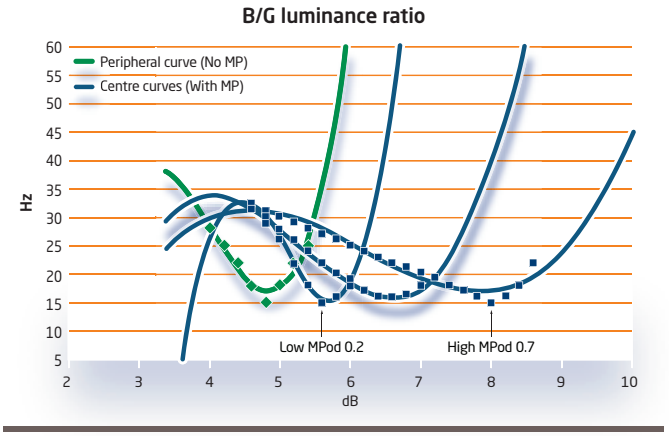

Figure 4 An illustration of the data obtained from observers with low, medium or high macular pigment levels. Notice the peripheral values in this example (green squares) are the same in each case. The central values (blue squares) differ in their minima depending on whether MP is low (0.2; left hand graph) or high (0.7; right hand group). The intermediate graph is not labelled for clarity of the figure

Concluding remarks

In the developed countries, more than 30 per cent of eyes older than 65 years exhibit soft confluent drusen, the precursor of age-related macular degeneration. Population demographics mean that in the next two decades there will be a steady increase in the incidence of AMD. Low MP is a well established risk factor for AMD and it is inevitable that patients will seek the advice of practitioners regarding MP-enhancing strategies.

There are many questions with respect to food supplements claiming to improve the health of the retina. Like other issues impinging on ocular health such as glaucoma, diabetes and hypertension, it is important that practitioners can provide balanced and well-informed advice.

In the case of AMD the advice is easy to say and more difficult to follow; eat a good diet, maintain a healthy weight, do not smoke and if the MP is low, improve the diet or take a supplement.

PATIENT TRIAL AND DEMONSTRATION

The authors are about to start a placebo-controlled, double-blind study of the effects of a lutein supplement on early stage macular disease. Macular pigment will be measured using the MPod. Contrast sensitivity, dark adaptation and a new test of rod function will also be used. Patients will take a daily dose of 10mg of lutein. Approximately 60 patients will be recruited. The authors would be delighted to hear from optometrists in the north of England who would like to be involved in the project either by sending patients or who would like to attend a small seminar on macular pigment and its relationship to macular disease. Anyone interested could come to the university to see a demonstration of the techniques. For the inclusion criteria and other details of the project email ian.j.murray@manchester.ac.uk, dave@armd.org.uk, maria.makridaki@postgrad.manchester or visit armd.org.uk. Maria Makridaki can be reached at 0161 306 3862.

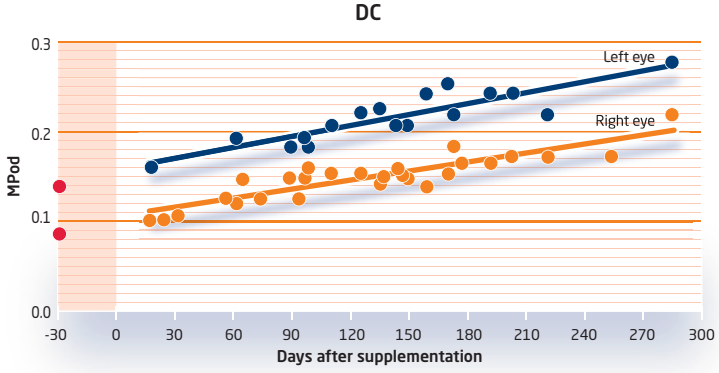

Figure 5 The slow increase in MP during the course of supplementation with a combined L and Z supplementation. Eye Promise Restore. (ZeaVision Inc USA). Subject DC. Vertical axis is MPod, horizontal axis is days following supplementation. The data points on the vertical axes are the means of six measurements taken prior to the start of the supplementation. Note that the observer DC now has MP levels that are within normal limits and he has probably reduced his risk of developing macular disease

References

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5 BBC programme, *The Truth About Food,* Spinach and Eyesight. (www.bbc.co.uk/sn/humanbody/truthaboutfood/young/spinach.shtml).

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