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Macular pigment and ocular biometry

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Abstract

This study is designed to investigate the relationship between macular pigment optical density (MPOD) and ocular biometric parameters. The following details were recorded for 180 healthy subjects: demographic profile; best-corrected visual acuity; refractive status; ocular biometric parameters [axial length (AL), anterior chamber depth (ACD), lens thickness (LT) and vitreous chamber depth (VCD)]; ocular dominance; MPOD; serum lutein (L) and zeaxanthin (Z). The mean MPOD ($\pm SD$) was 0.307 (0.155) and 0.305 (0.149) in the right and left eyes, respectively. No demonstrable relationship was observed between MPOD and AL, ACD or VCD [AL: $r = 0.091$, $p = 0.225$; ACD: $r = 0.091$, $p = 0.227$; VCD: $r = 0.146$, $p = 0.051$]. There was a significant and inverse relationship between LT and MPOD ($r = -0.204$; $p = 0.008$), which was attenuated to non-significance after correction for age and height ($r = -0.058$; $p = 0.466$). This study fails to identify an association between MPOD and ocular biometric parameters. This is an important negative finding, which allows investigators to study MP, and its relationship with potentially important variables, without the need to correct for ocular biometric parameters.

Keywords: Macular pigment; Axial length; Anterior chamber depth; Lens thickness; Vitreous chamber depth

1. Introduction

The macula is the specialized central region of the retina, and is essential for high-resolution visual acuity and colour vision. In primates, it has a characteristic yellow colour, due to the presence of macular pigment (MP), which is composed of two dietary xanthophylls, lutein (L) and zeaxanthin (Z) (Bone, Landrum, & Tarsis, 1985). Evidence is accumulating that MP confers protection against age-related macular degeneration (AMD), the commonest cause of blindness in Western countries, by acting as an optical filter to phototoxic blue light and/or via its powerful antioxidant properties (Beatty, Boulton, Henson, Hui-Hiang, & Murray, 1999; Landrum, Bone, & Kilburn, 1997).

Myopia is a common refractive error seen worldwide, with pathological myopia accounting for 27–33% of myopic eyes, which corresponds to a prevalence of 1.7–2% in the general population of the United States (Curtin, 1985). Pathological myopia describes an eye with greater than −6 dioptres of myopia and/or an axial length greater than 26–27 mm (Pruett, 1994). Interestingly, it is associated with the same visually consequential macular sequelae as are seen in AMD, namely choroidal neovascularization and atrophic changes.

Pathological myopia involves an excessive and progressive elongation of the globe, with consequential thinning of the retina at the posterior pole (Apple & Fabb, 1978; Yanoff & Fine, 1982). Interestingly, Aleman, Duncan, and Bieber (2001) have observed a relative lack of MP in association with thinner retinae. Therefore, it is tempting to hypothesize that eyes with pathological myopia may be deficient in MP, and that any such relative lack of MP may represent an antecedent common to the

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visually consequential sequelae of pathological myopia and AMD. The dietary origin of MP renders this hypothesis all the more provocative.

Furthermore, a relationship between ocular biometric parameters and macular pigment optical density (MPOD), if any, also rests on the possibility that axial length (alone or in combination with other biometric components) may be an important determinant of MPOD, potentially confounding any analysis of the relationship between this pigment and other variables.

We have designed a study to investigate the relationship between MP optical density and ocular biometric parameters.

2. Patients and methods

In this cross sectional study, 180 healthy subjects were recruited, by a self-selected sample in response to a campaign of posters and word of mouth. Informed consent was obtained from each subject, and the tenets of Declaration of Helsinki were adhered to.

The following data were recorded for each subject: demographic profile; smoking status; height; weight; best-corrected visual acuity (logMAR visual acuity chart); anterior and posterior segment photography; refractive status; ocular biometric parameters; ocular dominance; macular pigment optical density and serums L and Z.

2.1. Refractive status

Non-cycloplegic refraction was assessed using a Nidek auto refractor, and the average of three recordings was used for analysis. The refractive data was converted to spherical equivalent (SE), which is derived by adding the spherical component of refraction to half the cylindrical component.

2.2. Ocular dimensions

Ocular dimensions, including axial length, anterior chamber depth, lens thickness and vitreous chamber depth were measured with A-scan ultrasonography.

2.2.1. Instrumentation

The ophthalmic technologies (OTI) "i-scan" ultrasound system, with biometry X mode, was used to measure the ocular parameters. The probe consists of a hard-tipped ultrasound probe (X probe) operating at $10\,\text{MHz} \pm 10\%$. This instrument is prompted to take appropriate measurements upon automated identification of key structures within the eye.

2.2.2. Procedure

One drop of 0.5% proxymetacaine was instilled into the inferior conjunctival fornix, and appropriate settings for gain, sound velocity and measurement mode were verified, prior to each measurement. A fixation target was used for the fellow eye to help align the study eye appropriately, and the probe was placed on the central cornea and an automated sequence of ten measurements was recorded. Care was taken to ensure that the ultrasound probe did not compress the cornea. The average of ten readings for each ocular parameter under investigation was used for analysis.

2.2.3. Measurements

Axial length. Distance from the anterior surface of the cornea to the vitreoretinal interface at the macula.
Anterior chamber depth. Distance between the anterior corneal surface and the anterior lens surface.
Lens thickness. Distance between the anterior and posterior lens surfaces.
Vitreous cavity depth. Distance from the posterior lens surface to the anterior surface of the retina.

2.3. Ocular dominance

Ocular dominance was determined as follows: the subject was asked to focus, with both eyes open, on a target at 6 m, and to point at that target with his/her index finger. Then, each eye of the subject was occluded in turn, and the dominant eye was known to be in use when the subject saw the indicating finger directed exactly at the target. In contrast, when the non-dominant eye is looking under these conditions, the indicating finger will be seen pointing to an area to the side of the target.

2.4. Measurement protocol for heterochromatic flicker photometry

MP was measured psychophysically using the Maculometer, which utilizes the principle of heterochromatic flicker photometry (HFP). This instrument has been validated against motion photometry in normal subjects (Mellerio, Ahmedi-Lari, & Van Kuijk, 2002).

2.4.1. Principle

HFP is based on the principle of matching the luminance of two flickering light sources, one blue and one green, at the fovea and then at the parafovea. If the green light remains at constant luminance whereas, the luminance of the blue light is varied, a point of minimum flicker will be achieved when the luminance of the two light sources are matched. The logarithm ratio of the luminances of blue light required to achieve this end point, for foveal and parafoveal readings, is a measure of the optical density of MP. This is because MP is optically undetectable at an eccentricity of 6.5°, and has peak absorption at 460 nm corresponding to blue light.

It is important to note that when MP is measured using our HFP, most subjects report that some flicker is perceived at all settings, and that at no point does the flicker disappear completely. This is to be expected because, even at isoluminance, the target fields will change from blue to green. In addition, for the foveal test field, the MP is not evenly distributed across the 1° area that it subtends on the retina, and hence, no setting can be perfect for the whole area at once.

Furthermore, 5% of subjects with normal vision are unable to perform minimum match settings due to difficulty in grasping the concept of minimum flicker. Furthermore, some subjects try to make minute adjustments of the blue luminance so as to achieve a perfect setting, and are reluctant to stop fixation and relax by looking around the room. It is important to note that the subjects spend no more than 15–20 s fixating the test fields before relaxing: Troxler phenomena eventually bother subjects who continuously fixate, and this process of relaxing and looking away from the test fields is written into the SOP's (standard operating procedures) for our instrument. It is, therefore, for these reasons that "perfectionist" adjustment is strongly discouraged, and for most subjects, after a few non-recorded trials, the real measurements are easily made.

2.4.2. Apparatus

The Maculometer is a small and portable instrument, which uses light emitting diodes (LEDs) as light sources. LEDs provide good light sources for portable instruments because they are small, inexpensive, easily driven from simple power supplies and emit near monochromatic light.

The test stimulus consists of a 1° circular dot (foveal), flickering between a 460 nm measuring field (blue light; peak MP absorbance) and a 560 nm reference field (green light; minimal MP absorbance). This is surrounded by two arcs representing a parafoveal annulus (diameter: 10°; width: 1°) concentric with the fovea, also consisting of a flickering stimulus composed of the same wavelengths as the foveal stimulus. The measuring and the reference fields are superimposed, and presented out of phase at an alternating rate of 18 and 13 Hz at the fovea and parafovea, respectively.

The luminance of green light is fixed but the subject, using a dial, can alter the luminance of the blue light. Flicker is obvious when the perceived luminance of the blue and green lights differs, but is minimal/zero when these luminances are matched.

2.4.3. Procedure

Subjects were given brief instructions on the method, and a practice trial before actual readings were recorded.

For foveal matches, the subject was asked to look at a flickering blue/green light in the central field with parafoveal arcs extinguished, and to reduce the flicker to a minimum/zero by adjusting the blue light with the help of the dial. The subject's perception of the end point was then recorded. For parafoveal matches, the foveal field was changed from its flickering status to a dim red light to provide a fixation target, while the parafoveal arcs were flickering. The entire procedure was then repeated, with the test field imaged at the parafovea.

After recording each reading, the investigator sets the luminance control to some new arbitrary position so that the subject did not learn how far to adjust the dial to obtain a match. Between four and eight readings were recorded at the fovea and the parafovea for each eye, and then used to calculate MP optical density.

2.4.4. Intra-sessional and inter-sessional variability of MPOD readings

The reproducibility and test–retest variability for our maculometer has been assessed in 100 consecutive volunteers (Nolan, O'Donovan, & Kavanagh, 2004). The reproducibility of the MPOD readings recorded during a single session was expressed in terms of the coefficient of variation and the coefficient of repeatability, and was $16.14 \pm 18.48\%$ and $0.025 \pm 0.011\%$, respectively. Furthermore, agreement between the MPOD readings recorded on the two separate occasions was represented by a mean difference of 0.01 ± 0.08, and the 95% limits of agreement were -0.01 ± 0.16.

2.5. High performance liquid chromatography for serum analysis of L and Z

High performance liquid chromatography (HPLC) on reversed phase column is a powerful technique for separation, identification and quantification of various forms of carotenoids in human serum and other tissues.

2.5.1. Instrumentation

We have used a Hewlett-Packard (HP 1090 LC) system with photodiode array detection at 292, 325 and 450 nm, using Agilent Chem Station software. A 5 μm analytical/preparative 4.6×250 mm 201 TP speciality reverse phase column (Vydac) was used with an in-line guard column. The mobile phase consisting of 97% methanol and 3% tetrahydrofuran was degassed using an in-line degasser. The flow rate was 1 ml/min. Hoffmann-La Roche provided the standards for HPLC analysis.

2.5.2. Procedure

Blood samples (6–8 ml) were collected in two 5 ml vacutainer tubes containing 4.5 U of sodium or lithium heparin per milliliter of whole blood, and centrifuged immediately. The separated serum layer was then aliquoted into three light sensitive micro centrifuge tubes and stored at −70 °C until the time of analysis.

2.5.3. Extraction

A 0.4 ml aliquot of serum was pipetted into a light sensitive micro centrifuge tubes (2 ml total capacity). Ethanol (0.3 ml) containing 0.25 g/l butylated hydroxytoluene and internal standard (tocopherol acetate) was added to each tube. Heptane (0.5 ml) was then added and samples were vortexed vigorously for 1 min followed by centrifugation at 2000 rpm for 5 min (MSC Micro Centaur). The resulting heptane layer was retained, transferred to a second labelled light sensitive micro centrifuge tube, followed by a second heptane extraction. The combined heptane layers were immediately evaporated to dryness under a stream of pure nitrogen using a sample concentrator (Techne Sample Concentrator). These dried samples were reconstituted in methanol (200 μl) and 150 μl was injected for HPLC analysis. The total run time was 15 min. L and Z standard curves

were used for quantification of serum concentrations of these carotenoids for each subject. This assay has been validated against the National Institute of Standard and Technology (NIST) Standard Reference Material 968c for carotenoids in human serum.

2.6. Body mass index

Weight was measured on a single automatic weighing scale and recorded in kilograms. Height was recorded in meters, with the subject standing straight up without shoes. The body mass index (BMI) was derived from the ratio of the person's weight (kg) divided by the square of the person's height (m).

3. Data analysis

The data for this study was analysed using the SPSS statistical software package (SPSS Inc., Chicago, IL). As expected, there was a very strong correlation between ocular biometric parameters of fellow eye (AL: $r = 0.913$; ACD: $r = 0.772$; LT: $r = 0.825$; VCD: $r = 0.939$). Therefore, for the purpose of investigating the relationship(s) between MPOD and ocular biometric parameters, we used the data for one eye (the right eye) only. Correlations were evaluated by linear regression analysis and multiple linear regression models were used to assess cross-sectional relationships. The relationship in MPOD between dominant and non-dominant eye was compared with a paired-samples t test. A p value of <0.05 was deemed significant.

4. Results

This study comprised 180 healthy subjects (179 right eyes; 179 left eyes) recruited for the purpose of investigating the relationship between MPOD and ocular biometric parameters. In all participants, the best-corrected visual acuity was 0.2 or better, and there was no evidence of visually consequential cataract and/or macular pathology detected on anterior and posterior segment photography, respectively.

The mean age ($\pm SD$) of our study population was 41.25 (11.73) years, ranging between 21 and 63 years. Of the 180 subjects, 115 (63.9%) were females and 65 (36.1%) were males. The prevalences of myopia (<−0.50 D SE), emmetropia and hypermetropia (>0.50 D SE) were 47.8% ($n = 85$), 26.4% ($n = 47$), and 25.8% ($n = 46$), respectively. Moderate (−3.1 to −4.9 D SE) and high (<−5.0 D SE) myopia was seen in 10 (11.8%) and 14 (16.5%) subjects, respectively.

The mean MPOD (±SD) was 0.307 (0.155) and 0.305 (0.149) in the right and left eyes, respectively. There was a good degree of interocular agreement in MPOD with a maximum right–left eye difference of 0.222 ($r = 0.868$; $p < 0.0001$). There was no significant difference in mean MPOD between males and females (males: 0.326 ± 0.165; females: 0.296 ± 0.151, $p = 0.222$).

Using linear regression, a statistically significant age-related decline in MPOD was observed ($r = -0.230$; $p = 0.002$). MPOD was inversely related to weight and BMI, but not to a statistically significant degree (BMI: $r = -0.090$, $p = 0.233$; weight: $r = -0.027$, $p = 0.724$). Past and current smokers had lower MPOD than subjects who had never smoked, however, this relationship did not reach statistical significance (MPOD in past/current smokers: 0.295; MPOD in never smokers: 0.324; Independent samples t test, $p = 0.218$). Height was positively and significantly related to MPOD ($r = 0.195$; $p = 0.010$).

Multiple regression with a stepwise procedure has demonstrated age to be a negative predictor of MPOD, whereas, height and serum levels of lutein were positive predictors of MPOD (age: $p = 0.003$; height: $p = 0.027$; serum lutein: $p < 0.0001$). However, when gender is included in this model, height no longer remains a significant predictor of MPOD ($p = 0.125$).

4.1. Axial length

The mean AL ($\pm SD$) was 23.736 (1.259) and 23.685 (1.180) mm for right and left eyes, respectively. There was a strong positive relationship between axial lengths of fellow eyes ($r = 0.913$; $p < 0.0001$).

The relationships between AL and age, weight, height and BMI are given in Table 1. AL was significantly and inversely related to age ($r = -0.275$; $p < 0.0001$), but positively and significantly related to subject height ($r = 0.180$; $p = 0.018$). Females had significantly shorter AL when compared with males ([females: $n = 115$; mean AL $\pm SD$ for right eye: 23.57 ± 1.109] [males: $n = 65$; mean AL $\pm SD$ for right eye: 24.00 ± 1.45], $p = 0.028$). A trend towards a positive correlation

Table 1
Relationship between ocular biometric parameters and demographic and anthropometric profile

Ocular parameters	Age		Height		Weight		BMI	
	r value	p value	r value	p value	r value	p value	r value	p value
Axial length	−0.275	0.000	0.180	0.018	0.046	0.546	−0.046	0.542
Anterior chamber depth	−0.430	0.000	0.168	0.028	0.114	0.135	0.023	0.761
Lens thickness	0.718	0.000	−0.187	0.014	−0.022	0.775	0.133	0.077
Vitreous chamber depth	−0.388	0.000	0.200	0.009	0.017	0.824	−0.104	0.168

BMI, body mass index.
r, Pearson correlation.

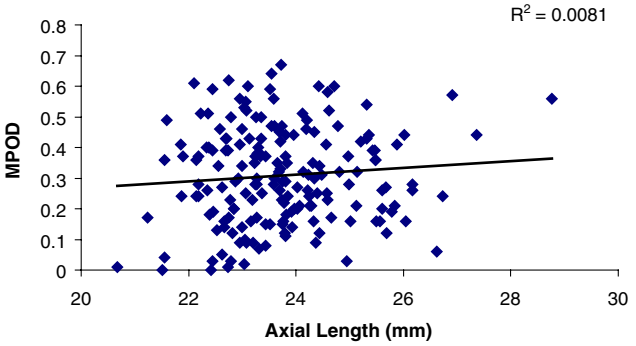

Fig. 1. Scatterplot showing the relationship between axial length and macular pigment optical density.

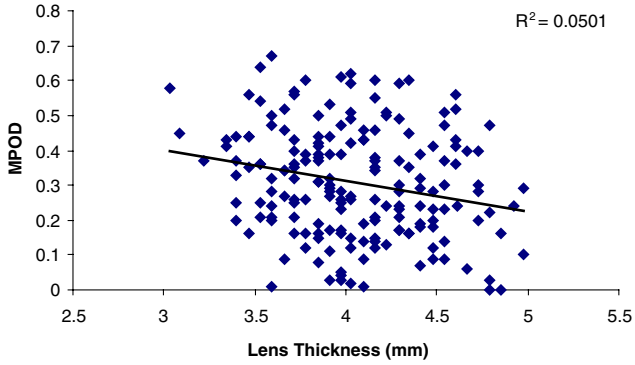

Fig. 2. Scatterplot showing the relationship between lens thickness and macular pigment optical density.

between AL and MPOD was observed ($r=0.091$; $p=0.225$; Fig. 1); however, this relationship ceased to exist after adjusting for age, gender and height ($r=0.002$; $p=0.983$).

Furthermore, after exclusion of eyes with high myopia and high hypermetropia from the data that has been adjusted for age, gender and height, the relationship between AL and MPOD remains unchanged ($r=-0.001$; $p=0.995$).

4.2. Anterior chamber depth

The mean ACD ($\pm SD$) was 3.225 (0.418) and 3.227 (0.375) mm for right and left eyes, respectively. The relationships between ACD and subject age, weight, height and BMI are given in Table 1. A slightly positive correlation was observed between ACD and MPOD ($r=0.091$; $p=0.227$) and interestingly, after controlling for age, gender and height the trend was reversed but remained insignificant ($r=-0.015$; $p=0.848$). After exclusion of eyes with high myopia and high hypermetropia from the data that has been controlled for age, gender and height, no demonstrable relationship existed between ACD and MPOD ($r=-0.020$; $p=0.808$).

4.3. Lens thickness

Mean LT ($\pm SD$) was 4.046 (0.410) and 4.061 (0.410) mm for right and left eyes, respectively. The relationships between LT and subject age, weight, height and BMI are given in Table 1. Lens thickness was positively related with age ($r=0.718$; $p<0.0001$), and inversely related with height ($r=-0.187$; $p=0.014$). A statistically significant inverse relationship was observed between LT and MPOD ($r=-0.225$; $p=0.002$; Fig. 2), and this relationship was attenuated to non-significance after correction for age and height ($r=-0.072$; $p=0.335$). After exclusion of eyes with high myopia and high hypermetropia from the data that has been corrected for age and height, there was no change in the strength of the inverse relationship ($r=-0.037$; $p=0.653$).

4.4. Vitreous chamber depth

The mean VCD ($\pm SD$) was 16.470 (1.181) and 16.379 (1.109) mm for right and left eyes, respectively. The relationships between VCD and subject age, weight, height and BMI are given in Table 1. VCD was inversely related to age ($r=-0.388$; $p<0.0001$), and positively related with height ($r=0.200$; $p=0.009$). A positive correlation with borderline significance was observed between VCD and MPOD ($r=0.146$; $p=0.051$); however, this relationship did not persist after adjustment for age and height ($r=0.030$; $p=0.700$). After exclusion of eyes with high myopia and high hypermetropia from the data that has been controlled for age and height, the relationship between VCD and MPOD remains unaltered ($r=0.025$; $p=0.760$).

4.5. Correlation of serum levels of L (and Z) with ocular biometric parameters

The mean serum levels ($\pm SD$) of L and Z were 0.083 (0.071) and 0.031 (0.038) μg/ml, respectively. A positive and significant relationship was observed between serum levels of L (and Z) and MPOD (serum L: $r=0.245$, $p=0.001$; serum Z: $r=0.185$, $p=0.013$).

However, serum L was not significantly related to AL, LT, VCD or ACD (AL: $r=-0.006$, $p=0.934$; ACD: $r=0.053$, $p=0.477$; LT: $r=-0.009$, $p=0.908$; VCD: $r=-0.002$, $p=0.766$). Similarly, serum Z was unrelated to any of these parameters in a statistically meaningful way (AL: $r=0.005$, $p=0.942$; ACD: $r=0.060$, $p=0.427$; LT: $r=-0.063$, $p=0.427$; VCD: $r=0.006$, $p=0.935$).

Multiple regression analysis found age ($p=0.002$) to be a significant positive predictor of serum L, and age ($p=0.005$) and weight ($p=0.036$) to be negative predictors for serum Z.

4.6. Ocular dominance

Of the 180 subjects, right ocular dominance was present in 67 (37.2%) subjects, and left ocular dominance in 54 (30%) subjects. Ocular dominance could not be reliably demonstrated in 54 subjects (30%), and was not evaluated in five subjects (2.7%). There was no statistically significant difference in MPOD between dominant and non-dominant eyes (MPOD: dominant eye 0.312; non-dominant eye 0.303, paired-samples t test, $p=0.234$).

5. Discussion

In this study, we have enrolled 180 healthy subjects for the purpose of investigating the relationship between MPOD and ocular biometric parameters. Our data demonstrate that MPOD exhibits no significant relationship with any of the ocular biometric parameters that we measured. Furthermore, no statistically meaningful relationship was observed between MPOD and ocular dominance. To our knowledge, this is the first study to report the relationship between MP and individual ocular dimensions.

The mean AL (23.736 ± 1.259) recorded in our study population is comparable with previously published data (Wickremasinghe, Foster, & Uranchimeg, 2004; Wong, Foster, & Ng, 2001a). Consistent with earlier studies, males and taller individuals have relatively longer axial dimensions than females and shorter individuals, respectively (Wong et al., 2001a; Wong, Foster, & Johnson, 2001b). A significant decline in AL was observed with increasing age, consistent with some, but not all, previous studies (Grosvenor, 1987; Lam, Goh, & Tang, 1999; Leighton & Tomlinson, 1972; van Rens & Arkell, 1991; Wickremasinghe et al., 2004; Wong et al., 2001a).

Our data have shown that there is no demonstrable relationship between AL and MPOD. This finding should be interpreted in the context of Liew et al. recent report, which demonstrated a significant and positive relationship between central retinal thickness and MPOD (Liew, Gilbert, & Spector, 2005). Eyes with pathological myopia have, in theory at least, thinner central retinae than emmetropic eyes. However, the results from four studies, which have investigated the relationship between central retinal thickness and AL, are inconsistent. Of the four studies, three have found that AL is unrelated to central retinal thickness (Gobel, Hartmann, & Haigis, 2001; Kanai, Abe, Murayama, & Yoneya, 2002; Wakitani, Sasoh, & Sugimoto, 2003) whereas Wong et al. have reported a significant and positive correlation between these variables (Wong, Chan, & Hui, 2005).

We have observed highly significant and positive relationship between VCD and AL ($r = 0.960$), consistent with the findings of previous investigators (Li, Wang, & Ji, 2000). As VCD is the main determinant of AL, it is likely that any relationship between MPOD and VCD simply reflects the relationship between MPOD and AL.

The optical and physical properties of the human lens change substantially with age, and in a complex manner. There is an increase in lens optical density concomitant with an increase in LT, suggesting a relationship between these age-related changes (Kashima, Trus, & Unser, 1993). However, it is important to note that the age-related increase in LT is linear whereas the age-related increase in lens optical density is exponential (Cook, Koretz, & Pfahnl, 1994).

Previous studies have demonstrated that there is a significant increase, approximately 0.02 mm per year, in LT with age (Brown, 1974). Our results, therefore, are consistent with these earlier reports. Furthermore, an inverse but insignificant relationship between MPOD and LT was demonstrated in our study. Indeed, Hammond et al. have demonstrated an inverse relationship between MPOD and lens optical density, and the inverse relationship between MPOD and LT that we demonstrate is, therefore, unsurprising (Hammond, Wooten, & Snodderly, 1997). Although the inverse relationship between MPOD and lens optical density remains unexplained, it is noteworthy that the macula and the lens accumulate L and Z to the exclusion of all other carotenoids in the diet and serum. Therefore, it is tempting to hypothesize that an individual who consumes high quantities of L and Z in the diet will, presumably, accumulate excessive amounts of L and Z both at the macula and in the crystalline lens. As a consequence, in theory at least, an individual with high macular pigment optical density will also have a parallel protective effect in the lens thus resulting in reduced cataractogenesis (and the associated increase in lens optical density and thickness).

The data from this study demonstrates a significant age-related decrease in axial length. This age-related decline in AL might relate to "adult ocular compensation", the coordinated changes occurring in the individual ocular components of the adult eye. This process is presumed to maintain emmetropia with increasing age. Alternatively, the reduction in the AL of the adult eye may be attributable to the shrinkage of connective tissue or increasing scleral rigidity, which are known to occur with increasing age (Grosvenor, 1987). Whatever the mechanism, AL is approximately 0.6 mm shorter in older subjects when compared with younger subjects (Grosvenor, 1987).

Similarly, a statistically significant decline in MPOD was observed with age, and this finding is consistent with most but not all studies that have investigated the relationship between age and MPOD. Of the 23 studies, which have reported the age effect on MPOD, 13 have shown an age-related decline in MPOD (Table 2). The possible mechanism for such a decline in MPOD with age, which may be attributable to a parallel age-related decrease in AL, warrants discussion. However, a correction for AL, when investigating the relationship between MPOD and age, was performed, and did not attenuate the observed age-related decline in MPOD, suggesting that any age-related decline in MPOD is not attributable to a reduction in AL with age.

In this study, serum levels of L (and Z) were positively and significantly related to MPOD, but unrelated to ocular biometric parameters. We also report an age-related decline in serum levels of Z, although no such age-related decline was observed for serum levels of L. The explanation for these observations remains unclear.

Ocular dominance, first described in 1593, is the tendency to prefer visual input from one eye over another, and is defined as the faculty whereby one of the eyes commonly dominates the other eye, both in fixation and in attention/perceptive function. Although ocular dominance is related to visual performance, the relationship between ocular dominance and ocular pathology, if any, is poorly understood

Table 2
List of studies which have investigated the relationship between macular pigment optical density and age

Principle author	Journal published	Year	Technique	Sample size	Age range (years)	Age effect	Correlation coefficient
Werner, J. S.	Vis. Res.	1987	HFP	50	10–90	Decline	−0.21
Hammond, B. R.	Invest. Ophthalmol. Vis. Sci.	2000	HFP	217	18–90	Decline	−0.14
Ciulla, T. A.	Ophthalmology	2001	HFP	280	18–50	None	Not given
Beatty, S.	Invest Ophthalmol Vis. Sci.	2000	HFP	46	21–81	Decline	−0.29
Nolan, J.	Invest Ophthalmol. Vis. Sci.	2004	HFP	100	22–60	Decline	−0.359
Neelam, K.	Invest Ophthalmol. Vis. Sci.	2004	HFP	125	20–60	Decline	−0.181
Ciulla, T. A.	Am. J. Ophthalmol.	2004	HFP	390	18–88	None	0.04
Bernstein, P. S.	Arch. Biochem. Biophys.	2004	HFP	40	18–61	Decline	−0.279
Kilbride, P. E.	Vis. Res.	1989	REF	7	Not given	Decline	Not given
Delori, F. C.	J. Opt. Soc. Am. A Opt. I Sci. Vis.	2001	REF	159	15–80	Increase	Not given
Chen, S. F.	Curr. Eye Res.	2001	REF	54	20–84	None	Not given
Berendschot, T. T. J. M.	Invest. Ophthalmol. Vis. Sci.	2002	REF	435	60–91	Increase	$r = 0.15$
Brockmans, W. M. R.	Am. J. Clin. Nutr.	2002	REF	376	18–75	None	Not given
Wustemeyer, H.	Graefes Arch. Klin. Exp. Ophthamol.	2003	REF	109	16–76	Decline	−0.218
Berendschot, T. T. J. M.	Arch. Biochem. Biophys.	2004	REF	138	18–76	Increase	0.14
Zagers	J. Opt. Soc. Am. A. Opt. I Sci. Vis.	2004	REF	38	18–64	None	0.058
Delori, F. C.	J. Opt. Soc. Am. A. Opt. I Sci. Vis.	2001	AF	159	15–80	Increase	Not given
Wustemeyer, H.	Graefes Arch. Klin. Exp. Ophthamol.	2003	AF	109	16–76	None	0.001
Gellermann, W.	J. Opt. Soc. Am. A. Opt. I Sci. Vis.	2002	RS	140	21–84	Decline	$r = -0.664^*$
Bernstein, P. S.	Ophthalmology	2002	RS	140	22–84	Decline	$r = -0.664^*$
Zhao, D. Y.	Arch. Ophthalmol.	2003	RS	140	23–84	Decline	$r = -0.664^*$
Bernstein, P. S.	Arch. Biochem. Biophys.	2004	RS	40	18–61	Decline	$r = -0.467$
Berendschot, T. T. J. M.	Exp. Eye Res.	2005	HFP, REF, AF	134	18–76	Decline (HFP only)	Not given

HFP—heterochromatic flicker photometry.
REF—reflectance spectroscopy.
AF—autoflorescence.
RS—Raman spectroscopy.
* Significant decline in macular pigment with age.

(Cheng, Yen, Lin, & Hsu, 2004). We hypothesized that an eye with higher MP than its fellow eye would become the dominant eye as a result of less chromatic aberration in that eye because MP reduces chromatic aberration by filtering blue light at a pre-receptorial level (Reading & Weale, 1974). This prompted us to investigate the possibility that ocular dominance may be associated with a relative surplus of this pigment. However, we were unable to demonstrate a relationship between MPOD and ocular dominance.

Some important limitations of this study warrant consideration. First, our data consist mainly of emmetropic subjects, and therefore the findings do not represent a population with high refractive errors. Second, the human eye undergoes daily axial length fluctuations, ranging from 15 to 40 μm. The small magnitude of such fluctuations cannot be identified by conventional A-scan ultrasonography, but instead require a method with greater resolution such as partial coherence interferometry (Stone, Quinn, & Francis, 2004).

In conclusion, our data failed to demonstrate a significant association between MPOD and ocular biometric parameters. Furthermore, no relationship was observed between MPOD and ocular dominance. These are important negative findings, which allow investigators to study MP, and its relationship with potentially important variables, without the need to correct for axial length, lens thickness, anterior chamber depth, vitreous chamber depth or ocular dominance.

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References

Aleman, T. S., Duncan, J. L., & Bieber, M. L. (2001). Macular pigment and lutein supplementation in retinitis pigmentosa and Usher syndrome. *Investigative Ophthalmology and Visual Science, 42*, 1873–1881.

Apple, D. J., & Fabb, M. F. (1978). *Clinicopathologic Correlation of Ocular Disease: A Text and Stereoscopic Atlas*. St Louis: CV Mosby (pp. 39–44).

Beatty, S., Boulton, M. E., Henson, D. B., Hui-Hiang, K., & Murray, I. J. (1999). Macular pigment and age-related macular degeneration. *British Journal of Ophthalmology, 83*, 867–877.

Bone, R. A., Landrum, J. T., & Tarsis, S. L. (1985). Preliminary identification of the human macular pigment. *Vision Research, 25*, 1531–1535.

Brown, N. (1974). The change in lens curvature with age. *Experimental Eye Research, 19*, 175–183.

Cheng, C. Y., Yen, M. Y., Lin, H. Y., & Hsu, W. M. (2004). Association of ocular dominance and anisometropic myopia. *Investigative Ophthalmology and Visual Science, 45*, 2856–2860.

Cook, C. A., Koretz, J. F., & Pfahnl, A. (1994). Aging of the human crystalline lens and anterior segment. *Vision Research, 34*(22), 2945–2954.

Curtin, B. J. (1985). The nature of pathologic myopia. In B. J. Curtin (Ed.), *The Myopias* (pp. 237–245). Philadelphia: Harper and Row.

Gobel, W., Hartmann, F., & Haigis, W. (2001). Determination of retinal thickness in relation to the age and axial length using optical coherence tomography. *Ophthalmologe, 98*(2), 157–162 [in German].

Grosvenor, T. (1987). Reduction in axial length with age: an emmetropizing mechanism for the adult eye? *American Journal of Optometry and Physiological Optics, 64*, 657–663.

Hammond, B. R., Wooten, B. R., & Snodderly, D. M. (1997). Density of the human crystalline lens is related to the macular pigment carotenoids, lutein and zeaxanthin. *Optometry and Visual Science, 74*(7), 499–504.

Kanai, k., Abe, T., Murayama, K., & Yoneya, S. (2002). Retinal thickness and changes with age. *Nippon Ganka Gakkai Zasshi, 106*(3), 162–165 [in Japanese].

Kashima, K., Trus, B. L., & Unser, M. (1993). Aging studies on normal lens using the scheimpflug slit lamp camera. *Investigative Ophthalmology and Visual Science, 34*, 263–269.

Lam, C. S., Goh, W. S., & Tang, Y. K. (1999). Changes in refractive trends and optical components of Hong Kong Chinese aged over 40 years. *Ophthalmic and Physiological Optics, 14*, 383–388.

Landrum, J. T., Bone, R. A., & Kilburn, M. D. (1997). The macular pigment: a possible role in protection from age-related macular degeneration. *Advance Pharmacology, 38*, 537–556.

Leighton, D. A., & Tomlinson, A. (1972). Changes in axial length and other dimensions of the eyeball with increasing age. *Acta Ophthalmology, 50*, 815–826.

Li, J., Wang, F., & Ji, H. (2000). A study on the effect of vitreous cavity length in primary ametropia. *Zhonghua Yan Ke Za Zhi, 36*(1), 59–61.

Liew, S. H., Gilbert, C. E., & Spector, T. D. (2005). Central retinal thickness is positively correlated with macular pigment optical density. *Experimental Eye Research*.

Mellerio, J., Ahmedi-Lari, S., & Van Kuijk, F. J. G. M. (2002). A portable instrument for measuring macular pigment with central fixation. *Current Eye Research, 25*(1), 37–47.

Nolan, J., O'Donovan, O., & Kavanagh, H. (2004). Macular pigment and percentage of body fat. *Investigative Ophthalmology and Visual Science, 45*(11), 3940–3950.

Pruett, R. C. (1994). Pathologic Myopia. In D. M. Albert & F. A. Jakobiec (Eds.), *Principles and Practise of Ophthalmology*. Philadelphia: WB Saunders Company.

Reading, V. M., & Weale, R. A. (1974). Macular pigment and chromatic aberration. *Journal of the Optical Society of America, 64*, 231–234.

Stone, R. A., Quinn, G. E., & Francis, E. L. (2004). Diurnal axial length fluctuations in human eyes. *Investigative Ophthalmology and Visual Science, 45*(1), 63–70.

van Rens, G. H., & Arkell, S. M. (1991). Refractive errors and axial length among Alaskan Eskimos. *Acta Ophthalmology, 69*, 27–32.

Wakitani, Y., Sasoh, M., & Sugimoto, M. (2003). Macular thickness measurements in healthy subjects with different axial lengths using optical coherence tomography. *Retina, 23*, 177–182.

Wickremasinghe, S., Foster, P. J., & Uranchimeg, D. (2004). Ocular biometry and refraction in Mongolian adults. *Investigative Ophthalmology and Visual Science, 45*, 776–783.

Wong, A. C. M., Chan, C. W. N., & Hui, S. P. (2005). Relationship of gender, body mass index, and axial length with central retinal thickness using optical coherence tomography. *Eye, 19*(3), 292–297.

Wong, T. Y., Foster, P. J., & Johnson, G. J. (2001b). The relationship between ocular dimensions and refraction with adult stature: The Tanjong Pagar Survey. *Investigative Ophthalmology and Visual Science, 42*, 1237–1242.

Wong, T. Y., Foster, P. J., & Ng, T. P. (2001a). Variations in ocular biometry in an adult Chinese population in Singapore: The Tanjong Pagar Survey. *Investigative Ophthalmology and Visual Science, 42*, 73–80.

Yanoff, M., & Fine, B. S. (1982). *Ocular Pathology: A Text and Atlas*. Philadelphia: Harper and Row (pp. 513–514).