

Nagra, M., Gilmartin, B. & Logan, N. S. (2014). Estimation of ocular volume from axial length. *British Journal of Ophthalmology*, 98(12), pp. 1697-1701. doi: 10.1136/bjophthalmol-2013-304652



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Original citation: Nagra, M., Gilmartin, B. & Logan, N. S. (2014). Estimation of ocular volume from axial length. *British Journal of Ophthalmology*, 98(12), pp. 1697-1701. doi: 10.1136/bjophthalmol-2013-304652

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Estimation of ocular volume from axial length

Journal:	<i>British Journal of Ophthalmology</i>
Manuscript ID:	bjophthalmol-2013-304652.R1
Article Type:	Clinical science
Date Submitted by the Author:	26-May-2014
Complete List of Authors:	Nagra, Manbir; Aston University, School of Life and Health Sciences Gilmartin, Bernard; Aston University, Optometry Logan, nicola; Aston University, Optometry
Keywords:	Optics and Refraction, Eye (Globe), Imaging

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5 **Title:** Estimation of ocular volume from axial length
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33 **Keywords:**

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35 myopia, ocular biometry, ocular volume, refractive error
36

37 **Word count (excluding title page, abstract, references, figures and tables and**
38 **figure/table legends): 1847 words**
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3 **Title:** Estimation of ocular volume from axial length
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6 **ABSTRACT**
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8 **BACKGROUND/AIMS:**
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10 To determine which biometric parameters provide optimum predictive power for ocular
11 volume.
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15 **METHODS:** Sixty-seven adult subjects were scanned with a Siemens 3-T MRI scanner.
16 Mean Spherical Error, MSE (D) was measured with a Shin-Nippon autorefractor and a
17 Zeiss *IOLMaster* used to measure (mm) axial length (AL), anterior chamber depth
18 (ACD) and corneal radius (CR). Total ocular volume (TOV) was calculated from T2-
19 weighted MR images (voxel size 1.0mm³) using an automatic voxel counting and
20 shading algorithm. Each MR slice was subsequently edited manually in the axial,
21 sagittal and coronal plane, the latter enabling location of the posterior pole of the
22 crystalline lens and partitioning of TOV into anterior (AV) and posterior (PV) regions.
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31 **RESULTS:** Mean values (\pm sd) for MSE (D), AL (mm), ACD (mm) and CR (mm) were -
32 2.62 \pm 3.83, 24.51 \pm 1.47, 3.55 \pm 0.34, 7.75 \pm 0.28, respectively. Mean values (\pm sd) for TOV,
33 AV and PV (mm³) were 8168.21 \pm 1141.86, 1099.40 \pm 139.24, 7068.82 \pm 1134.05,
34 respectively. TOV showed significant correlation with MSE, AL, PV (all $p < 0.001$), CR
35 ($p = 0.043$), and ACD ($p = 0.024$). Bar CR, the correlations were shown to be wholly
36 attributable to variation in PV. Multiple linear regression indicated that the combination
37 of AL and CR provided optimum R² values of 79.4% for TOV.
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44 **CONCLUSION:** Clinically useful estimations of ocular volume can be obtained from
45 measurement of AL and CR.
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INTRODUCTION

A recent comprehensive review of factors contributing to the aetiology of myopia included an analysis of the association between myopia and ocular disease.¹ It was demonstrated that the risk of disease, traditionally linked to dioptric levels greater than 6D, was also significant between 1 and 3D, a level generally described as physiological myopia.² Further, the review demonstrated that risk was not confined to myopia as hyperopia is associated with higher rates of exudative age-related maculopathy and angle closure glaucoma.¹ Longitudinal axial length is the principal structural correlate for refractive error^{3,4} and a recent cross-sectional study on 120 Hong Kong children used binary logistic regressions to demonstrate that after adjusting for myopia over -8D, age, gender, duration of myopia, family retinal history and intraocular pressure, an axial length longer than 26.5 mm was a significant risk factor for peripheral retinal changes, optic nerve crescents and white-without-pressure.⁵

Ocular volume is more directly relevant than longitudinal axial length to the structural and biomechanical integrity of the globe, particularly in myopia.⁶ If the eye is treated as a simple sphere then a 12.8% increase in axial length from 23.5mm (typical for an emmetropic individual) to 26.5mm (typical for a highly myopic individual) results in an increase in ocular volume of 43.4% (i.e. from 6795 mm³ to 9744 mm³). A 6.4% decrease in axial length to 22mm (typical for a hyperopic individual) results in a decrease in volume of 17.9% (i.e. from 6795 mm³ to 5575 mm³). A systematic analysis of *in vivo* measures of ocular volume and longitudinal axial length has yet to be reported.

Ocular MRI has been used in ophthalmic research in areas such as accommodation^{7, 8} and myopia.⁹⁻¹² Our laboratory was the first to use 3-D ocular MRI to report ocular volume in emmetropic and myopic eyes.^{9,10} The technique can also account for the differences between emmetropia and myopia in the shape of the posterior vitreous chamber.¹¹ Our MRI studies to date have generated ocular volume data across a range of refractive error and the aim of the present study is to investigate the utility of generally available biometric measures in estimating ocular volume.

MATERIALS AND METHODS

The study was approved by the Aston University Research and Ethics Committee; all aspects of the investigation were carried out in accordance with the tenets of the Declaration of Helsinki. Informed consent was obtained from all subjects.

Subjects

Sixty-seven adult subjects were recruited from the Aston University student and staff population. Subject age ranged from 18 to 40 years (mean age 26.20 ± 6.24 years); the cohort comprised of 23 males and 44 females of predominantly white European and South Asian ethnicities (54% white European; 40% South Asian; 3% African-Caribbean; 3% Chinese).

Refraction, axial length, keratometry, and anterior chamber depth measurements

Objective measurements of refractive error for both eyes were obtained under cycloplegia (one drop of tropicamide ophthalmic solution 0.5%, *Minims*® Bausch and Lomb, Surrey, UK). An open-view binocular infrared autorefractor (Shin Nippon SRW-5000, Ryusyo Industrial Co. Ltd, Osaka, Japan) was used to obtain five readings per eye and average refractive error expressed as Mean Spherical Error (MSE, D).

Partial coherence interferometry (PCI) longitudinal axial length (AL) measurements, central corneal radius (CR) and anterior chamber depth (ACD) were determined (mm) using the Zeiss *IOLMaster* (Carl Zeiss Meditec, Inc., Dublin, California, USA). AL was expressed as the mean of five measurements. Mean CR was expressed as the mean of the horizontal and vertical corneal radii following three measurements, and a single capture automatically generated mean ACD based on five measurements.

Ocular volume

The MRI protocol, verification, and repeatability statistics for the MRI technique employed in this study have been previously reported.⁹⁻¹¹ Calculation of ocular volume followed the acquisition of T2-weighted MR images using a Siemens trio 3-T whole body MR scanner (Siemens Medical Systems, Iselin, NJ) with an eight phase head coil (voxel dimensions 1.0 x 1.0 x 1.0 mm). Images were optimised to reveal the fluid-filled

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3 chambers of the eyes. An automatic voxel shading algorithm was applied and if
4 required, shading was subsequently edited manually following visual inspection of each
5 MR slice in each of the axial, sagittal and coronal planes (approximately 25 slices per
6 plane). The program provided a standard voxel count to calculate volume.^{9,10}
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12 With reference to the longitudinal visual axis, the anterior volume was defined as the
13 region from the posterior corneal surface to the posterior pole of the lens; the posterior
14 volume was defined as the region from the posterior pole of the lens to the retinal
15 surface (vitreous-retinal interface). The approximate location of the posterior pole of the
16 lens was taken to be the first MR coronal slice to fall wholly within the posterior vitreous
17 chamber i.e. the slice that indicated the delineation of the non-fluid lens from the fluid
18 vitreous. Shaded voxels were then removed for slices in the coronal plane between the
19 posterior corneal surface and the posterior lens pole (i.e. the anterior volume); the
20 remaining voxels were counted by the *mri3dX* program (developed by Professor Krish
21 Singh, 2005) to generate posterior volume in mm³ (PV). Subtracting the posterior
22 volume from the total volume (TOV) gave values for the anterior volume (AV).
23 Correlations were calculated between MSE, AL, CR, ACD and volume (PV, AV, and
24 TOV). All statistical analyses were undertaken using SPSS version 21.0 (IBM, IL,
25 USA).
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39 RESULTS

40 A two-tailed paired student's t-test for MSE, AL, CR, ACD, PV, AV and TOV showed no
41 overall group difference between right and left eye data (all $p > 0.05$). Right eye data are
42 presented.
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47 Mean data

48 Mean Spherical Error, MSE (D) mean -2.62 ± 3.83 (range -10.56 to $+4.38$, see Figure 1),
49 mean AL (mm) 24.51 ± 1.47 (range 21.72 to 28.12), mean CR (taken as the mean of the
50 horizontal and vertical corneal radii) were (in mm) 7.75 ± 0.28 (range 6.95 to 8.38) and
51 mean ACD (in mm) 3.55 ± 0.34 (range 2.23 - 4.39).
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3 Mean TOV (mm³) was 8168.21±1141.86 (range 5036.00-11777.00); mean AV was
4 1099.40 ±139.24 (range 633.00-1422.00) and mean PV was 7068.82±1134.05 (range
5 4017.00-10646.00).
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8 9 10 **Pearson's correlation coefficients**

11 A more negative MSE was significantly correlated with a longer AL ($p<0.001$, $R^2=0.76$),
12 a steeper CR ($p=0.002$, $R^2=0.14$), and a deeper ACD ($p=0.046$, $R^2=0.06$). A greater
13 TOV was also significantly correlated with a longer AL ($p<0.001$, $R^2=0.74$), an
14 increasingly negative MSE ($p<0.001$, $R^2=0.43$), a flatter mean CR ($p=0.043$, $R^2=0.06$),
15 and a deeper ACD ($p=0.024$, $R^2=0.08$). Mean CR was not correlated with AL ($p=0.91$,
16 $R^2=0.002$), but a significant increase in ACD was noted with increasing AL ($p=0.006$,
17 $R^2=0.11$).
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26 **Anterior ocular volume (AV)**

27 AV did not bear any significant correlation with MSE, AL (Figures 2 and 3), CR, ACD,
28 PV, or TOV (all $p>0.05$)
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33 **Posterior ocular volume (PV)**

34 An increase in PV significantly correlated with a longer AL ($p<0.001$, $R^2=0.76$), an
35 increase in negative MSE ($p<0.001$, $R^2=0.46$), a larger TOV ($p<0.001$, $R^2=0.99$) (Figure
36 2 and 3) and a deeper ACD ($p=0.030$, $R^2=0.07$), but the relationship with mean CR just
37 failed to reach statistical significance ($p=0.060$, $R^2=0.05$).
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44 **Regression analysis**

45 Simple linear regressions showed that mean CR accounted for 6.2% of the variance in
46 TOV ($F=4.28$, $p=0.043$); ACD for 7.6% ($F=5.36$, $p=0.024$), MSE for 42.6% ($F=48.32$,
47 $p<0.001$), and AL for 73.8% of the variance in TOV ($F=183.08$, $p<0.001$).
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53 A Stepwise method of multiple regression was employed; AL and corneal radius were
54 automatically selected by SPSS as the predictors which created the best model of
55 ocular volume prediction. AL alone contributed to 73.8% of the variance in TOV; mean
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CR contributed a further 5.6%; hence both AL and mean CR could account for 79.4% of the variance in TOV.

Simple linear regressions showed that mean CR accounted for 5.3% of the variance in PV (F=3.67, p=0.060); ACD for 7% (F=4.91, p=0.030), MSE for 45.8% (F=55.03, p<0.001), and AL for 75.6% of the variance in PV (F=201.73, p<0.001).

Equations to determine ocular volume

From the multiple linear regression analysis, the following equation for TOV (in mm³) was derived; AL and mean CR are expressed in mm:

$$\text{TOV} = -15565.86 + (662.62 \cdot \text{AL}) + (967.18 \cdot \text{Mean CR}) \quad \text{Eq 1}$$

The robustness of the equation may be gauged from examining the difference between unadjusted and adjusted R² values, 0.794 and 0.788, respectively. The difference of 0.006 thus indicates that that if the equation were derived from a larger population it would account for only 0.6% less variance.

From multiple linear regression analysis, the following equation for PV (in mm³) was derived; AL and mean CR are expressed in mm:

$$\text{PV} = -16155.62 + (666.41 \cdot \text{AL}) + (889.41 \cdot \text{Mean CR}) \quad \text{Eq 2}$$

The R² for the PV multiple regression was 0.805 and the adjusted R²=0.798; i.e. a difference of 0.007 (0.7%).

The regression equations in Table 1 may be used to calculate volumes in situations where only one biometric parameter may be available. Two-tailed significance p-values are shown in brackets.

Predictor	Posterior volume	Total volume
Axial length (mm)	y = 668.70x - 9319.50 R ² = 0.76 (p<0.001)	y = 665.11x - 8132.00 R ² = 0.74 (p<0.001)

MSE (D)	$y = -200.65x + 6543.98$ $R^2 = 0.46$ (p<0.001)	$y = -194.83x + 7658.57$ $R^2 = 0.43$ (p<0.001)
Anterior chamber depth (mm)	$y = 890.29x + 3909.35$ $R^2 = 0.07$ (p=0.030)	$y = 933.54x + 4855.27$ $R^2 = 0.08$ (p=0.024)
Mean corneal radius (mm)	$y = 937.17x - 193.51$ $R^2 = 0.05$ (p=0.060)	$y = 1014.663x + 305.33$ $R^2 = 0.06$ (p=0.043)

Total MRI derived volume was also compared to the equivalent volume for a sphere using the formula $\frac{4}{3} * \pi * r^3$ where 'r' is half the axial length. A paired Student's t-test indicated significant differences between the two volume datasets (p<0.001). Volume for eyes with axial lengths less than 26mm were underestimated by the sphere formula (by 17.54% for an axial length of 22mm) and overestimated for axial lengths greater than 26mm (by 6.43% for an axial length of 28mm) (see Figure 4 and Table 2).

PCI AL	MRI regression vol	Sphere regression vol	Difference (MRI-Sphere)	Percentage difference
22	6500.42	5360.34	1140.08	17.54
23	7165.53	6327.81	837.72	11.69
24	7830.64	7295.28	535.36	6.84
25	8495.75	8262.75	233.00	2.74
26	9160.86	9230.22	-69.36	-0.76
27	9825.97	10197.69	-371.72	-3.78
28	10491.08	11165.16	-674.08	-6.43

DISCUSSION

As expected, total ocular volume increased with a longer axial length. However, anterior volume bore no significant relationship to either axial length or to ametropia (expressed as MSE). Conversely, posterior eye volume showed a strong correlation with axial length and MSE, supporting previous findings^{9,11,12} that an increase in posterior vitreous chamber depth is the main contributor to increased axial length in myopia.

Whereas the correlation between linear measurements of AL and ACD was calculated solely from measurements made using the Zeiss IOLMaster, the correlation between AL and AV was calculated from a combination of PCI (AL) and volumetric data based on an MRI 1mm³ voxel count (AV). The resolution of volumetric data will thus be

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3 significantly less than PCI data and less able therefore to reflect the significant
4 correlation evident between AL and ACD.
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9 Estimation of ocular volume from axial length may facilitate further investigation of the
10 effect of intravitreal injection of ophthalmic drugs on intra ocular pressure (IOP).¹³⁻¹⁷

11 Several reports have suggested a link between axial length, refractive error and IOP
12 increase following injection,¹⁵⁻¹⁷ but others have found evidence to the contrary.¹⁸

13 Although injection volumes are generally small (of the order of 0.05ml) a recent study on
14 post-mortem porcine globes demonstrated increases in IOP of approximately 15mmHg
15 following one-second 15ml (0.015ml) micro-infusions of phosphate buffered saline.¹⁹ A
16 clinical research application of this study could be, therefore, to examine whether ocular
17 volume is a structural correlate for IOP change following intravitreal injections.
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25 Using a similar subject group to the present study Santodomingo et al²⁰ demonstrated
26 that axial length determined using the Zeiss *IOLMaster* did not differ significantly from
27 that determined by 10MHz A-scan applanation ultrasonography (Storz Omega Compu-
28 Scan Biometric Ruler, Storz International, St Louis, MO, USA). Ultrasound measures of
29 axial length can therefore be used to estimate total ocular volume and posterior ocular
30 volume from Equations 1 and 2 respectively.
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38 REFERENCES AND ACKNOWLEDGEMENTS

39
40 **Acknowledgements:** We acknowledge Krish D Singh, Elizabeth Wilkinson, Jade Thai,
41 and Jon Wood for assistance with data collection. We thank Richard Armstrong and
42 Chinyere Nzekwe-Excel for their advice on statistical analysis.
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47 **Funding:** The College of Optometrists and The Lord Dowding Fund for Humane
48 Research are acknowledged for funding support.
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LEGENDS FOR DISPLAY ITEMS:

Fig 1 Histogram showing distribution of Mean Spherical Error (MSE, in D).

Fig 2 Anterior and Posterior ocular volume (mm^3) plotted as a function of MSE (D). Unfilled circles represent anterior volume; filled circles represent posterior volume.

Fig 3 Anterior and Posterior ocular volume (mm^3) plotted as a function of AL (mm). Unfilled circles represent anterior volume; filled circles represent posterior volume.

Fig 4 Total MRI volume (mm^3) plotted as a function of AL (mm) represented by the filled circles, and the equivalent volume of a sphere (mm^3) also plotted as a function of AL, represented by the unfilled circles.

Table 1 Linear regression equations for both total ocular volume and posterior ocular volume based on axial length and MSE.

Table 2 AL values (mm) from 22mm to 28mm were inputted into the linear regression equations representing total MRI volume (mm^3), and sphere formula volume (mm^3) from Fig 4.

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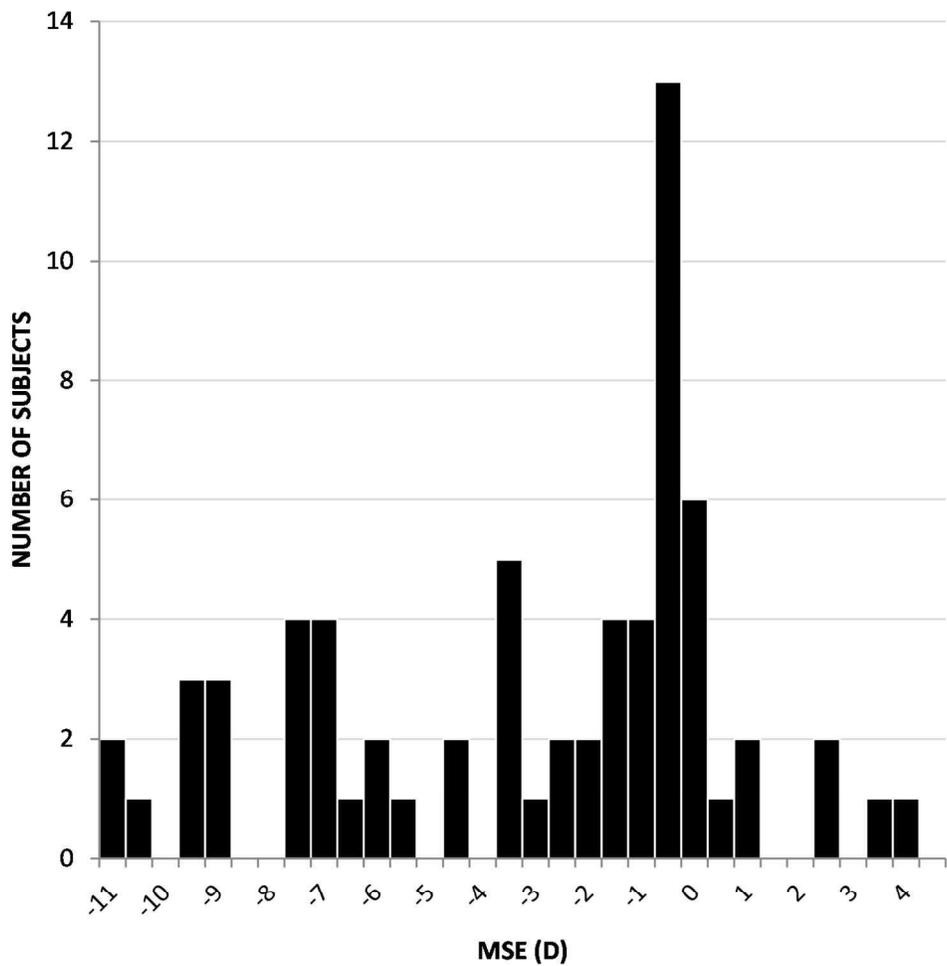


Fig 1 Histogram showing distribution of Mean Spherical Error (MSE, in D).
127x128mm (300 x 300 DPI)

View Only

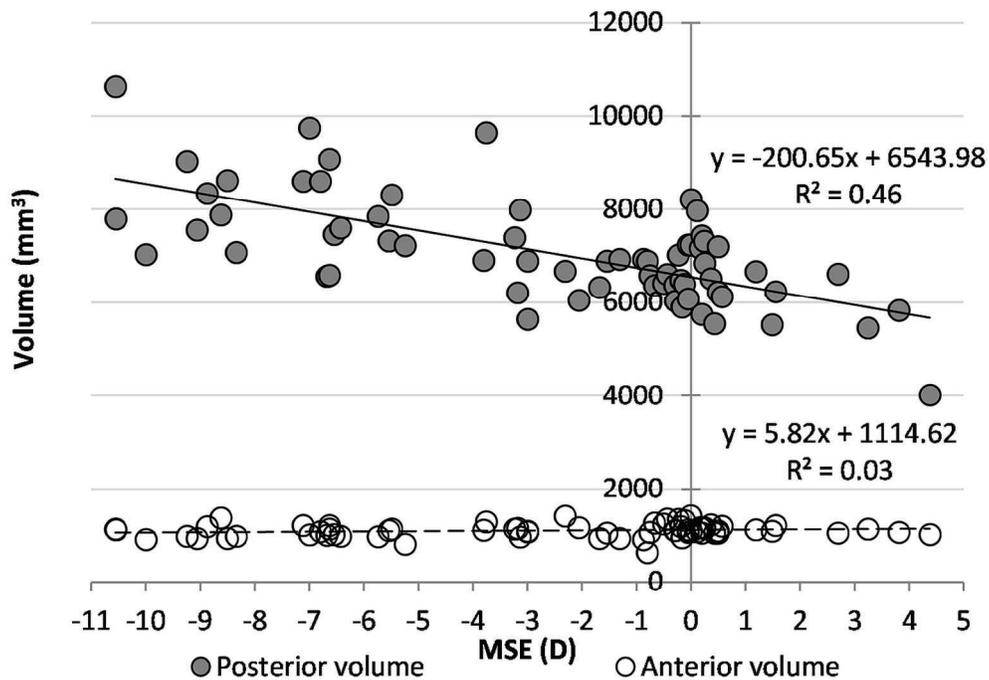


Fig 2 Anterior and Posterior ocular volume (mm³) plotted as a function of MSE (D). Unfilled circles represent anterior volume; filled circles represent posterior volume.
131x90mm (300 x 300 DPI)

Review Only

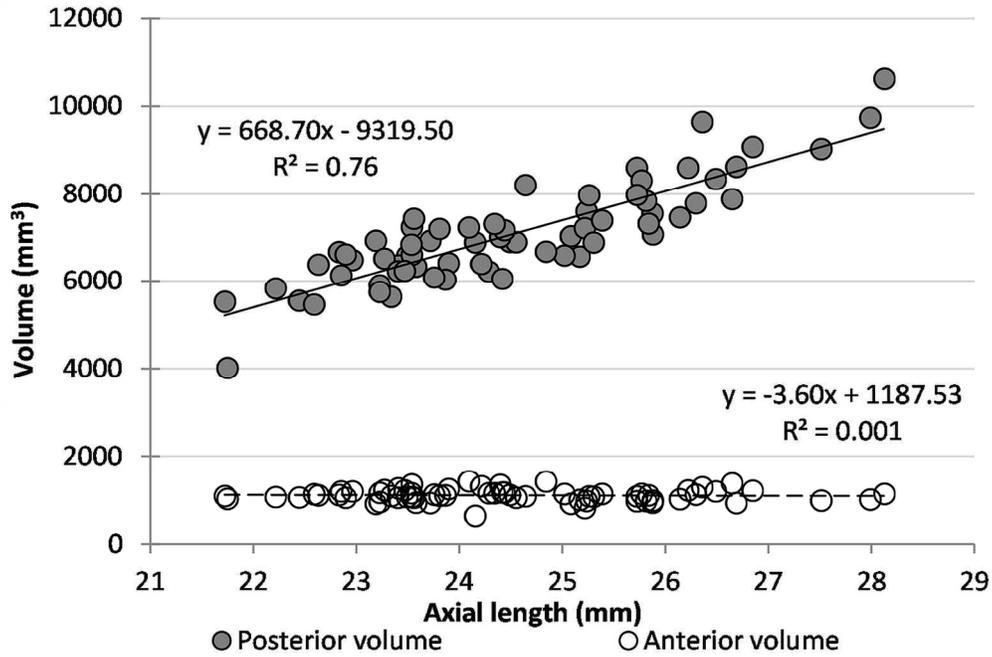


Fig 3 Anterior and Posterior ocular volume (mm³) plotted as a function of AL (mm). Unfilled circles represent anterior volume; filled circles represent posterior volume.
135x90mm (300 x 300 DPI)

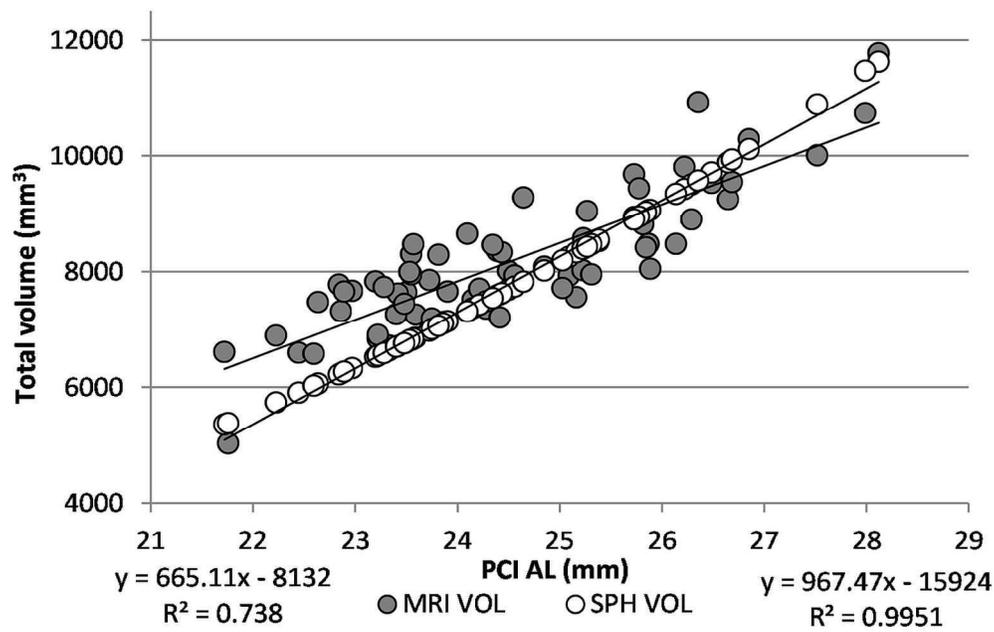


Fig 4 Total MRI volume (mm³) plotted as a function of AL (mm) represented by the filled circles, and the equivalent volume of a sphere (mm³) also plotted as a function of AL, represented by the unfilled circles.
140x90mm (300 x 300 DPI)