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In Vivo Measurement of the Human Vitreous Chamber Volume Using Computed Tomography Imaging of 100 Eyes

Ariel M. Azhdam, Robert A. Goldberg, and Shoaib Ugradar

Stein Eye Institute, Division of Orbital and Ophthalmic Plastic Surgery, University of California, Los Angeles, Los Angeles, CA, USA

Correspondence: Ariel M. Azhdam, Stein Eye Institute, 300 Stein Plaza, 1st Floor, Los Angeles, CA 90095, USA. e-mail: arielazhdam1@gmail.com

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Purpose: To accurately measure the vitreous chamber volume (VCV) in humans using high-resolution computed tomography (CT) scanning techniques combined with three-dimensional analysis software. Potential relationships between age, axial length, and VCVs were also explored.

Methods: In this retrospective study, the eyes of 100 healthy individuals were studied. Scans were acquired during clinical care and did not show any signs of orbital pathology. Exclusion criteria included any ocular history. CT scans were acquired with a slice thickness of 0.7 mm, and volumetric analysis was carried out using the MIMICS image analysis software version 19.0 (Materialise, Leuven, Belgium).

Results: The final sample included 100 eyes from 50 patients (30 women, 20 men). The mean age was 48.67 $\pm$ 20.72 years, and the age range was 18 to 91 years. The mean VCV was 4.649.99 $\pm$ 0.426.54 mm^3 for women and 4.969.0 $\pm$ 0.465.20 mm^3 for men. We found a significant correlation between age and VCV ($P < 0.001$), axial length and VCV ($P < 0.001$), and age and axial length ($P < 0.005$).

Conclusions: The VCV appears to be greater than the current consensus suggests. This work also suggests that the VCV is associated with age and axial length, indicating that it is dynamic and may change throughout adulthood.

Translational Relevance: This information regarding the volume of the vitreous chamber is useful for our understanding of proper dosage and behavior of agents we commonly insert into the vitreous chamber.

Introduction

The vitreous body typically occupies up to 80% of the volume of the normal human eye.[1] Despite this, it is perhaps the least understood ocular structure. It is by design invisible, posing a major challenge to any endeavors to study its structure and function. The earliest histologic studies that looked at the vitreous chamber volume (VCV) were biased by the use of acidic tissue fixatives and frozen sections, which resulted in the precipitation of glycosaminoglycans and subsequent changes to the vitreous and, therefore, volume of the eye.[2]

The introduction of slit-lamp biomicroscopy contributed by facilitating the in vivo study of vitreous structure. Although this technique did not suffer the challenges of tissue fixation, it led to a variety of sometimes conflicting descriptions that included the presence of membranelles,[3] cisterns,[4] fibers,[2] and pockets.[5] These accounts highlight the difficulty in characterizing the vitreous body.

The current consensus suggests that the volume of the vitreous ranges between 4 and 4.4 mls[3].[2] These figures have been derived from early postmortem studies. However, constitution of the vitreous changes after death, and this is confounded by the treatment of the tissue during processing.[6]

Previously considered a quiescent structure, there is a growing body of evidence that underscores the importance of the vitreous and its role in pathologic conditions that involve the posterior segment.[7] Information regarding the VCV could influence common procedures that require the instillation of substances such as oil and gas into the eye. Frequent problems of over/underfilling the eye could potentially be avoided.

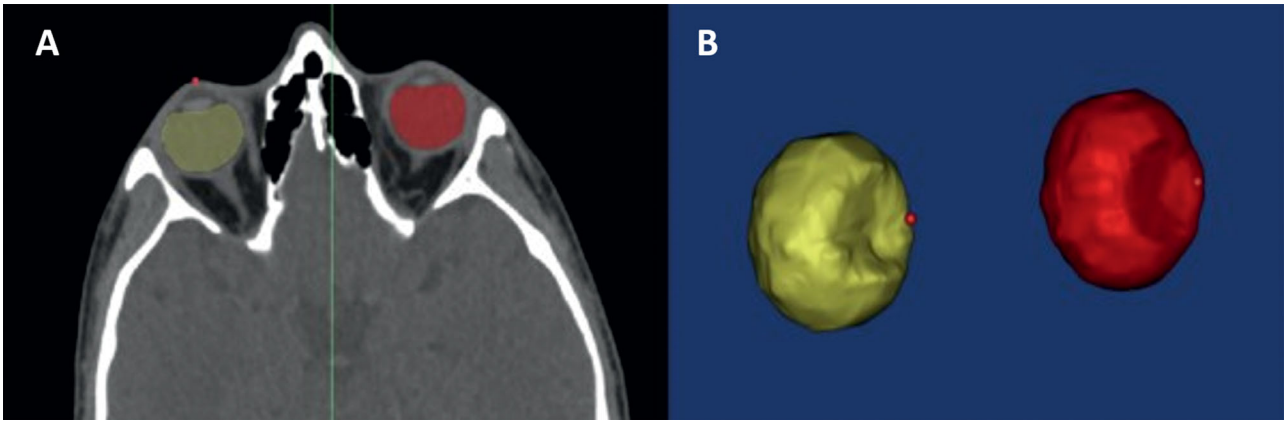

Figure 1. (A) Manual segmentation of the vitreous chamber on axial CT scans. The vitreous chamber was manually segmented (filled in), slice by slice, using axial, sagittal, and coronal slices simultaneously to create a mask. A three-dimensional model (B) was created from this mask. The outer surface area of this model was calculated using the software. Total retina and choroidal volumes were calculated by multiplying the surface area of each vitreous cavity by the average choroid/retina thickness.

Furthermore, knowledge of these parameters could aid in determining drug concentrations and volumes of medication injected into the vitreous chamber (VC).

Despite the potential clinical implications, we found few studies that sought to specifically report on the VCV. Xu and colleagues[8] used magnetic resonance imaging (MRI) to study the biometric properties of 31 patients. They reported VCVs of 5.482 ± 0.440 mL. Interestingly, these figures are greater than the currently accepted volumes for the vitreous, and their method has not been validated. Furthermore, they did not take the thickness of the choroid and retina into account when measuring the VCV. Finally, with only 15 women and 16 men with ages ranging from 18 to 32 years, their study may not be generalizable to a wider age group.

The purpose of this study was to accurately measure the VCV using high-resolution computed tomography (CT) scans to provide key anthropometric data.

Methods

Patients

We retrospectively reviewed the CT scans of 50 patients (30 women and 20 men) from patients at the Chelsea and Westminster Hospital, London, UK. Patients with any ocular or orbital pathology or a history of ocular surgery were excluded from the study. The study adhered to the tenets of the Declaration of Helsinki, and institutional review board approval was provided by the Chelsea and Westminster Hospital, London, UK. CT scans were carried out as part of the patient's clinical care using a SOMATOM Definition AS/AS+ 64 slice CT scanner (Siemens, Munich, Germany). Continuous scanning with a slice thickness of 0.7 mm had been applied. Patients were in the supine position and asked to look at a fixed point. No gantry tilt was applied.

Volume Calculation Method

The Mimics (Materialise, Leuven, Belgium) image analysis tool was used to calculate the VC volume. Three-dimensional reconstructions of the eyes within the orbit were created. The MIMICS image analysis software was chosen since it provides visualization in the axial, coronal, and sagittal planes on the same display screen, allowing for simultaneous visibility of segmentation in each stack. Segmentation in one plane immediately appears on the other two planes. On the axial scans, the VC of each eye was manually delineated in every slice to ensure accuracy. The software calculated the tissue volume and surface area by means of voxel addition, and this was expressed in cubic millimeters (Fig. 1). Since the choroid and retina are not easily identified on CT or MRI, their volume was calculated using average thickness maps (0.458 mm^2 for the choroid and retina combined) defined in previous studies[9] and multiplying this by the internal surface area. These figures were obtained using OCT (Cirrus HD-OCT, Carl Zeiss Meditec, Inc., Dublin, CA). The standard deviation across all regions of the in this study was between 76 and 81 µm. This volume was then subtracted from the VC volume (Fig. 1).

Calculation of Axial Length

The CT scans were oriented so that a plane that passes through the transverse dimensions of the globe

showing the scleral rim, lens, optic nerve, and horizontal recti on either side was outlined. The axial length was measured by using the distance between two points on a horizontal line drawn along the corneal apex anteriorly and along the scleral rim posteriorly.

Intraobserver Variability

For intraobserver variability, one observer calculated the VC volume of 10 different eyes on five consecutive working days. Intraobserver variability was expressed using the coefficient of variation, calculated as the SD divided by 100 × the mean of the measurements.

Statistical Analysis

The statistical computer program SPSS version 22.0 (SPSS, Inc., Chicago, IL) was used for statistical analysis. Intraclass correlation coefficients (ICCs) and their 95% confidence intervals were calculated for all parameters to determine the intraobserver variability (0 = no agreement, 1 = perfect agreement between measurement occasions). The association between age and axial length with VCV was analyzed following the creation of a Gaussian generalized estimating equation with exchangeable correlation structure.

Results

A total of 100 eyes from 50 patients (30 women, 20 men) were included in this study. The mean (SD) age was 44.3 (22.9) years for men and 51.7 (18.9) years for women. The mean (SD) VCV was 4.649.97 mm^3 (0.426.54) for women and 4.969.0 mm^3 (0.465.20) for men. The mean (SD) volume of the posterior chamber for men was 4969 (465) mm^3, while that for women was 4650 (426) mm^3 ($P < 0.05$). We found significant correlations between age and VCV ($P < 0.001$; −17.15 to −2.88) (Fig. 2a), axial length and VCV ($P < 0.001$; 360.8 to 460.24) (Fig. 2b), and age and axial length ($P < 0.05$; −0.04 to 0) (Fig. 2c). The mean (SD) axial length for men was 24.7 (1.13) mm, while that for women was

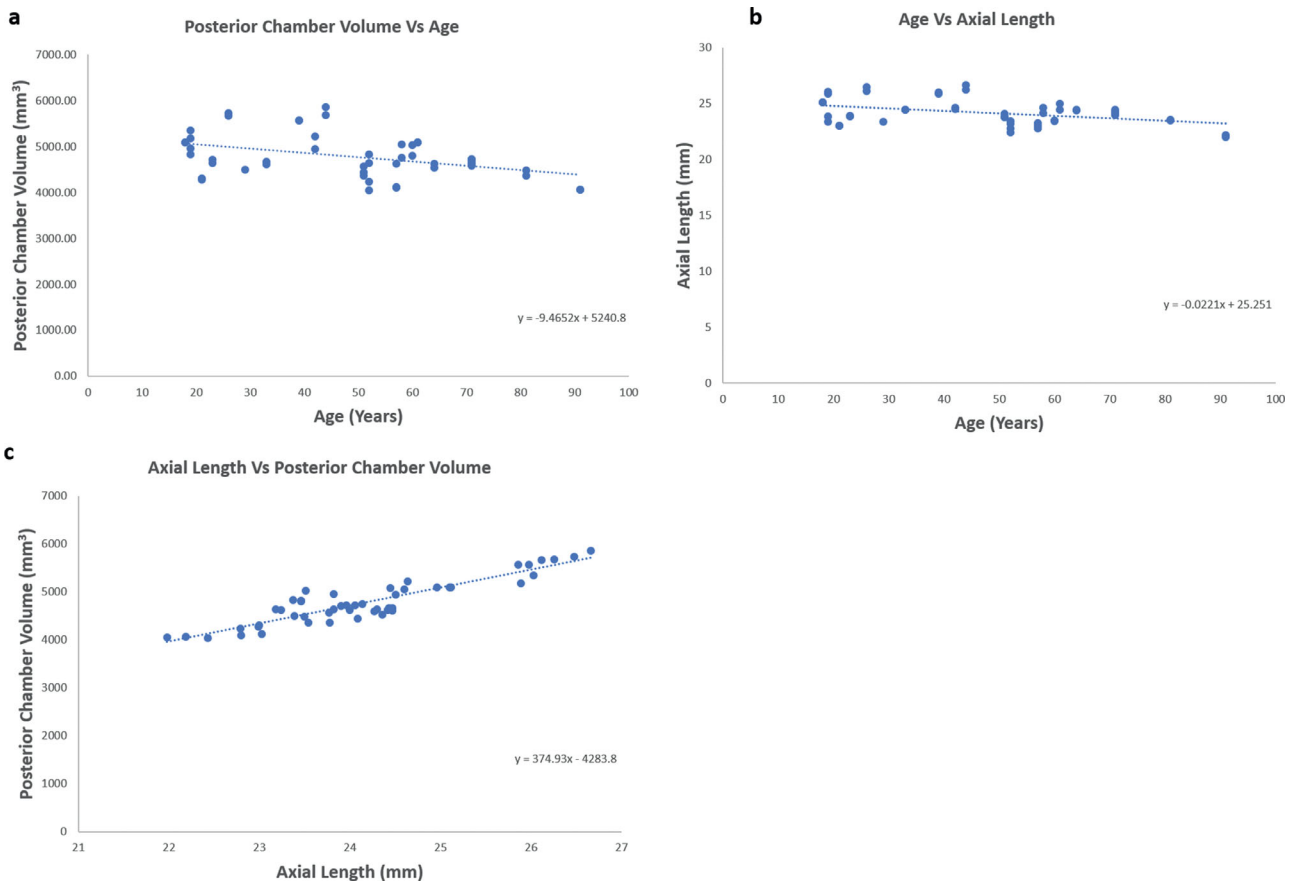

Figure 2. (a) The relationship between age (years) and posterior chamber volume (mm^3). (b) The relationship between age (years) and axial length (mm). (c) The relationship between the axial length (mm) and posterior chamber volume (mm^3).

23.7 (0.97) mm ($P < 0.05$). On separating men and women, the correlations between age and VCV (men, $P < 0.05$; women, $P < 0.01$), axial length and VCV (men, $P < 0.05$; women, $P < 0.05$), and axial length versus age (men, $P < 0.05$; women, $P < 0.03$) were maintained.

Intraobserver Variability

Intraobserver variability of the AL and VC volume measurements on 10 different eyes was 0.07% for AL and 0.83% for VC volume measurement. The ICC was found to range between 0.99 (95% CI, 0.984–0.993) and 0.989 (95% CI, 0.99–0.99).

Discussion

The VC is becoming an increasingly important arena for the pharmaceutical industry. Aside from conventional therapy that requires the insertion of gas and oil into the chamber, new therapeutic agents are increasingly being used to target the retina. Information regarding the VCV would be useful in aiding our understanding of the behavior of these agents once deposited into the VC. To our knowledge, this is the first study that has sought to specifically measure the VCV.

In our sample of 100 eyes, we found that the average VCV is greater than the currently accepted volume of 4 to 4.4 mm^3. We found a volume of $4.649.99 \pm 0.426.54$ mm^3 for women and $4.968.81 \pm 0.465.20$ mm^3 for men. A previous study using MRI, by Xu and colleagues,[8] found a greater average VC volume of 5.482 ± 0.440 mm^3 in their 31 patients. However, their study did not account for the choroid and retina tissues that are not visible on a MRI scan, therefore explaining the larger volumes found in their study. Further, their study had fewer patients (32), and the age range of their patients was only between 18 and 32 years.

In our study, we designated a volume for the retina and choroid by using previously published thickness maps of both tissues. Although the retina and choroid have different thicknesses throughout the fundus, we used an average thickness to create our volume. This may introduce an error. However, had we used the minimum thickness of the choroid (nasal portion) and the retina (foveola), the possible error introduced would have been less than 5% of the overall volume measured. Further, we did not account for the posterior surface area of the lens. Typically, the posterior lens in adults measures 6.11 (SD 1.4) mm in diameter when looking at a target 2 m away (using MRI).[10] Using this measurement, the area of the posterior surface of the lens would be 29.3 mm^2. Given that the average surface area of the vitreous cavity was 1481 mm^2, omission of this value could only result in an error of 1.97%.

We found that the VCV and axial length decrease with age in , and this is in agreement with previous studies.[11,12] This phenomenon may contribute to emmetropization of the aging eye, caused by age-related cross-linking of the cornea and the sclera.[13–15] Cross-linking of these tissues involves formation of bonds between adjacent collagen fibrils in the aforementioned tissues, possibly leading to shrinkage of these tissues as the collagen is packed more closely.[14]

We also found that the average VCV was greater in men, and this is supported by the findings of Wong et al.[16] and Shufelt et al.,[17] who found that the length of vitreous was greater in male patients. Our study revealed a positive correlation between axial length and VCV measurements (410.52; 95% CI, –360.8 to 460.24; $P < 0.001$), implying that the axial length is a reliable indicator of VCV.

Although MRI has previously been used as the modality of choice for studying the dimensions of the eye, we found that CT scans with a slice thickness of 0.7 mm provided highly accurate information for volume calculation. The lens and inner dimensions of all eyes studied were clearly visible, allowing for an accurate three-dimensional reconstruction.

This work indicates that the volume of the vitreous chamber might be greater than previously suspected. Furthermore, it adds to previous work that suggests that eyes may decrease in size with age. While it is difficult to draw broad conclusions about the vitreous chamber volume from a sample of 100 eyes, this study provides evidence to suggest that a reappraisal of the currently accepted dimensions for the vitreous chamber is required.

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