

## **A longitudinal study of accommodative changes in biometry during incipient presbyopia**

**Running title: Accommodative changes during incipient presbyopia**

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## Abstract

**Purpose:** To profile accommodative biometric changes longitudinally and to determine the influence of age-related ocular structural changes on the accommodative response prior to the onset of presbyopia.

**Methods:** Twenty participants (aged 34 to 41 years) were reviewed at six, 6 monthly intervals over 2.5 years. At each visit, ocular biometry was measured with the LenStar biometer (Haag-Streit, Switzerland) in response to 0.00, 3.00 and 4.50 D stimuli. Accommodative responses were measured by the WAM 5500 Auto Ref/Keratometer (Grand Seiko, Japan).

**Results:** During accommodation, anterior chamber depth reduced ( $F=29$ ,  $p<0.001$ ), whereas crystalline lens thickness ( $F=39$ ,  $p<0.001$ ) and axial length ( $F=5.4$ ,  $p=0.009$ ) increased. The accommodative response ( $F=5.5$ ,  $p=0.001$ ) and the change in anterior chamber depth ( $F=3.1$ ,  $p=0.039$ ), crystalline lens thickness ( $F=3.0$ ,  $p=0.042$ ) and axial length ( $F=2.5$ ,  $p=0.038$ ) in response to the 4.50 D accommodative target reduced after 2.5 years. However, the change in anterior chamber depth ( $F=2.2$ ,  $p=0.097$ ), crystalline lens thickness ( $F=1.7$ ,  $p=0.18$ ) and axial length ( $F=1.0$ ,  $p=0.40$ ) per dioptre of accommodation exerted remained invariant after 2.5 years. The increase in disaccommodated crystalline lens thickness with age was not significantly associated with the reduction in accommodative response ( $R=0.32$ ,  $p=0.17$ ).

**Conclusion:** Despite significant age-related structural changes in disaccommodated biometry, the change in biometry per dioptre of accommodation exerted remained invariant with age. The present study supports the Helmholtz theory of accommodation and suggests an increase in lenticular stiffness is primarily responsible for the onset of presbyopia.

## Introduction

Current presbyopia theories are derived from our understanding of the mechanism of accommodation in young eyes, based on the Helmholtz theory.<sup>1</sup> However, despite at least a century of investigation, the exact mechanism of accommodation, and the impact of age-related changes in the accommodative apparatus, remains equivocal.<sup>2,3</sup>

Present understanding of the mechanism of accommodation suggests the contractile increase in ciliary muscle thickness<sup>4,5</sup> reduces zonular tension, which instigates a reduction in crystalline lens equatorial diameter,<sup>6,7</sup> a reduction in the radii of curvature of the anterior and posterior crystalline lens surfaces<sup>8,9</sup> and an increase in crystalline lens axial thickness.<sup>6,7</sup> The increase in lenticular thickness during accommodation is produced entirely by an increase in the thickness of the nucleus<sup>10</sup> and the increase in steepness of the crystalline lens surfaces is greater anteriorly than posteriorly.<sup>8,9</sup> Moreover, the posterior axial movement of the posterior crystalline lens surface during accommodation is smaller than the anterior movement of the anterior crystalline lens surface.<sup>9,11</sup>

The force of ciliary muscle contraction is thought to be transmitted along the uveal tract; pulling the equatorial choroid centripetally and therefore necessitating posterior pole elongation to maintain a constant ocular volume.<sup>12,13</sup> Indeed, a significant increase in ocular axial length has been observed with accommodation.<sup>12-15</sup> The recoil of the choroid, assisted by the posterior zonules,<sup>16</sup> is thought to restore the accommodative apparatus to a disaccommodated **state** following the cessation of accommodation.<sup>1</sup>

With age, Strenk *et al.*<sup>4</sup> and Sheppard & Davies<sup>17</sup> reported ciliary muscle contractility remains invariant, despite an increase in ciliary muscle mass with age.<sup>18</sup> However, more recent research by Croft *et al.*<sup>19</sup> has suggested the contractile response may attenuate with age. Additionally, the increase in the stiffness of the choroid<sup>20,21</sup> and sclera<sup>22,23</sup> with age may dampen the ability of the choroid to restore the accommodative apparatus to a disaccommodated **state** following the cessation of accommodation. However, significant age-related change in crystalline lens size and

shape,<sup>7, 24, 25</sup> and the increase in lenticular stiffness with age,<sup>26</sup> have led to age-related crystalline lens changes becoming central to several presbyopia theories.<sup>2, 3, 27</sup>

Incipient presbyopia represents the phase of presbyopia where the decline in the amplitude of accommodation is critical in functional terms,<sup>28</sup> with a loss of approximately 3.00 D between 35 and 45 years of age.<sup>29</sup> Therefore, understanding the influence of age-related structural changes on the mechanism of accommodation during this period will aid the refinement of models for presbyopia development.

The aim of this study was to profile accommodative biometric changes longitudinally and to determine the influence of age-related ocular structural changes on the accommodative response during incipient presbyopia.

## **Method**

The study was approved by the Aston University Audiology and Optometry Research Ethics Committee and was conducted in accordance with the tenets of the Declaration of Helsinki. Informed written consent was obtained from all the participants after an explanation of the nature and possible consequences of the study.

Incipient presbyopic individuals with an amplitude of accommodation >4.50 D (measured by the push-up, pull-down RAF rule method) and astigmatic error of <0.75 D in their right eye were recruited. In order to collect longitudinal data, the following experimental protocol was repeated every 6 months over 2.5 years. To control for diurnal fluctuations in axial length,<sup>30, 31</sup> the allotted appointment time for each participant was kept as similar as possible for each review visit. One UK registered optometrist (DL) collected the data at each visit.

## ***Stimulus response***

Change in objective refractive error during accommodation was measured by the binocular open-field Grand Seiko WAM-5500 autorefractor (<http://www.grandseiko.com/english/WAM-5500e.htm>).

The right eye of all myopic participants was fitted with a soft daily disposable spherical contact lens (Focus Dailies, nelfilcon A, 69% water content; Ciba Vision, Duluth, GA) **for the duration of the study.** A bespoke +5.00 D Badal lens system with a 90% high contrast Maltese cross target was mounted on the WAM-5500 autorefractor. The fixation target was placed 20 cm, 8 cm and 2 cm away from the Badal lens in order to stimulate 0.00, 3.00 and 4.50 D of accommodation, respectively. The left eye of each patient was occluded and participants were asked to focus on the centre of the Maltese cross as accurately as possible throughout data collection.<sup>32</sup> Participants were exposed to the stimulus for 20 seconds prior to the acquisition of data, which is adequate time to achieve the maximal accommodative response.<sup>33</sup> A 1 minute distance-viewing break was permitted between the presentation of each stimulus level. Three consecutive measurements of refraction were acquired and the change in mean sphere was calculated.

#### ***LenStar biometry***

**Sequentially,** optical biometry was measured by the Haag-Streit LenStar LS-900 (<http://www.haag-streit.com/products/biometry/lenstar-ls-900r.html>), with the addition of a bespoke Badal lens system incorporating a 92% transmission, 8% reflection pellicle beamsplitter (<http://www.edmundoptics.co.uk>), as described previously.<sup>34</sup> The LenStar provides accurate measurements of biometry (**with a resolution of 0.01 mm**) even with a contact lens in place.<sup>34, 35</sup>

In order to provide a 0.00 D, 3.00 D and 4.50 D accommodative stimulus, the target was positioned 10 cm, 7 cm and 5.5 cm away from the +10.00 D Badal lens, respectively. Each participant wore an eye patch over their left eye and was encouraged to maintain clear focus of the fixation target throughout data collection.<sup>32</sup> The presentation order of each accommodative level was randomised and participants were exposed to the stimulus for 20 seconds prior to acquisition of data and were permitted a 1 minute distance-viewing break between stimulus levels. The average of three repeat measures of corneal thickness (CT), anterior chamber depth (ACD), crystalline lens thickness (LT) and

axial length (AXL) were recorded at each accommodative level. Anterior segment length (ASL=CT+ACD+LT) and vitreous chamber depth (VCD=AXL-ASL) were calculated from these values.

### ***Visante AS-OCT crystalline lens thickness measurements***

Where the LenStar biometer was unable to obtain crystalline lens thickness values, presumably due to high light transmittance of the posterior crystalline lens surface, measures were substituted with data collected from a Zeiss Visante AS-OCT ([http://www.zeiss.co.uk/meditec/en\\_gb/home.html](http://www.zeiss.co.uk/meditec/en_gb/home.html)) with version 3.0 software.

Accommodated crystalline lens OCT images were acquired by a Visante AS-OCT (with a resolution of 0.01 mm) by modulating the internal Badal lens optometer to stimulate 0.00, 3.00 and 4.50 D of accommodation. Three crystalline lens images with the vertical fixation line visible<sup>36</sup> were acquired in raw image mode each and were subsequently exported in binary form (512 x 995 pixels) for analysis with custom-designed Matlab R2012b software (<http://uk.mathworks.com>). A pixel:mm conversion factor of 93 pixels per millimetre was derived by comparing disaccommodated Visante crystalline lens pixel thickness values to disaccommodated LenStar crystalline lens millimetre thickness data obtained on the same day from 46 individuals (mean age 39.1 (SD 3.2 years), mean spherical equivalent -1.17 (SD 2.09 DS)).

### ***LenStar error calculations***

The LenStar uses an average refractive index to convert an optical path length into a geometrical AXL. Therefore, to correct for an overestimation of AXL due to the increase in LT with accommodation, the induced error was estimated using equations 1 to 6.

In line with previous publications,<sup>14, 37</sup> the relative proportions of the crystalline lens taken up by the anterior cortex, nucleus and posterior cortex during accommodation were kept constant because, despite the well-established thickening of the nucleus during accommodation,<sup>38</sup> the exact nature of the change in refractive index during accommodation is not fully understood.<sup>9, 39, 40</sup> In order to

compensate for age-related changes in anterior cortex thickness (ACT), nucleus thickness (NT) and posterior cortex thickness (PCT), equations 1, 2 and 3 were used to modify the segmentation of the crystalline lens according to age (in years).<sup>38</sup> OPL and the average refractive index of the eye ( $n_{av}$ ) were calculated using the refractive indices specified by Gullstrand's No. 1 (exact) eye with shell lens (equations 4 and 5).<sup>41</sup> Equation 6 was used to calculate the error (E), which is subtracted from the geometric AXL reported by the LenStar to provide corrected AXL values.

$$ACT = LT * \frac{(0.51 + 0.012 * \text{age})}{(0.51 + 0.012 * \text{age}) + (2.11 + 0.003 * \text{age}) + (0.33 + 0.0082 * \text{age})} \quad (1)$$

$$NT = LT * \frac{(2.11 + 0.003 * \text{age})}{(0.51 + 0.012 * \text{age}) + (2.11 + 0.003 * \text{age}) + (0.33 + 0.0082 * \text{age})} \quad (2)$$

$$PCT = LT * \frac{(0.33 + 0.0082 * \text{age})}{(0.51 + 0.012 * \text{age}) + (2.11 + 0.003 * \text{age}) + (0.33 + 0.0082 * \text{age})} \quad (3)$$

$$OPL = (CT * 1.376) + (ACD * 1.336) + (ACT * 1.386) + (NT * 1.406) + (PCT * 1.386) + (VCD * 1.336) \quad (4)$$

$$n_{av} = \left[ \left( \frac{CT}{AXL} \right) * 1.376 \right] + \left[ \left( \frac{ACD}{AXL} \right) * 1.336 \right] + \left[ \left( \frac{ACT}{AXL} \right) * 1.386 \right] + \left[ \left( \frac{NT}{AXL} \right) * 1.406 \right] + \left[ \left( \frac{PCT}{AXL} \right) * 1.386 \right] + \left[ \left( \frac{VCD}{AXL} \right) * 1.336 \right] \quad (5)$$

$$E = \frac{OPL}{n_{av}} - AXL_{unaccommodated} \quad (6)$$

### **Statistical analysis**

Repeated measures ANOVA testing was used to determine whether the changes in biometry during accommodation (0.00, 3.00 and 4.50 D) were significant at visit 1, and whether any dependency on ametropia classification existed (SPSS, <http://www-01.ibm.com/software/uk/analytics/spss/>). Repeated measures ANOVAs were also used to investigate whether the change in axial biometry at each accommodative level was degraded over the course of the study and whether the response per

diopetre of accommodation exerted changed. The association between changes in disaccommodated LT and changes in the accommodative response were investigated using linear regression analysis.

The target sample size for repeated measures ANOVA testing (within and between interaction), including an effect size (f) of 0.25, an error probability ( $\alpha$ ) of 0.05 and required power (1- $\beta$ ) of 0.80 for 6 repeat measurements amongst 2 groups, was 20 participants (G\*Power, <http://www.gpower.hhu.de/en.html>).

## Results

### Participants

Twenty individuals aged 34 to 41 years were recruited and completed all study visits. Ten participants were emmetropic (mean MSE -0.25 (SD 0.24 D); range -0.62 to +0.17 D) and ten were myopic (mean MSE -3.18 (SD 1.27 D); range -1.29 to -6.06 D). The change in refractive error during the course of the study was not statistically significantly ( $F=1.3$ ,  $p=0.28$ ). All of the myopic participants had previous contact lens wear experience. The baseline average ages of the myopic (37.2 (SD 2.1 years)) and emmetropic (38.2 (SD 2.0 years)) groups were not statistically significantly different ( $t=1.2$ ;  $p=0.26$ ).

The reduction in subjective amplitude of accommodation after 2.5 years was statistically significant ( $F=20$ ,  $p<0.001$ ; Figure 1), however was not dependent on refractive error classification ( $F=1.4$ ,  $p=0.25$ ).

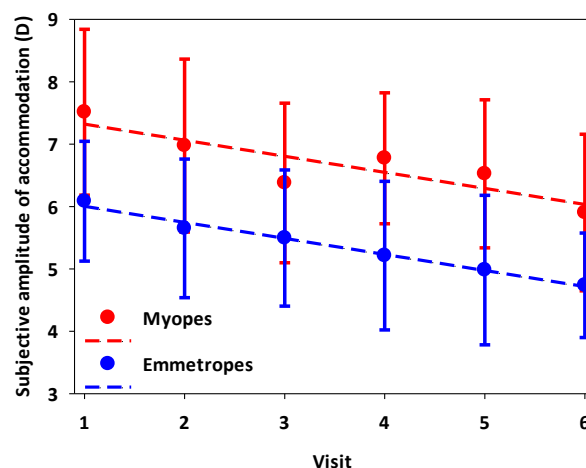




Figure 1. Right eye amplitude of accommodation (with  $\pm 1$  standard deviation error bars) measured in myopic (red; n=10; mean age 37.2 (SD 2.1 years)) and emmetropic (blue; n=10; mean age 38.2 (SD 2.0 years)) participants at each visit.

### Changes in refractive response

Repeated measures ANOVA testing revealed that the objective accommodative response elicited by the 3.00 D accommodative target decreased significantly over the 2.5 year study ( $F=3.9$ ,  $p=0.003$ ; Figure 2A) and was not dependent on refractive error classification ( $F=1.7$ ,  $p=0.13$ ). Similarly, the accommodative response produced by the 4.50 D accommodative target reduced significantly over the course of the study ( $F=5.5$ ,  $p=0.001$ ; Figure 2B) and was not dependent on refractive error classification ( $F=1.5$ ,  $p=0.23$ ). The magnitude of the accommodative response exerted by the myopic cohort was significantly greater than the emmetropic response at the 4.50 D level ( $F=5.8$ ,  $p=0.028$ ).

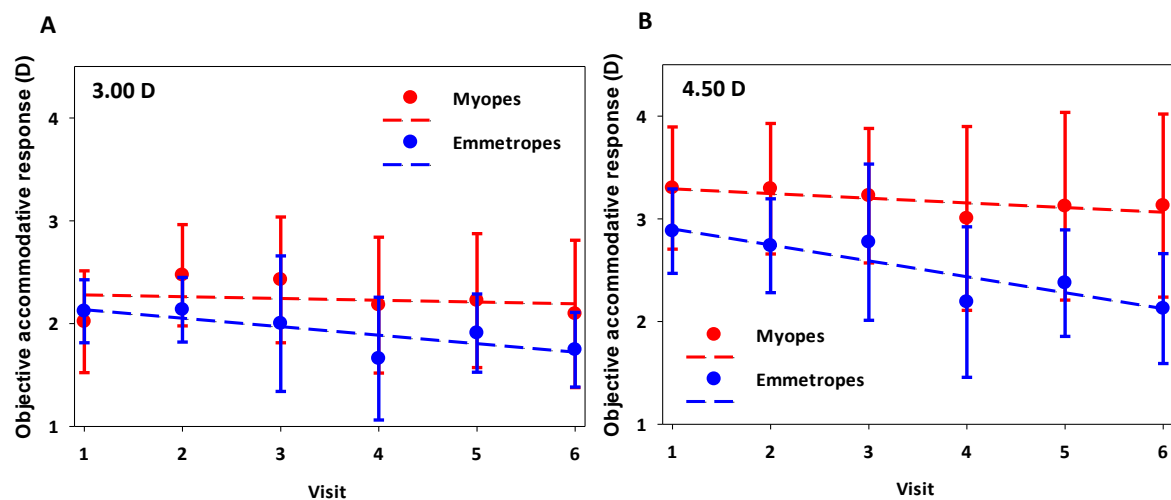


Figure 2. Mean objective accommodative response (with  $\pm 1$  standard deviation error bars) measured in myopic (red) and emmetropic (blue) participants whilst viewing a 3.00 D (A) and 4.50 D (B) accommodative target at each visit.

### Changes in ocular biometry

At 0.00 D accommodative stimulus, a statistically significant reduction in ACD and an increase in LT and ASL was observed after 2.5 years (Table 1). The change in disaccommodated LT was significantly larger amongst the emmetropic participants (+0.208 (SD 0.157 mm)) when compared to the myopic participants (+0.088 (SD 0.119 mm);  $F=3.6$ ,  $p=0.023$ ), however changes in CT ( $F=0.90$ ,  $p=0.49$ ), ACD ( $F=2.3$ ,  $p=0.056$ ), ASL ( $F=0.63$ ,  $p=0.68$ ), VCD ( $F=0.82$ ,  $p=0.51$ ) and AXL ( $F=0.43$ ,  $p=0.74$ ) were not dependent on refractive error classification.

Table 1. Mean ocular biometric parameters and the mean disaccommodated change in the myopic and emmetropic groups after 2.5 years with the level of statistical significance. Bold  $p$  values denote statistically significant changes with time.

Parameter	Mean baseline value (mm $\pm$ SD)		Mean change after 2.5 years (mm $\pm$ SD)		Statistical significance ( $p$ ) of changes after 2.5 years
	Myopes	Emmetropes	Myopes	Emmetropes	
CT	0.53 $\pm$ 0.04	0.54 $\pm$ 0.04	+0.01 $\pm$ 0.04	+0.03 $\pm$ 0.08	0.342
ACD	3.08 $\pm$ 0.29	2.96 $\pm$ 0.41	-0.08 $\pm$ 0.05	-0.18 $\pm$ 0.05	<b>0.003</b>
LT	3.84 $\pm$ 0.20	3.76 $\pm$ 0.42	+0.09 $\pm$ 0.10	+0.21 $\pm$ 0.16	<b>&lt;0.001</b>
ASL	7.45 $\pm$ 0.30	7.25 $\pm$ 0.36	+0.01 $\pm$ 0.11	+0.04 $\pm$ 0.18	<b>0.045</b>
VCD	17.41 $\pm$ 1.15	16.42 $\pm$ 0.55	+0.02 $\pm$ 0.12	-0.03 $\pm$ 0.18	0.067
AXL	24.86 $\pm$ 1.25	23.67 $\pm$ 0.55	+0.03 $\pm$ 0.04	+0.01 $\pm$ 0.05	0.296

The changes in ACD ( $F=29$ ,  $p<0.001$ ), LT ( $F=39$ ,  $p<0.001$ ) and AXL ( $F=5.4$ ,  $p=0.009$ ) stimulated by the 3.00 and 4.50 D accommodative targets were statistically significant at visit 1, however changes in ASL ( $F=1.1$ ,  $p=0.35$ ) and VCD ( $F=1.1$ ,  $p=0.34$ ) were not. No differences in accommodative response emerged according to refractive error classification (ACD  $F=0.86$ ,  $p=0.43$ ; LT  $F=1.1$ ,  $p=0.34$ ; ASL  $F=0.001$ ,  $p=0.99$ ; VCD  $F=0.016$ ,  $p=0.98$ ; AXL  $F=0.76$ ,  $p=0.48$ ), however VCD ( $F=6.6$ ,  $p=0.019$ ) and AXL ( $F=5.4$ ,  $p=0.009$ ) values were significantly longer in myopic eyes (ACD  $F=1.5$ ,  $p=0.23$ ; LT  $F=0.057$ ,  $p=0.81$ ; ASL  $F=0.19$ ,  $p=0.19$ ).

Whilst viewing the 3.00 D accommodative target, the changes in ACD ( $F=2.0$ ,  $p=0.14$ ), LT ( $F=1.9$ ,  $p=0.15$ ) and AXL ( $F=0.45$ ,  $p=0.81$ ) were not significantly attenuated over the course of the 2.5 year

study (Figure 2) and were not dependent on refractive error classification (ACD  $F=2.8$ ,  $p=0.055$ ; LT  $F=1.7$ ,  $p=0.15$ ; AXL  $F=1.5$ ,  $p=0.21$ ).

The change in ACD ( $F=3.1$ ,  $p=0.039$ ), LT ( $F=3.0$ ,  $p=0.042$ ) and AXL ( $F=2.5$ ,  $p=0.038$ ) whilst viewing the 4.50 D accommodative target significantly reduced over the 2.5 year study (Figure 3). The changes in biometry at 4.50 D were not dependent on refractive error classification (ACD  $F=1.7$ ,  $p=0.18$ ; LT  $F=1.7$ ,  $p=0.15$ ; AXL  $F=1.5$ ,  $p=0.21$ ).

The biometric response per dioptre of accommodation exerted to the 4.50 D accommodative target was not significantly attenuated over the 2.5 year study (ACD  $F=2.2$ ,  $p=0.097$ ; LT  $F=1.7$ ,  $p=0.18$ ;  $p=0.46$ ; AXL  $F=1.0$ ,  $p=0.40$ ; Table 2) and did not depend on refractive grouping (ACD  $F=1.2$ ,  $p=0.33$ ; LT  $F=1.5$ ,  $p=0.23$ ; AXL  $F=0.97$ ,  $p=0.44$ ). The magnitude of the change per dioptre of accommodation was not statistically dependent on whether the participant was classified as myopic or emmetropic (ACD  $F=0.72$ ,  $p=0.72$ ; LT  $F=3.5$ ,  $p=0.079$ ; AXL  $F=0.049$ ,  $p=0.83$ ). The magnitude of the change in AXL per dioptre of accommodation was not dependent on baseline AXL at visit 1 ( $r=0.084$ ,  $p=0.73$ ).

Table 2. Mean changes in axial biometry per dioptre of accommodation exerted (whilst viewing the 4.50 D accommodative target) at visit 1 (baseline) and visit 6 (after 2.5 years) for the myopic and emmetropic groups individually. The  $p$  values denote the significance of the change in accommodative response at each parameter over 2.5 years for myopic and emmetropic individuals.

Biometry	Mean change per dioptre of accommodation exerted at Visit 1 (mm ± SD)		Mean change per dioptre of accommodation exerted at Visit 6 (mm ± SD)		Statistical significance ( <i>p</i> ) of changes over 2.5 years
	Myopes	Emmetropes	Myopes	Emmetropes	
	ACD	-0.063 ± 0.020	-0.101 ± 0.078	-0.051 ± 0.025	
LT	+0.066 ± 0.023	+0.104 ± 0.079	+0.054 ± 0.023	+0.073 ± 0.020	0.178
AXL	+0.005 ± 0.004	+0.002 ± 0.006	+0.000 ± 0.005	+0.004 ± 0.008	0.395

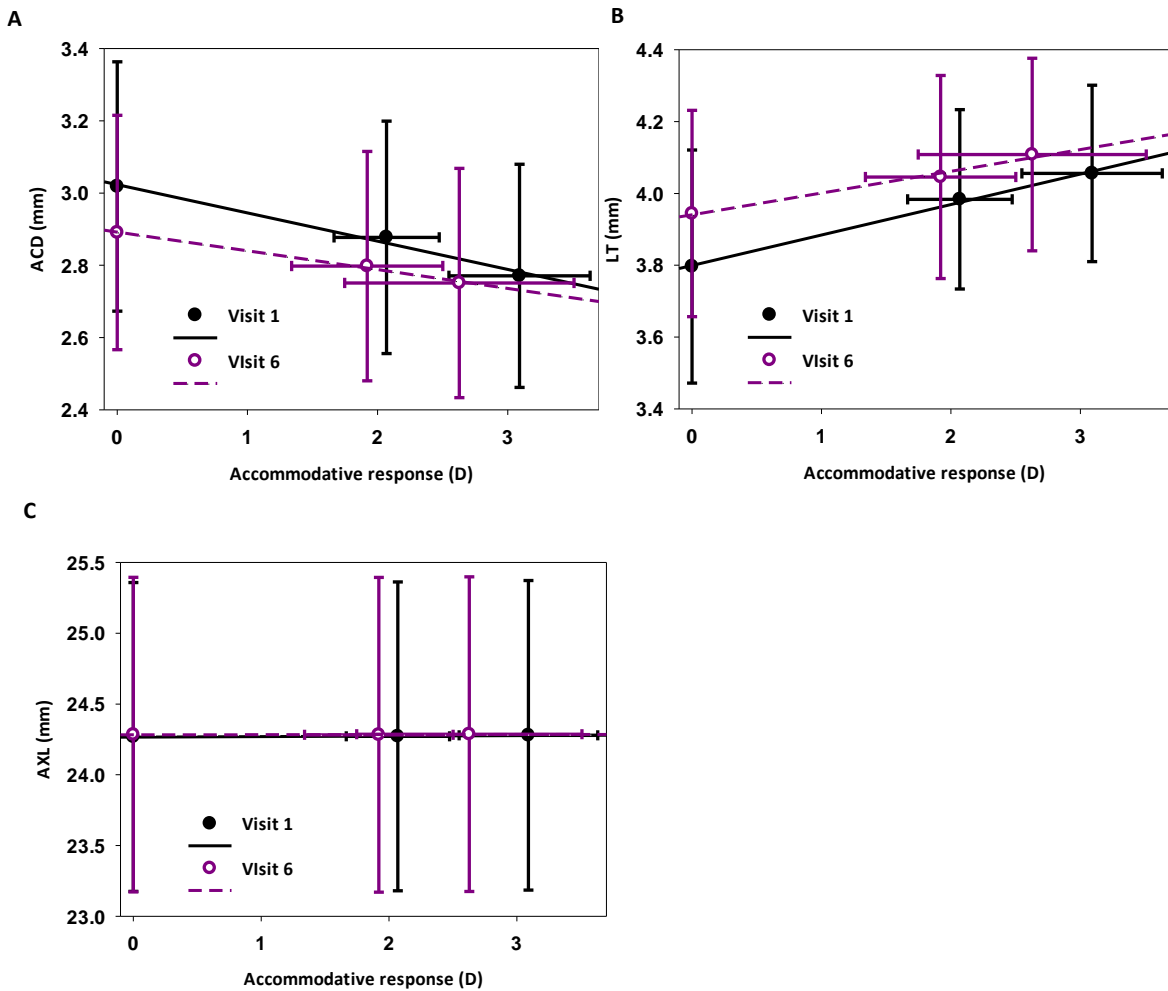


Figure 3. Mean ACD (A), LT (B) and AXL (C) (with  $\pm 1$  standard deviation error bars) at visit 1 (black filled circles and solid regression line) and after 2.5 years at visit 6 (purple open circles and dashed regression line) according to the accommodative response exerted at visit 1 and 6, respectively, to the 0.00, 3.00 and 4.50 D targets.

The increase in disaccommodated LT with age was not statistically significantly related to the reduction in accommodative lenticular response ( $R=0.43$ ,  $p=0.059$ ) or the refractive response at 4.50 D ( $R=0.32$ ,  $p=0.17$ ).

## Discussion

The present investigation is the first to document an age-related attenuation of changes in ACD, LT and AXL with accommodation in an incipient presbyopic population longitudinally. A significant decrease in ACD and an increase in LT and AXL accompanied accommodation. Despite significant age-related structural changes in disaccommodated biometry, the change in biometry per dioptre of accommodation exerted remained invariant with age, as reported by Koretz *et al.*<sup>42</sup>

The magnitude of the change in anterior biometry per dioptre of accommodation exerted was similar to the results from earlier studies utilising a variety of imaging techniques (Table 3). The majority of the increase in LT was compensated for by the reduction in ACD, which supports previous findings that the movement of the crystalline lens surface and reduction in radii of curvature is significantly greater anteriorly than posteriorly,<sup>8, 9</sup> and the Helmholtz theory of accommodation.<sup>1</sup>

The increase in disaccommodated LT with age was not statistically significantly related to the reduction in accommodative response at 4.50 D. Therefore, it is unlikely age-related changes in lenticular geometry alone are responsible for the reduction in accommodative ability. Consequently, the results of the current study suggest the increase in lenticular stiffness with age is primarily responsible for reduction in lenticular accommodative response.

Table 3. Summary of previous research investigating changes in anterior biometry per dioptre of accommodation exerted  $\pm$  standard deviation (where possible).

Study	Age range (years)	Technique	Change per dioptre of accommodation exerted $\pm$ SD (mm/D)		
			ACD	LT	ASL
<b>Current study</b> <b>Visit 1</b> n=20	34 to 41	LCR, AS-OCT	-0.082 $\pm$ 0.061	+0.085 $\pm$ 0.060	+0.003 $\pm$ 0.050
<b>Richdale <i>et al.</i><sup>7</sup></b> n=26 Emmetropes	30 to 50	AS-OCT MRI	-	+0.064 +0.065	-
<b>Sheppard <i>et al.</i><sup>6</sup></b> n=19	19 to 30	MRI	-	+0.08 $\pm$ 0.05	-
<b>Richdale <i>et al.</i><sup>36</sup></b> n=22	36 to 50	AS-OCT	-	+0.051 $\pm$ 0.019	-
<b>Bolz <i>et al.</i><sup>43</sup></b> n=10 Myopes	19 to 31	PCI	-0.057	+0.072	+0.013
<b>Bolz <i>et al.</i><sup>43</sup></b> n=10 Emmetropes	19 to 31	PCI	-0.047	+0.063	+0.009
<b>Ostrin <i>et al.</i><sup>44</sup></b> n=22	21 to 30	A-scan US	-0.051 $\pm$ 0.008	+0.067 $\pm$ 0.008	+0.017 $\pm$ 0.005
<b>Garner and Yap<sup>45</sup></b> n=11	18 to 28	A-scan US	-0.054	+0.054	-
<b>Koretz <i>et al.</i><sup>42</sup></b> n=42 Emmetropes	18 to 40	Scheimpflug	-0.038 $\pm$ 0.139	+0.043 $\pm$ 0.145	+0.003 $\pm$ 0.174

The change in ASL and VCD with accommodation was not significant. However, previous studies have reported a significant increase in ASL occurs with accommodation in younger individuals.<sup>14, 43, 44,</sup>

<sup>46</sup> The negligible change in ASL observed during incipient presbyopia may suggest the mobility of the posterior crystalline lens surface diminishes with age.<sup>19</sup> Indeed, the accommodative movement of the posterior lens surface in individuals aged between 18 to 36 years has been reported to be bi-phasic<sup>47</sup>; that is to say the posterior lenticular movement is negligible until the accommodative

demand reaches approximately 2.00 D (eliciting an accommodative response of approximately 1.50 D). The initial static phase is thought to originate from vitreous humour resistance.<sup>47</sup> It is feasible age-related anterior migration of the anterior zonules<sup>48</sup> and decreased flexibility of the posterior crystalline lens<sup>26</sup> and capsule<sup>49</sup> may perpetuate the initial static phase of accommodative posterior crystalline lens surface movement in older individuals. Nevertheless, as demonstrated by the large ASL standard deviation values in Table 3, significant intersubject variability in the response of the posterior crystalline lens surface occurs. Further research investigating the link between crystalline lens placement, zonular architecture and accommodative changes in ASL is indicated.

Similarly to research in young adults,<sup>12-14, 37</sup> a statistically significant elongation of AXL during accommodation was observed within the current cohort. No differences in AXL response arose according to refractive error grouping, as reported previously.<sup>14</sup> The AXL elongation per dioptre of accommodation exerted remained invariant after 2.5 years, thus suggesting the susceptibility of the choroid to the force of ciliary muscle contraction did not decrease. It would be of interest to investigate whether AXL change during accommodation is attenuated over the lifespan due to increases in choroidal<sup>20, 21</sup> and scleral stiffness<sup>22, 23</sup> and also to investigate longitudinally whether the ciliary muscle contractile response is attenuated with age.

The magnitude of the accommodative response exerted by the myopic group was significantly larger than exerted by the emmetropic group. Indeed, anecdotal and published evidence<sup>50</sup> suggests hypermetropic and emmetropic patients manifest presbyopia before myopic patients. The origin of this phenomenon has been traditionally thought to arise from near vision effectivity of myopic spectacle lenses (reducing the accommodative demand for myopic spectacle wearers)<sup>51</sup> or the increased vitreous chamber depth associated with myopia (requiring a smaller change in axial ocular distances to produce accommodation due to the relatively more distant retinal plane).<sup>52</sup> However, it is feasible myopic structural changes occurring during adolescence, perhaps lenticular thinning<sup>53, 54</sup> and lenticular equatorial expansion,<sup>54</sup> may preserve the accommodative ability and delay the onset

of presbyopia. The biomechanical reason for this putative association requires further investigation. It would also be of interest to document the reduction in the accommodative response longitudinally over the lifespan to investigate the influence of ametropia on accommodation further.

A possible limitation of this study is the inclusion of LT measurements derived from both LenStar and Visante instruments. However, the pixel thickness measurements of the Visante were calibrated against LenStar measurements, therefore minimising any potential disparity. Nonetheless, the LT for each participant was either wholly measured by the LenStar (11 participants) or by the Visante (9 participants) to minimise any potential inaccuracies.

The current study provides the first prospective, longitudinal insight into how accommodative changes in axial ocular biometry attenuate during incipient presbyopia. In conclusion, the accommodative decrease in ACD and increase in LT and AXL are significantly attenuated with age, however the response per dioptre of accommodation exerted remains constant with age. The mobility of the posterior crystalline lens surface also appears to reduce with age. Further longitudinal research is required to investigate how accommodative changes in ocular biometry change over the lifespan. The present study supports the Helmholtz theory of accommodation and suggests the increase in lenticular stiffness is likely to be primarily responsible for the onset of presbyopia.

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