

# Accommodation lags are higher in myopia than in emmetropia: Measurement methods and metrics matter

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## Abstract

**Purpose:** To determine whether accommodative errors in emmetropes and myopes are systematically different, and the effect of using different instruments and metrics.

**Methods:** Seventy-six adults aged 18–27 years comprising 24 emmetropes (spherical equivalent refraction of the dominant eye  $+0.04 \pm 0.03$  D) and 52 myopes ( $-2.73 \pm 0.22$  D) were included. Accommodation responses were measured with a Grand Seiko WAM-5500 and a Hartmann–Shack Complete Ophthalmic Analysis System aberrometer, using pupil plane (Zernike and Seidel refraction) and retinal image plane (neural sharpness—NS; and visual Strehl ratio for modulation transfer function—VSMTF) metrics at 40, 33 and 25 cm. Accommodation stimuli were presented to the corrected dominant eye, and responses, referenced to the corneal plane, were determined in the fellow eye. Linear mixed-effects models were used to determine influence of the refractive group, the measurement method, accommodation stimulus, age, race, parental myopia, gender and binocular measures of heterophoria, accommodative convergence/accommodation and convergence accommodation/convergence ratios.

**Results:** Lags of accommodation were affected significantly by the measurement method ( $p < 0.001$ ), the refractive group ( $p = 0.003$ ), near heterophoria ( $p = 0.002$ ) and accommodative stimulus ( $p < 0.05$ ), with significant interactions between some of these variables. Overall, emmetropes had smaller lags of accommodation than myopes with respective means  $\pm$  standard errors of  $0.31 \pm 0.08$  D and  $0.61 \pm 0.06$  D ( $p = 0.003$ ). Lags were largest for the Grand Seiko and Zernike defocus, intermediate for NS and VSMTF, and least for Seidel defocus.

**Conclusions:** The mean lag of accommodation in emmetropes is approximately equal to the previously reported depth of focus. Myopes had larger (double) lags than emmetropes. Differences between methods and instruments could be as great as 0.50 D, and this must be considered when comparing studies and outcomes. Accommodative lag increased with the accommodation stimulus, but only for methods using a fixed small pupil diameter.

## KEYWORDS

aberrometer, accommodation errors, autorefractor, emmetropia, metrics, myopia

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## INTRODUCTION

Educational factors<sup>1,2</sup> and near work<sup>3-5</sup> are associated with myopia development and/or its progression rate (reviewed in Huang et al.<sup>6</sup>). During near work, the accommodation response is usually less than the demand, which results in a lag of accommodation (reviewed by Charman<sup>7</sup>). Animal studies have shown that hyperopic defocus, induced with lenses, increases axial eye growth leading to myopia.<sup>8</sup> As accommodation lags induce hyperopic defocus, high lags are considered a risk factor for myopia.<sup>9-12</sup>

Accommodative responses can be calculated by measuring the refractive state of the eye when viewing objects at different distances. Instruments such as the Grand Seiko autorefractors use an annulus beam in the pupil in combination with the 'image-size' principle. However, the further out the annulus, the more that higher order aberrations, such as spherical aberrations, can influence refraction.<sup>13,14</sup> Other autorefractors and most aberrometers use circular beams, and again, the larger the beam, the larger the influence of higher order aberrations.

Refractions using aberrometers can be determined from different metrics, based on the aberration coefficients, and classified into pupil plane and retinal image plane metrics.<sup>15</sup> The pupil plane metrics are based directly on Zernike aberration coefficients, such as using only the second order (Zernike refraction), or using second order and one or more of the higher orders (Seidel refraction), which give greater emphasis to the more central parts of the pupil.<sup>14</sup> Retinal image plane metrics optimise a measure of image quality, sometimes weighted by neural sensitivity. These include the Strehl intensity ratio, the intensity variance of the point spread function, the volume under the modulation transfer function (MTF) and the volume under the contrast sensitivity function (CSF). Neural sharpness (NS) is designed to capture the effectiveness of a point spread function for stimulating the neural part of the visual system.<sup>15</sup> The visual Strehl ratio for the modulation transfer function (VSMTF) weights the MTF by the neural CSF, and emphasises the modulation near the peak of the CSF (e.g., 6 cycles/degree).<sup>15</sup> Subjective refraction and the refraction for best visual acuity occur intermediate between the pupil plane Zernike and Seidel defoci. The retinal image plane metrics are considered to be better than pupil plane metrics in estimating subjective refractions.<sup>15-17</sup>

There are issues with determining accommodative lag using automated instruments. Hazel et al.<sup>18</sup> reported that an autorefractor appeared to overestimate the increase in lag with increasing accommodation stimulus relative to aberrometer measures. They suggested that the bias could be due to the autorefractor calibration being influenced by aberrations determined with relaxed accommodation, while accommodating eyes have increasing negative spherical aberration as accommodation increases. Further differences may be observed if the pupil diameter used by the autorefractor does not match natural pupil sizes, and this is not considered when calculating refraction with

### Key points

- Across all confounding variables, myopes had double the lag of accommodation of emmetropes, for whom the lags were similar to the depth of focus.
- Autorefractor measures and second-order Zernike defocus approximation were the most unreliable in establishing the differences in accommodative errors between the refractive groups.
- The most reliable method of establishing differences in accommodative lags between refractive groups was the iterative method with appropriate merit functions.

the aberrometer. Accommodative lags may also differ depending on the near task given, and not just on the object distance, with Sreenivasan et al.<sup>11</sup> finding that tasks with higher cognitive demand elicit higher levels of accommodation than those with low cognitive demand conducted at the same object distance.

Accommodative responses determined with the aberrometer depend on the measure of image quality adopted.<sup>19,20</sup> The challenge with this technique is to find suitable optical quality metrics (OQMs) that quantify image quality using the same criteria as the accommodative system.<sup>19</sup>

Labhishetty et al.<sup>20</sup> argued that objective refractions based on either autorefractor or wavefront sensor measurements provide much higher accommodative lags or leads than those indicated by subjective measurements based on maximising the visual acuity. However, they acknowledged that objective refraction based on wavefront measurements and certain merit functions, such as the visual Strehl ratio, provides reasonably accurate and consistent measures of accommodative response with a constant lag of  $\approx 0.33$  D, and could predict the real subjective responses if a fixed offset of  $\approx 0.33$  D was applied to objective measurements. Therefore, they should not bias the estimates of the difference in accommodative errors between refractive groups.

The International Myopia Institute report on accommodation<sup>21</sup> compiled published studies of accommodation in children and adults. It remains contentious as to whether the lag of accommodation varies with refractive error. Some studies reported larger lags in myopes than in emmetropes,<sup>22-24</sup> but Tarrant et al.<sup>19</sup> found the opposite. Others did not find a difference,<sup>12,18,25</sup> but one study found a dependence on myopia progression rate such that progressive myopes had larger lags than stable myopes.<sup>12</sup>

Most of these studies used autorefractors and may have a systematic bias for higher accommodative lags than one would expect from a more accurate assessment. This is

particularly true for some investigations involving children as subjects, where mean accommodative lags of around 1 D or more have frequently been reported. Such blur levels, which exceed the objectionable blur limits,<sup>26,27</sup> raise doubts as to whether the subjects were able to perform the task given to them, that is, to make the image of the target clear. It is known from an earlier study<sup>28</sup> that higher-level attentional factors ('effort-to-see') play a significant role in accommodative responses, and could inhibit the performance of children who may have insufficient development of attention.

Accurate determination of the lag of accommodation is important if it is to be used as an indicator for myopia control. Furthermore, lags may be associated with other factors such as near heterophoria, accommodation functions such as the accommodative convergence/accommodation (AC/A) ratio,<sup>29</sup> race<sup>30</sup> and parental history of myopia. This information may be important in overall determination of myopia progression risk.

The aim of this study was to investigate differences between accommodation responses in emmetropes and myopes and to assess whether these were affected by instruments that operate on different principles, that is, measurement with an autorefractor vs. an aberrometer. The aberrometer data were analysed using both pupil plane (Seidel and Zernike defocus) and retinal image plane (NS and VSMTF) metrics. A further aim was to determine associations between responses and potential risk factors.

## METHODS

### Participants

This study adhered to the tenets of the Declaration of Helsinki. The Queensland University of Technology (QUT) Human Research Ethics Committee approved the protocol. All participants signed the informed consent form before starting measurements.

This is the first report of a study, which included a clinical trial of myopes wearing two types of progressive spectacle lenses for a period of 12 months, with regular follow-ups to measure the change in accommodative error over time. At the baseline visit, there were two groups of myopes of approximately equal size and an emmetropic group of similar size for comparison. In this paper, the two myopic groups were combined, as they were wearing the same type of correction.

Seventy-six young adults (24 emmetropes and 52 myopes) aged between 18 and 27 years were recruited from QUT students and their acquaintances. All participants had good ocular and general health. Emmetropes had non-cycloplegic subjective spherical equivalent refractions (SER) between Plano and +0.50 D, and myopes had non-cycloplegic SER between -0.75 D and -6.00 D. Subjective refraction included monocular subjective refraction using best vision sphere—maximum plus to maximum visual

acuity; cylindrical power; and axis refinement using the Jackson cross-cylinder and binocular balancing using the monocular fogging balance (modified Humphriss) method. As high myopia ( $\leq -6.00$  D) carries a risk of pathological changes such as myopic maculopathy and retinal detachment (reviewed by Jagadeesh et al.<sup>31</sup>) and can affect accommodation measurements, individuals with high myopia were excluded. People with anisometropia  $>1.50$  D and/or cylinder  $>1.50$  D, or with a past or current history of myopia control treatment, for example orthokeratology and multifocal lenses, were also excluded. There was a high correlation between the SER and axial length of the right and left eyes (Pearson's correlation coefficient = 0.97 for each), and thus, the average of both eyes was used to characterise the participants.

### Measurements

Eye and vision testing included ocular health assessment, slit-lamp biomicroscopy, intraocular pressure measurement, direct ophthalmoscopy, automated refraction (Grand Seiko Auto Ref/Keratometer WAM-5500, [grand seiko.com](http://grandseiko.com)), and subjective refraction. Best-corrected visual acuity was logMAR 0.0 (6/6) or better in all participants. Subjective amplitude of accommodation was measured with a handheld Badal optometer (luminance 500 cd/m<sup>2</sup>, Rodenstock, [rodenstock.com](http://rodenstock.com)).<sup>32</sup> Distance refractive error was corrected with lenses in a trial frame. Axial length was measured using the Lenstar LS 900 biometer (Haag-Streit, [haag-streit.com](http://haag-streit.com)). Near and distance heterophoria were measured using a Maddox rod and prisms. The dominant eye was determined by a sighting alignment (pointing-a-finger) test.<sup>33</sup> Demographic characteristics such as age, gender, race and family history of myopia were collected through a questionnaire. Other tests were conducted as described below.

### Accommodative convergence-to-accommodation (AC/A) and convergence accommodation-to-convergence (CA/C) ratios

The stimulus AC/A ratio was determined using the gradient method.<sup>34</sup> Briefly, this involved distance correction, a Thorington card at 40 cm, a Maddox rod and penlight to produce a monocular vertical streak. Heterophoria was determined for each added lens power in one dioptre steps from +2.00 D to -2.00 D, and the heterophorias were plotted against the lens powers to obtain the slope, that is, the AC/A ratio. For calculations, exophorias and esophorias were assigned negative and positive values, respectively.

The CA/C ratio was determined using a pseudo-Gaussian target with the Grand Seiko WAM 5500.<sup>35,36</sup> The target was a 5-mm-diameter red light-emitting diode behind a diffusing screen at 40-cm distance. To eliminate potential accommodation inducing stimuli,<sup>36,37</sup> the instrument screen

brightness was reduced to 30%, room lights were turned off, and the examiner covered himself and the screen with a dark cloth. Right eye refractions were obtained for five prism conditions: 10 Δ base-in, 5 Δ base-in, no prism, 5 Δ base-out and 10 Δ base-out in front of the left eye. To avoid adaptation effects, measurements were taken immediately when fusion was reported. The CA/C ratio was determined across the prism values similar to the determination of AC/A ratio across lens powers.

## Accommodation response: Grand Seiko Autorefractor

Accommodation response was measured with the Grand Seiko autorefractor. It uses approximately a 1.5-mm to 2.3-mm sampling annulus.<sup>14,38</sup> The dominant eye viewed the target and drove the accommodation response, while the refraction of the other eye, that is, the consensual response, was measured. This was achieved by placing a distance trial lens correction in front of the dominant eye, while an infrared pass filter (87C, Kodak, [kodak.com](http://kodak.com)) close to the non-dominant eye occluded its view but transmitted the instrument's infrared radiation (Figure 1a). The luminance of the targets was approximately 100 cd/m<sup>2</sup>. For distance, the fixation target was a high-contrast cross equivalent to 6/15 letter size presented at 4 m. For near, five high-contrast printed letters in a row were presented in decreasing size at 40, 33, 25 and 20 cm, such that each row of letters subtended 12.5 min of arc vertically (0.40 log-MAR or 6/15 letter size).<sup>19,39</sup> For myopes, the trial lens was decentred according to the inter-pupillary distance, vertex distance and target distance.

Proximal accommodation may be considered to play a role in this situation, and for the Complete Ophthalmic Analysis System (COAS) described below. However, under vergence open-loop and accommodation closed-loop

conditions, Hung et al.<sup>40</sup> calculated that the contribution of proximal accommodation to total accommodation was about four per cent. This indicates that the contribution of proximal accommodation in our experiment should be negligible.

The wording of instructions can also influence accommodation responses.<sup>41</sup> Thus, participants were asked to focus on the letters and keep them 'as clear as possible' during the measurement.<sup>42</sup> For instrument alignment, room lights were dimmed so that targets appeared at the centre of the instrument's red alignment ring. The participant's non-dominant eye was measured along the axis of the instrument by translating, as necessary, the external letter target to align at the centre of the instrument's ring. Five measurements were taken for each testing distance in decreasing order of distance. If any measure was different from the others by 0.25 D or more with an obvious reason, for example, eye movement, head tilt or blinking while measuring, it was excluded. Average spherical equivalent refraction and  $J_0$  and  $J_{45}$  astigmatism were calculated using power vector analysis.<sup>43</sup>

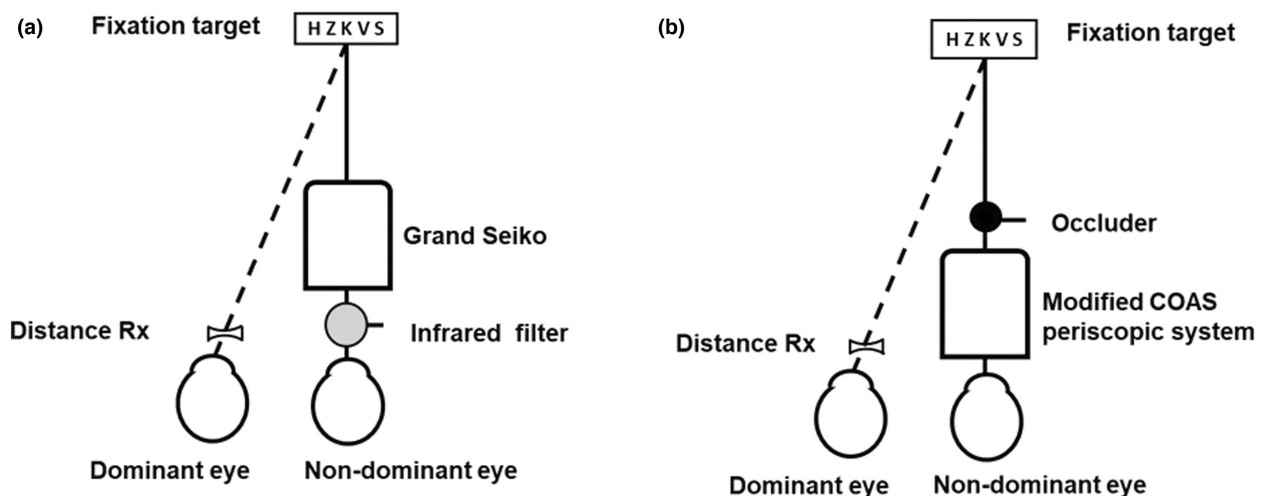
Lag of accommodation (LoA) was calculated as the difference between the accommodative stimulus (AS) and accommodative response (AR) using the equations of Atchison and Varnas:<sup>44</sup>

$$AS = \frac{Rx}{1 - VD \cdot Rx} - \frac{1 + (TD + VD) \cdot (Rx)}{TD - VD \cdot (TD + VD) \cdot (Rx)}$$

$$AR = [OR(4\text{ m}) + 0.25] - OR(SVL_{\text{near}})$$

$$LoA = AS - AR$$

Here, Rx is spherical equivalent subjective refraction of the dominant eye at the spectacle plane, VD is the distance from the spectacle plane to the cornea (varies between



**FIGURE 1** Experimental set-up for measuring the accommodation response with: (a) the Grand Seiko autorefractor and (b) the Complete Ophthalmic Analysis System (COAS) aberrometer. Not to scale. See text for details.

participants), TD is near testing distance, OR (4 m) is the objective SER at the corneal plane for a target at infinity, OR ( $SVL_{near}$ ) is the objective SER at the corneal plane at one of the three near testing distances, and the sign of LoA is positive for a lag of accommodation. The form of the latter equation shows that the accommodation response is set to zero for a stimulus at infinity and the responses for other distances are relative to this. Target distances of  $-0.4$ ,  $-0.33$ ,  $-0.25$  and  $-0.20$  m were measured from the target plane to the eye plane. The distances for the dominant eye to the target were larger (Figure 1) at

$$TD_{adj} = -\sqrt{(TD)^2 + (IPD)^2}$$

where IPD is inter-pupillary distance, taken as 64 mm. Adjusted testing distances ( $TD_{adj}$ ) were  $-0.405$ ,  $-0.336$ ,  $-0.258$  and  $-0.210$  m.

### Accommodation response: Complete Ophthalmic Analysis System (COAS) aberrometer

The Complete Ophthalmic Analysis System (COAS) Hartmann–Shack aberrometer (Johnson & Johnson Vision, [jnvision.com](http://jnvision.com)) was modified by adding a periscopic system<sup>45</sup> to measure the consensual accommodation response. The internal fixation target of the COAS was turned off. Like the Grand Seiko, the dominant eye drove the response while the response of the non-dominant eye was measured along the instrument axis. This was achieved by placing the distance Rx trial lens in front of the dominant eye and an occluder in front of the non-dominant eye (Figure 1b). The non-dominant eye was measured along the axis of the instrument by translating, as necessary, the external letter target to align with the super-luminescent diode source of the instrument seen faintly by the non-dominant eye. For myopes, the horizontal position of the distance Rx was shifted inwards based on the participant's inter-pupillary distance and vertex distance during near measurements.

Distance and near targets consisted of 5 high contrast letters in a row on a tablet at 5 m and on a smartphone screen at 40, 33 and 25 cm. Five letters of each line subtended 12.5 min of arc vertically at the eye (0.40 logMAR or 6/15 letter size). As for the Grand Seiko autorefractor, participants were asked to focus on the letters and keep them 'as clear as possible' during the measurement. The order of measurements was a decreasing order of distance. Four measurements were taken for each distance and results averaged. Target luminance was 80–100 cd/m<sup>2</sup> by keeping the brightness settings of tablet and phone screen at 40% for both far and near testing distances.

Aberration data were exported as Zernike coefficients up to the sixth order for a 550-nm wavelength. Spherical equivalents were calculated using Zernike defocus for a

3 mm pupil diameter, as this was considered to provide values similar to the Shin-Nippon NVision K5001 (Grand Seiko, [grandseiko.com](http://grandseiko.com)) autorefractor,<sup>46</sup> and Seidel defocus for second- to sixth-order coefficients for natural pupil diameters. Zernike defocus was calculated using

$$M = -4\sqrt{3}C_2^0/r^2$$

where  $M$  is defocus,  $C_2^0$  is the Zernike defocus coefficient, and  $r$  is pupil semi-diameter. Seidel defocus for the natural pupil diameter was calculated using

$$M = \left(-4\sqrt{3}C_2^0 + 12\sqrt{5}C_4^0 - 24\sqrt{7}C_6^0\right)/r^2$$

where  $C_4^0$  and  $C_6^0$  are fourth- and sixth-order symmetric coefficients, respectively.

Objective refractions from the wavefront sensor measurements for natural pupil diameters, taking into account the contribution of all the higher order aberrations up to the sixth order and maximising visual quality using the NS and VSMTF metrics, were computed using a MATLAB (MathWorks, [mathworks.com](http://mathworks.com)) program developed at the University of Indiana and described by Thibos et al.<sup>15</sup>

Optimisation of the NS and VSMTF metrics involved several steps including remapping of the aberration distribution using Fourier transforms of the aberration maps and numerical integration of certain integrals of the remapped distributions provided in Equations (A22) and (A31) of Thibos et al.<sup>15</sup> The starting values of the second-order Zernike coefficients corresponded to the paraxial curve matching set that produces zero curvature at the centre of the pupil. The first step of the first iteration searched for the optimal  $C_2^0$ , while the other two were fixed. The second step searched for the optimal  $C_2^2$  using the new  $C_2^0$  and the original  $C_2^{-2}$ , and the third step searched for the optimal  $C_2^{-2}$  using the new  $C_2^0$  and  $C_2^2$  values. The second iteration used the new values as starting values, and so on until all three coefficients changed less than 0.0001  $\mu\text{m}$  between the last two iterations.

Lag of accommodation (LoA) was calculated as the difference between the accommodation stimulus (AS) and accommodation response (AR) as described for the Grand Seiko instrument. Here, the accommodation response is now

$$AR = [OR(5\text{ m} + 0.2)] - OR(SVL_{near})$$

where, similar to the equation for the Grand Seiko instrument, OR (5 m + 0.2) is the objective SER at the corneal plane for a target at infinity and OR ( $SVL_{near}$ ) is the objective SER at the corneal plane at one of the three near testing distances. The form of the latter equation shows that the accommodation response is set to zero for a stimulus at infinity and the responses for other distances are relative to this. Accommodation stimulus was determined with the

same equation as for the Grand Seiko. The lag of accommodation was calculated for the metrics using the same equations as for the Grand Seiko autorefractor.

## Data analysis

Data analysis was performed using the Statistical Package for the Social Sciences (SPSS) (version 26; IBM, [ibm.com](http://ibm.com)). Characteristics of emmetropes and myopes were compared using unpaired t-tests for numerical variables (age, SER, axial length, heterophoria, AC/A and CA/C ratios) and chi-squared tests for categorical variables (gender, race and parental history of myopia). The level of significance was 0.05 for two-tailed tests.

For the COAS aberrometer metrics, data of one emmetrope were excluded for 25 cm and data of two myopes were excluded for 40 cm because of unreliable values that did not match the pattern of the other testing distances. Lags were measured at 40, 33, 25 and 20 cm for the Grand Seiko autorefractor, and at 40, 33 and 25 cm for the COAS aberrometer. For analysis comparing the measurements of the two instruments, lags at 40, 33 and 25 cm were used. The target distances were converted to accommodative stimuli in dioptres. Since the accommodative stimuli were dependent on the power of the lenses worn and their back vertex distances, this conversion for the corrected myopes resulted in a small range of dioptric stimuli for each discrete target distance.

To investigate differences in lags between accommodative stimuli (within-subject factor), measurement methods (within-subject factor), refractive group (between-subject factor) and race (between-subject factor), linear mixed-effects models were performed. These models enabled us to calculate the adjusted mean values of accommodative lags for the main factors so that an unbiased comparison between them could be made. The adjusted means are also referred to in the literature as the estimated marginal means or the least squares means.

For the linear mixed-effects approach, the associations between the lags and the demographic variables (age, gender, race, family history) and binocular measures (near and distance heterophorias, AC/A and CA/C ratios) were investigated by univariate linear mixed models. The main multivariate linear mixed-effects model used the calculated lags of accommodation for a range of accommodative stimuli derived from the autorefractor and COAS aberrometer measurements using all four metrics: Zernike defocus for a fixed 3-mm pupil, and Seidel, NS and VSMTF metrics for the natural pupil size. The variables that had significance level  $p < 0.20$  in the univariate linear mixed-effects models and/or those variables that were different between emmetropes and myopes at  $p < 0.20$  in the descriptive analysis (Table 1) were entered into the multivariate linear mixed-effects model. The backward fitting approach was performed; that is, the variable with the highest  $p$ -value was

excluded from the model, one at a time, until the remaining variables were significant at the  $p < 0.10$  level. Several factors (measurement method, race, refractive status) had different numbers of observations for different testing conditions because of missing values as described in the previous paragraph, and hence, these factors had different degrees of freedom. Also, a linear mixed-effects model was run with all of the significant independent variables and their interactions, which identified two highly significant interactions between the method and near heterophoria, as well as the method and race. For pairwise comparisons of measurement methods and race, the Sidak test was performed. The residuals assessed using histograms and normal probability plots showed normal distributions for all analyses.

## RESULTS

### Characteristics of participants

Participant characteristics are presented in Table 1. There were 76 participants (24 emmetropes and 52 myopes) with a mean ( $\pm$ standard error, SE) age of  $21.9 \pm 0.3$  years, and 46 (60%) were females. The mean spherical equivalent refractions for emmetropes and myopes were  $+0.04 \pm 0.03$  D and  $-2.73 \pm 0.22$  D, respectively. The mean axial lengths for emmetropes and myopes were  $23.14 \pm 0.14$  mm and  $24.61 \pm 0.15$  mm, respectively. The mean amplitude of accommodation was  $8.4 \pm 0.1$  D, with a range of 6–10 D, and was similar for emmetropes and myopes; this means that stimulus levels up to 4 D are well within the amplitude of all subjects. Participants exhibited physiological exophoria at near. Myopes were more likely to have one or more parents with myopia than were emmetropes.

### Lags of accommodation

Figure 2 shows the unadjusted mean accommodation lag as a function of the accommodative stimulus for each of the five methods of determining the refractive state of the eye. Table 2 shows the main multivariate linear mixed-effects model results. Accommodative lags were affected significantly by the measurement method ( $F_{4,1042} = 67.5$ ,  $p < 0.001$ ), the refractive group ( $F_{1,76} = 9.6$ ,  $p = 0.003$ ), near heterophoria ( $F_{1,75} = 10.2$ ,  $p = 0.002$ ), accommodative stimulus ( $F_{1,1018} = 4.0$ ,  $p = 0.05$ ), race ( $F_{2,74} = 2.6$ ,  $p = 0.08$ ) and two interactions: method  $\times$  near heterophoria and method  $\times$  race (both  $p < 0.001$ ). Overall, myopes had larger lags than emmetropes by  $0.30 \pm 0.10$  D with the estimated mean lags of emmetropes and myopes being  $0.31 \pm 0.08$  D and  $0.61 \pm 0.06$  D, respectively. Lags were highest and increased with the increase in stimulus when metrics involved a small pupil (with the

TABLE 1 Characteristics of participants

Characteristics	Emmetropes (n = 24)	Myopes (n = 52)	p	Overall (n = 76)
Age, years	21.3 ± 0.7	22.1 ± 0.4	0.40	21.9 ± 0.3
Gender, female (%)	15 (62.5)	31 (59.6)	0.87	46 (60.5)
Race <sup>a</sup> , n (%)				
Caucasian	7 (29.2)	6 (11.5)	0.07	13 (17.1)
East Asian	6 (25.0)	25 (48.1)		31 (40.8)
South Asian	11 (45.8)	21 (40.4)		32 (42.1)
Refractive error, D <sup>b</sup>				
SER	+0.04 ± 0.01	-2.70 ± 0.23	<b>&lt;0.001</b>	NA
J <sub>0</sub>	+0.03 ± 0.04	+0.18 ± 0.04	<b>0.02</b>	
J <sub>45</sub>	-0.01 ± 0.02	0.00 ± 0.02	0.24	
Axial length <sup>b</sup> , mm	23.14 ± 0.14	24.61 ± 0.15	<b>&lt;0.001</b>	NA
Amplitude of accommodation, D	8.3 ± 0.2	8.4 ± 0.2	0.34	8.4 ± 0.1
Near heterophoria, Δ <sup>c</sup>	-5.1 ± 0.9	-2.9 ± 0.8	0.09	-3.5 ± 0.6
Distance heterophoria, Δ <sup>c</sup>	-0.5 ± 0.5	-0.6 ± 0.4	0.61	-0.5 ± 0.3
AC/A ratio, (Δ/D)	2.4 ± 0.2	2.6 ± 0.1	0.35	2.5 ± 0.1
CA/C ratio, (D/Δ)	0.068 ± 0.001	0.039 ± 0.001	<b>&lt;0.001</b>	0.049 ± 0.001
Parental history of myopia, n (%)				
Neither parent	15 (62.5)	8 (15.4)	<b>&lt;0.001</b>	23 (30.3)
One parent <sup>d</sup>	7 (29.2)	30 (57.7)		37 (48.7)
Both parents	2 (8.3)	14 (26.9)		16 (21.0)

Note: Significant values are bolded. Data are presented as means ± standard errors except for gender, race and parental history.

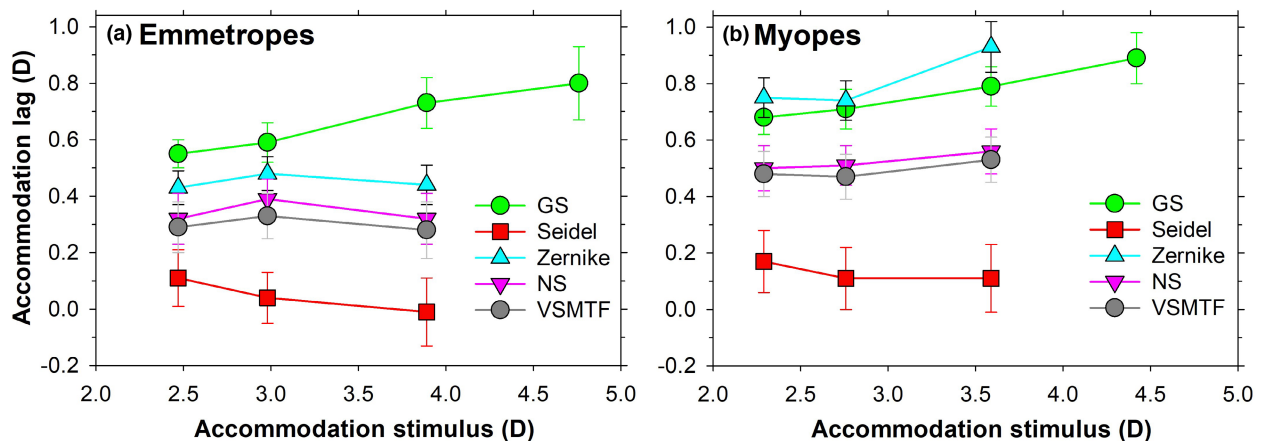
Abbreviation: NA, not applicable.

<sup>a</sup>East Asian comprised 19 Chinese, 2 Japanese, 1 South Korean and 9 others, which included 3 Vietnamese, 3 Indonesians, 2 mixed and 1 Filipino; South Asian comprised 18 Nepalese, 13 Indians and 1 Sri Lankan.

<sup>b</sup>SER, J<sub>0</sub>, J<sub>45</sub> and axial length are averages of two eyes.

<sup>c</sup>Minus sign indicates exophoria.

<sup>d</sup>Includes 5 participants with a myopic sibling.



**FIGURE 2** Accommodation lag as a function of accommodative stimulus for (a) emmetropes and (b) myopes according to five metrics: Grand Seiko (GS), Seidel defocus, Zernike defocus, neural sharpness (NS) and visual Strehl ratio for modulation transfer function (VSMTF). Data are presented as mean and standard error (SE). Accommodation stimulus depended upon refraction and vertex distance, and as shown, each accommodation stimulus is a mean value. There are horizontal error bars for the accommodation stimulus, but these are too small to be legible.

Grand Seiko autorefractor and for the Zernike defocus), were intermediate in magnitude and with no clear trend with changes in stimulus for NS and VSMTF metrics, and were smallest with Seidel defocus.

A separate linear mixed-effects model was run for each measurement method. Table 3 gives estimated marginal means of accommodative errors for emmetropes and myopes, and their differences and significance. For the Grand

**TABLE 2** Association of lags of accommodation with explanatory variables using linear mixed-effects models

Parameter	Levels	Full model		
		Parameter estimate (SE)	F	p
Intercept	1	0.31 (0.14)	8.64	0.004
Method <sup>a</sup>	5		67.49	<0.001
Refractive status (RS)	2	0.30	9.63	<b>0.003</b>
Acc. stimulus (AS)	1	0.04 (0.02)	4.03	<b>0.05</b>
Near heterophoria	1	−0.02 (0.01)	10.75	<b>0.002</b>
Race <sup>b</sup>	3		2.61	0.08
East Asian		−0.38 (0.14)		
South Asian		−0.24 (0.14)		
Method*Near Heterophoria <sup>a</sup>	5		7.23	<0.001
Method*Race <sup>a</sup>	15		4.40	<0.001

Note: Significant values are bolded.

Abbreviation: SE, standard error.

<sup>a</sup>There are multiple parameter estimates for the multi-level factors and their interactions that have been omitted

<sup>b</sup>Caucasian was the reference group for the race.

**TABLE 3** Estimated adjusted mean accommodative errors (SE) in emmetropes and myopes derived from the linear mixed-effects models for each method including three confounding variables: refractive group (emmetropes or myopes), near heterophoria and either accommodative stimulus (in measurements using a small, fixed pupil diameter—autorefractor and Zernike defocus) or race (in measurements using natural pupils)—Seidel, visual Strehl ratio for modulation transfer function (VSMTF) and neural sharpness (NS)

Method	Grand Seiko	Zernike	Seidel	VSMTF	NS
Emmetropes	0.58 (0.08)	0.40 (0.09)	−0.01 (0.13)	0.27 (0.09)	0.31 (0.09)
Myopes	0.75 (0.05)	0.82 (0.06)	0.25 (0.10)	0.59 (0.07)	0.61 (0.07)
Difference	0.16 (0.09)	0.42 (0.11)	0.27 (0.16)	0.32 (0.12)	0.30 (0.12)
p-value	0.08	<0.001	0.10	<0.01	<b>0.01</b>

Note: Significant values are bolded.

Seiko and for COAS Seidel defocus, the lag differences between emmetropes and myopes were not significant ( $p > 0.05$ ). For the other three COAS-related methods, myopes had greater lags than emmetropes by  $0.30 \pm 0.12$  D (NS) to  $0.42 \pm 0.11$  D (Zernike defocus).

Subjects were divided into three groups by race: Caucasian, East Asian and South Asian, with the Caucasian group used as the reference. The Caucasians had lags of accommodation that were higher, but not significantly so, than the East Asian group (difference  $0.28 \pm 0.13$  D,  $p = 0.10$ ) and the South Asian group ( $0.13 \pm 0.12$  D,  $p = 0.67$ ).

## Pupil size

Natural pupil sizes varied considerably with accommodation. For completion, Table 4 includes pupil size data with the COAS. Differences between emmetropic and myopic groups were not significant.

## DISCUSSION

This study compared the lag of accommodation in emmetropes and myopes using the Grand Seiko autorefractor

and the COAS aberrometer with four metrics. Myopes

**TABLE 4** Mean pupil diameters in millimetres (SE) in emmetropes and myopes at different testing distances with the Complete Ophthalmic Analysis System (COAS)

Testing distance	Emmetropes	Myopes
500 cm	5.58 (0.15)	5.79 (0.17)
40 cm	5.01 (0.19)	5.07 (0.16)
33 cm	4.93 (0.20)	5.11 (0.20)
25 cm	4.69 (0.19)	4.89 (0.16)

had larger overall lags than emmetropes (Tables 2 and 3), with respective adjusted mean lags of 0.61 D and 0.31 D. Considerable differences were found between the metrics. The largest lag estimates were found for the Grand Seiko and for Zernike defocus when the small pupil diameter of 3 mm was used. For the natural pupil metrics, Seidel defocus gave the lowest lag estimates but also the largest scatter within and between subjects, while the NS and VSMTF metrics gave more consistent estimates. Accommodative lag appears to increase with an increase in stimulus by around 0.1/1 D, but only for the methods using a fixed small pupil diameter (Zernike defocus and Grand Seiko,



as indicated by the coefficients of AS in the corresponding LME models). No such dependence was found for the merit functions using the natural pupil diameters. This appears to suggest that the increase in accommodative lag with increasing stimulus in young subjects is an artefact of keeping the pupil diameter constant, and hence not considering how the higher order aberrations affect the measured refraction. The estimates of lags of accommodation derived using the metrics with the natural pupil size are insensitive to the changes in stimulus in the range of 2.5 and 4.0 D.

The increase in negative spherical aberration that occurs with accommodation would not be measured by an instrument that only measures across a small pupil diameter. Thus, the accommodative response with increasing stimulus would be underestimated and the calculated lag would appear to increase, but this would not reflect the actual retinal image.

The Zernike defocus was obtained with a much smaller pupil at 3 mm than the other aberrometer metrics (natural pupils ranged from 3.7 to 7.9 mm), while the Grand Seiko autorefractor uses an approximately 1.5-mm to 2.3-mm sampling annulus at the cornea.

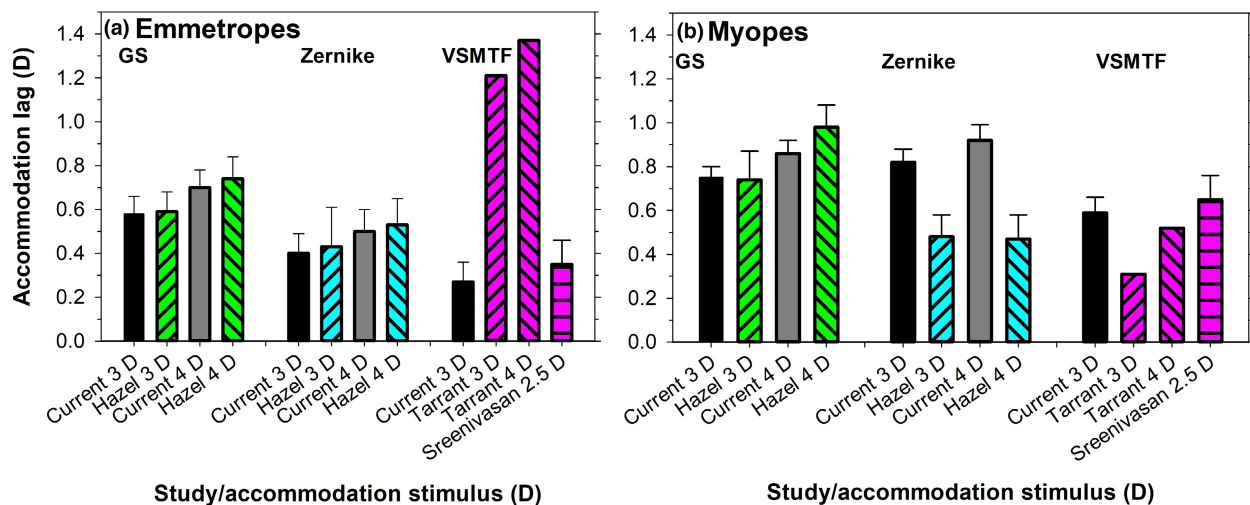
There are three previous studies of young adults<sup>11,18,19</sup> that can be compared with the current study, but this can be done for only some of the metrics and some stimuli levels (Figure 3). Here, the comparisons are made with the adjusted mean accommodative errors (Table 3) rather than the values shown in Figure 2. The autorefractor findings of Hazel et al.<sup>18</sup> are in excellent agreement with the current Grand Seiko results for both emmetropes and myopes (e.g., for a 3 D stimulus, they have lags of 0.58 and 0.74 D, respectively, compared with 0.58 and 0.75 D, respectively, in the current study). This is despite the use of different methods

of stimulus presentation in the two studies—negative lens series approach in the Hazel et al. study<sup>18</sup> and decreasing distance series in our study. Previously published studies have shown the two methods of presenting the stimulus giving significantly different outcomes when refraction was measured with the Canon R1 autorefractor<sup>9,12,18,47</sup> but not, to our knowledge, for the Grand Seiko or Shin-Nippon autorefractors. Comparison was made of the Zernike defocus values derived here with the COAS measurements for the fixed 3-mm pupil with the Hazel et al. equivalent calculated for a fixed 2.9-mm pupil, which they termed the ‘total spherocylindrical error for the eye’ and described as ‘the sum of the paraxial and spherical aberration correction’. Their values agree well with the present findings for emmetropes (e.g., 0.42 and 0.40 D, respectively, at 3 D stimulus) but not for myopes (0.48 and 0.82 D at 3 D stimulus).

For the Tarrant et al.<sup>19</sup> study with myopes, recalculated results for the Seidel defocus, VSMTF and NS using natural pupil sizes are in reasonable agreement with those of the current study for the 4 D stimuli, but are about 0.2 D lower for the 3 D stimulus. However, for emmetropes, the Tarrant et al. lags are approximately 1 D higher than those measured here. The VSMTF, but not NS, results are compared in Figure 3.

Sreenivasan et al.<sup>11</sup> determined lags of accommodation with the COAS aberrometer using natural pupils, which were large due to low lighting levels, with the VSMTF metric. For a monocular visual acuity task at a 2.5 D stimulus, mean accommodative lags were 0.35 D for emmetropes and 0.65 D for myopes, similar to the values in the current study of 0.27 D and 0.59 D, respectively.

Reduced accommodation increases the hyperopic defocus, which is a risk factor for myopia development. As has been pointed out by Rosenfield & Carrel,<sup>48</sup> accommodative



**FIGURE 3** Accommodation lag as a function of accommodation stimulus for: (a) emmetropes and (b) myopes for the mean values for the current study adjusted for the 3.0 D and 4.0 D stimuli (GS, Zernike, and VSMTF), Hazel et al.<sup>18</sup> (GS, Zernike), Tarrant et al.<sup>19</sup> (VSMTF) and Sreenivasan et al.<sup>11</sup> (VSMTF). Data are presented as mean and standard errors of the mean. Hazel et al.<sup>18</sup> used the Shin-Nippon SRW-5000 autorefractor, a predecessor of the Grand Seiko WAM-5500, which samples an annulus of 2.9 mm outer diameter in the pupil plane, and a laboratory Hartmann–Shack aberrometer, which was analysed for a 2.9-mm pupil. The Tarrant et al. aberrometer results for natural pupils required ‘zeroing’ at 0 D stimulus for the results to be comparable with the current study. Sreenivasan et al.’s<sup>11</sup> results are for monocular viewing and natural pupils.

errors that do not exceed the depth of focus of the eye (typically about  $\pm 0.3$  D) will not be observed by the subject. The accommodative lags are very close to the value of the depth of focus in emmetropes, but they are around twice that amount in myopes.

The investigation included the binocular accommodation and vergence measures of near and distance heterophorias, as well as the AC/A and CA/C ratios. Of these, the CA/C ratios were significantly lower for myopes than for emmetropes, but did not appear in the final model. The near heterophoria contributed significantly to the accommodative lag model, an outcome consistent with the fact that the accommodation and vergence systems are connected to ensure a coordinated near response and thus enable clear and single vision at all distances.<sup>49</sup>

So, why would myopes tolerate higher accommodative errors than emmetropes? Jiang<sup>50</sup> modelled accommodative behaviours of adult emmetropes and late-onset myopes (LOMs) using a modified control theory model of static accommodation, which included a new linear operator accommodative sensory gain (ASG) to account for the degradation of the error signal (blur) by sensory factors. In their clinical trial, a range of accommodation-related parameters in young adult emmetropes and late-onset myopes was measured. Modelling of the collected accommodative responses averaged across all stimuli suggested that the ASG is significantly impaired in late-onset myopes compared with emmetropes.

Labhishetty and Bobier<sup>51</sup> conducted a similar investigation to that of Jiang<sup>50</sup> with emmetropic and myopic children, as well as young adults for comparison. They collected data on the transient aspects of accommodation in emmetropes and myopes and used a similar control theory model to see whether their observed results could be simulated. They concluded that reduced blur sensitivity coupled with a motor recalibration of the accommodation convergence cross-link predicts the transient accommodative behaviour of progressive myopes. Although a link was not found between accommodative lag and the AC/A ratio here, the differences between the accommodative responses of young adult myopes and emmetropes are consistent with reduced sensitivity to hyperopic blur in myopia, which may facilitate progressive myopia in children.

The main goal of this study was to establish the most reliable and accurate method of objectively measuring and calculating accommodative errors for the purpose of comparing them between groups. Racially diverse cohorts of young adult emmetropes and myopes were compared. Pooling the measurement and calculation methods together, the mean adjusted difference in accommodative lags was 0.34 D, with myopes having higher lags than emmetropes. Of the two methods that sample small areas of the pupil (autorefractometry and Zernike defocus calculation for the 3-mm pupil), the Grand Seiko difference is considerably smaller than the mean difference by about a factor of two, while the Zernike defocus difference is larger. This reinforces the need for caution in making conclusions about

the differences between accommodative lags in different refractive groups based on measurements using autorefractors such as the Grand Seiko WAM-5500. Of the three merit functions used to calculate accommodative lags from the aberrometer measurements using natural pupil sizes, Seidel defocus was less reliable (higher standard errors) than the calculations of the full wavefront refraction using Zernike coefficients up to the sixth order in minimising the merit functions of VSMTF or NS. It is thus suggested that future studies of the accommodation response in myopes use aberrometer measurements, natural pupil sizes and VSMTF or NS merit functions, if this methodology is available.

There are limitations to the study. First, the measured accommodative responses were to a monocular stimulus, while everyday experiences are mostly binocular. Second, the measurements were indirect in that we did not measure the response of the eye exposed to the stimulus, but rather the consensual accommodative response of the other eye; however, there is no evidence to indicate that this affected the results. Third, results were not referenced to cycloplegic refractions. There is a need in children to use cycloplegia to ensure the accuracy of the refraction, for both epidemiological and treatment studies, but the value of this is less clear for studies of accommodation in myopic young adults. Without cycloplegia, there are errors in the estimation of myopia, emmetropia and hyperopia in the 20–50 year age range, just as in children, but these are small and less than 0.2 D in the case of young adult myopes.<sup>52</sup> Hence, we do not think that this caused errors in the value of the lag of clinical significance.

## AUTHOR CONTRIBUTIONS

**Dinesh Kaphle:** Formal analysis (equal); investigation (equal); methodology (equal); writing – original draft (equal). **Saulius R Varnas:** Resources (equal); writing – original draft (equal). **Katrina L Schmid:** Conceptualization (equal); funding acquisition (equal); methodology (equal); project administration (equal); supervision (equal); writing – original draft (equal). **Marwan Suheimat:** Resources (equal); writing – review and editing (equal). **Alexander Leube:** Resources (equal); writing – review and editing (equal). **David Atchison:** Conceptualization (equal); funding acquisition (equal); methodology (equal); project administration (equal); supervision (equal); writing – original draft (equal).

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employee of Carl Zeiss Vision Open access publishing facilitated by Queensland University of Technology, as part of the Wiley - Queensland University of Technology agreement via the Council of Australian University Librarians.

## CONFLICT OF INTEREST

Saulius Varnas is an employee of Carl Zeiss Vision.

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