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The relationship between refractive and biometric changes during Edinger–Westphal stimulated accommodation in rhesus monkeys

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Abstract

Experiments were undertaken to understand the relationship between dynamic accommodative refractive and biometric (lens thickness (LT), anterior chamber depth (ACD) and anterior segment length (ASL=ACD+LT)) changes during Edinger–Westphal stimulated accommodation in rhesus monkeys. Experiments were conducted on three rhesus monkeys (aged $11 \cdot 5$, $4 \cdot 75$ and $4 \cdot 75$ years) which had undergone prior, bilateral, complete iridectomies and implantation of a stimulating electrode in the Edinger–Westphal (EW) nucleus. Accommodative refractive responses were first measured dynamically with video-based infrared photorefraction and then ocular biometric responses were measured dynamically with continuous ultrasound biometry (CUB) during EW stimulation. The same stimulus amplitudes were used for the refractive and biometric measurements to allow them to be compared. Main sequence relationships (ratio of peak velocity to amplitude) were calculated. Dynamic accommodative refractive changes are linearly correlated with the biometric changes and accommodative biometric changes in ACD, ASL and LT show systematic linear correlations with increasing accommodative amplitudes. The relationships are relatively similar for the eyes of the different monkeys. Dynamic analysis showed that main sequence relationships for both biometry and refraction are linear. Although accommodative refractive changes in the eye occur primarily due to changes in lens surface curvature, the refractive changes are well correlated with A-scan measured accommodative biometric changes. Accommodative changes in ACD, LT and ASL are all well correlated over the full extent of the accommodative response.
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1. Introduction

In primates, the accommodative refractive change of the eye is brought about by a change in the crystalline lens surface curvatures (Young, 1801; Cramer, 1853; Helmholtz von, 1909). When accommodation occurs, lens equatorial diameter decreases (Storey and Rabie, 1987; Wilson, 1997; Glasser and Kaufman, 1999; Strenk et al., 1999), the lens anterior and posterior surface curvatures steepen (Brown, 1973; Koretz et al., 1984, 1987; Garner and Yap, 1997), anterior chamber depth decreases, lens axial thickness increases (Storey and Rabie, 1983; Koretz et al., 1987; Beers and Van der Heijde, 1996) and the posterior lens surface generally moves posteriorly (Brown, 1973;

Beauchamp and Mitchell, 1985; Drexler et al., 1997). The accommodative change in shape of the young lens is brought about by the force the capsule exerts on the lens (Fincham, 1925, 1937; Glasser and Campbell, 1998, 1999; Glasser et al., 2001). The accommodative change in optical power of the eye is primarily due to an increase in lens surface curvatures. There is also a lesser contribution to the optical change in power of the eye from the axial changes in optical distances due to the increase in lens thickness, the decrease in anterior chamber depth and the decrease in vitreous chamber depth. The accommodative increase in lens surface curvatures is biomechanically coupled to the increase in lens thickness. To understand more fully how the lens produces accommodative optical changes, it is of interest to precisely quantify the accommodative axial biometric changes as a function of the accommodative dioptric change.

Axial biometric accommodative changes that can be measured with A-scan ultrasonography are lens thickness

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(LT) and associated changes in anterior chamber depth (ACD) and vitreous chamber depth (VCD) (Storey and Rabie, 1983; Beauchamp and Mitchell, 1985; Koretz et al., 1997). Anterior segment length (ASL=ACD+LT) can also be determined as an indication of the extent of movement of the posterior lens surface. A-scan ultrasonography has been used to measure static changes in ocular biometry with accommodation in monkeys using both Edinger–Westphal (EW) and pharmacological stimulated accommodation (Koretz et al., 1987). Partial coherence interferometry (Drexler et al., 1997) and Scheimpflug photography (Brown, 1973; Koretz et al., 1984, 1987, 1997; Dubbelman et al., 2003) have also been used to measure static biometric changes during accommodation in humans.

Van der Heijde and colleagues developed and used continuous high-resolution A-scan ultrasound biometry to measure and analyse dynamic accommodative biometric changes in human eyes (de Vries et al., 1987; Van der Heijde and Weber, 1989; Beers and Van der Heijde, 1994a, b, 1996; Van der Heijde et al., 1996). The transducer of the continuous ultrasound biometer (CUB) was attached to the eye with negative vacuum pressure (Beers and Van der Heijde, 1994b). This provides stable, reliable biometry recorded during accommodation at a rate of 100 Hz, uncontaminated by convergent eye movements. The subjects viewed a far and near accommodative stimulus with the contralateral eye while lying supine.

Efforts to relate the biometric changes to the refractive changes are challenging because the biometry instrument generally covers the eye being measured so it has not so far been possible to simultaneously measure the accommodative biometric and refractive changes in the same eye (Beers and Van der Heijde, 1996; Drexler et al., 1997; Dubbelman et al., 2003). Therefore, accommodative biometric changes have typically been compared with stimulus dioptric demand rather than actual accommodative dioptric response amplitudes. The actual accommodative response generally lags behind the stimulus demand, so a comparison with stimulus demands provide an inaccurate representation of the biometry changes per diopter of accommodation. The lag of accommodation increases with increasing stimulus amplitude and varies in extent for different individuals (Gwiazda et al., 1993; Kasthurirangan et al., 2003). Biometric changes could be compared with the true dioptric changes in human subjects by, for example, presenting the subject with a fixed amplitude stimulus and first objectively measuring the accommodative refractive change and subsequently measuring the accommodative biometric change, or by measuring the refractive change in one eye and simultaneously measuring the biometric change in the contralateral eye. However, variability in the latency of the visual stimulus driven accommodative responses from one stimulus presentation to the next, fluctuations in the accommodative response, intraocular differences and convergence introduce complexities.

Accommodative biometric and objectively measured optical refractive changes have been compared in rhesus monkeys (Koretz et al., 1987). The relationship between the biometric and refractive changes was described using averaged data from several different methods in which static refractive and biometric measurements were made only at several discrete accommodative states. It is of interest to characterize the dynamic relationship between the refractive and biometric changes in individual monkeys to determine if this relationship changes with the amplitude of the response, is different between different monkeys or different eyes, or changes systematically with increasing age.

The goal of this study was to understand dynamic biometric changes during accommodation and how they relate to dynamic refractive changes. In a previous preliminary study it was established that refraction and biometry could be correlated using EW stimulated accommodation in rhesus monkeys (Vilupuru and Glasser, 2003). However, the low resolution A-scan ultrasound used in that study precluded accurate comparisons for low amplitude responses or for the small changes that occur in ASL, for example. In this current study, a higher resolution, high dynamic acquisition frequency A-scan ultrasound instrument has been used that provides sufficient resolution to allow small changes to be measured with improved resolution and accuracy.

EW stimulated accommodation in anesthetized rhesus monkeys allows rigorous and reliable control of the amplitude and duration of dynamic accommodative response (Vilupuru and Glasser, 2002; Ostrin and Glasser, 2004). The EW nucleus provides parasympathetic innervation to the ciliary muscles of the eye via the ciliary ganglion. A controlled stimulus current can be presented repeatedly to the EW nucleus to reliably elicit accommodative responses of the same amplitude and duration while first refraction and then subsequently biometry can be recorded dynamically. This study was undertaken to characterize the dynamic accommodative biometric and optical relationships in normal adolescent rhesus monkeys to better understand how the lens undergoes accommodative changes.

2. Materials and methods

All experiments conformed to the ARVO Statement for the Use of Animals in Ophthalmic and Vision Research and were in accordance with institutionally approved animal protocols. Experiments were performed on both eyes each of three rhesus monkeys (*Macaca mulatta*) #4, #38, #70, aged 11·5, 4·75 and 4·75 years, respectively. Each monkey had previously had a stimulating electrode surgically implanted in the EW nucleus of the brain (Crawford et al., 1989; Glasser and Kaufman, 1999; Vilupuru and Glasser, 2002). The monkeys had previously undergone bilateral

complete iridectomies (Kaufman and Lütjen-Drecoll, 1975; Vilupuru and Glasser, 2002). The monkeys are used in multiple experimental protocols and the iridectomies (Kaufman and Lütjen-Drecoll, 1975), the justification for them (Glasser and Kaufman, 1999; Vilupuru and Glasser, 2002, 2003), and the absence of an effect on the accommodative mechanism and amplitude (Crawford et al., 1990; Glasser and Kaufman, 1999) have been described previously.

Monkeys were anesthetized with intramuscular injection of $10 \, mg \, kg^{-1}$ ketamine and $0.5 \, mg \, kg^{-1}$ acepromazine and then anesthetized to surgical depth using constant infusion of propofol (Propoflo, Abbott Laboratories, North Chicago, IL) anesthesia delivered as initial bolus of $1.5 \, mg \, kg^{-1}$ and then as a constant perfusion of $0.5 \, mg \, kg^{-1} \, min^{-1}$. The monkeys were held prone with their heads held in a head holder, facing forward. The eye lids were held open with lid speculums, sutures were passed through the lateral and medial rectus muscles to stabilize the eyes and clear, plano contact lenses were placed on the corneas to prevent dehydration and loss of optical clarity.

At the start of each experiment, the relationship between the stimulus current amplitude delivered to the EW nucleus and the resulting accommodative refractive change was established by generating an accommodative stimulus response function for each eye of each monkey. Static accommodative responses were measured with a Hartinger coincidence refractometer. From the stimulus response function, seven or eight increasing stimulus current amplitudes were chosen to be used subsequently for stimulating increasing amplitude, dynamic accommodative responses spanning the full range of accommodation available to each eye. Details of these methods have been described previously (Vilupuru and Glasser, 2002).

3. Dynamic refractive measurements

Video-based infrared photorefraction (Schaeffel et al., 1993) was used to measure dynamic refractive changes during EW stimulated accommodation at 30 Hz. Three, 4-sec long stimuli were delivered at each current amplitude to elicit accommodation and the refractive responses were recorded to video tape for later off-line analysis. The stimulus onset, duration and termination were also recorded to the video tape with a text overlay. The three individual responses were averaged and fit with appropriate functions for accommodative and disaccommodative phases of the responses. Refraction was recorded for the range of stimulus amplitudes used in one eye and then the other eye and immediately following that the biometry measurements were recorded for the same range of stimulus amplitudes. Details of these methods have been described previously (Vilupuru and Glasser, 2002, 2003).

4. Dynamic biometric measurements

A CUB developed by Dr Van der Heijde (Beers and Van der Heijde, 1994b) was used to measure dynamic changes in ocular biometry in each eye of each monkey. The same stimulus current amplitudes used for the dynamic refractive measurements were used for the dynamic biometric measurements. The CUB has a 10 MHz transducer, is able to detect a movement of $\pm 2 \, \mu m$ and records ocular biometry data to a computer via the RS232 port at a frequency of 100 Hz (Beers and Van der Heijde, 1994b).

A 1 cm long rubber tubing stand-off sleeve was placed over the transducer tip and filled with ultrasound transmission gel (Liquasonic Ultrasound Gel, Chester Labs Inc., Cincinnati, OH 45237). The transducer was clamped in a micromanipulator (D-10 positioner, Research Instruments, London, UK). The contact lens was removed from the eye. The tip of the rubber tube was positioned in contact with a bead of ultrasound transmission gel on the cornea to give sharp A-scan peaks for all ocular surfaces. The instrument records the time between the peaks associated with the different intraocular interfaces. Times were subsequently converted to distances by multiplication with accepted sound velocities (ACD = $1532 \, m \, s^{-1}$; LT = $1641 \, m \, s^{-1}$) (Koretz et al., 1987; Wallman and Adams, 1987; Van der Heijde and Weber, 1989; Troilo and Judge, 1993; Vilupuru and Glasser, 2003). ACD was measured from the first corneal surface. ASL was determined as the sum of ACD and LT and identifies the extent of movement of the posterior lens surface. VCD was measured but not considered further. For each stimulus amplitude, three accommodative responses were recorded and averaged. For comparison with the 30 Hz video-based refractive measurements, 100 Hz CUB data was re-sampled at 30 Hz.

5. Function fitting

Functions were fitted to the accommodative and disaccommodative biometric and refractive phases of the responses as described previously (Vilupuru and Glasser, 2002). For the 30 Hz refraction measurements, based on visual inspection of the responses, the accommodative response was considered to begin two video frames ($\sim 66 \, msec$) after the stimulus onset (to remove the latency between stimulus onset and the start of the response), and to continue until the stimulus terminated. The disaccommodative response was considered to begin two video frames after the stimulus termination and to continue until the refraction reached baseline 2 sec after the stimulus termination, i.e. 58 frames in total. For the 100 Hz biometric responses the baseline prior to the onset of the response was removed by visual inspection and the accommodative and
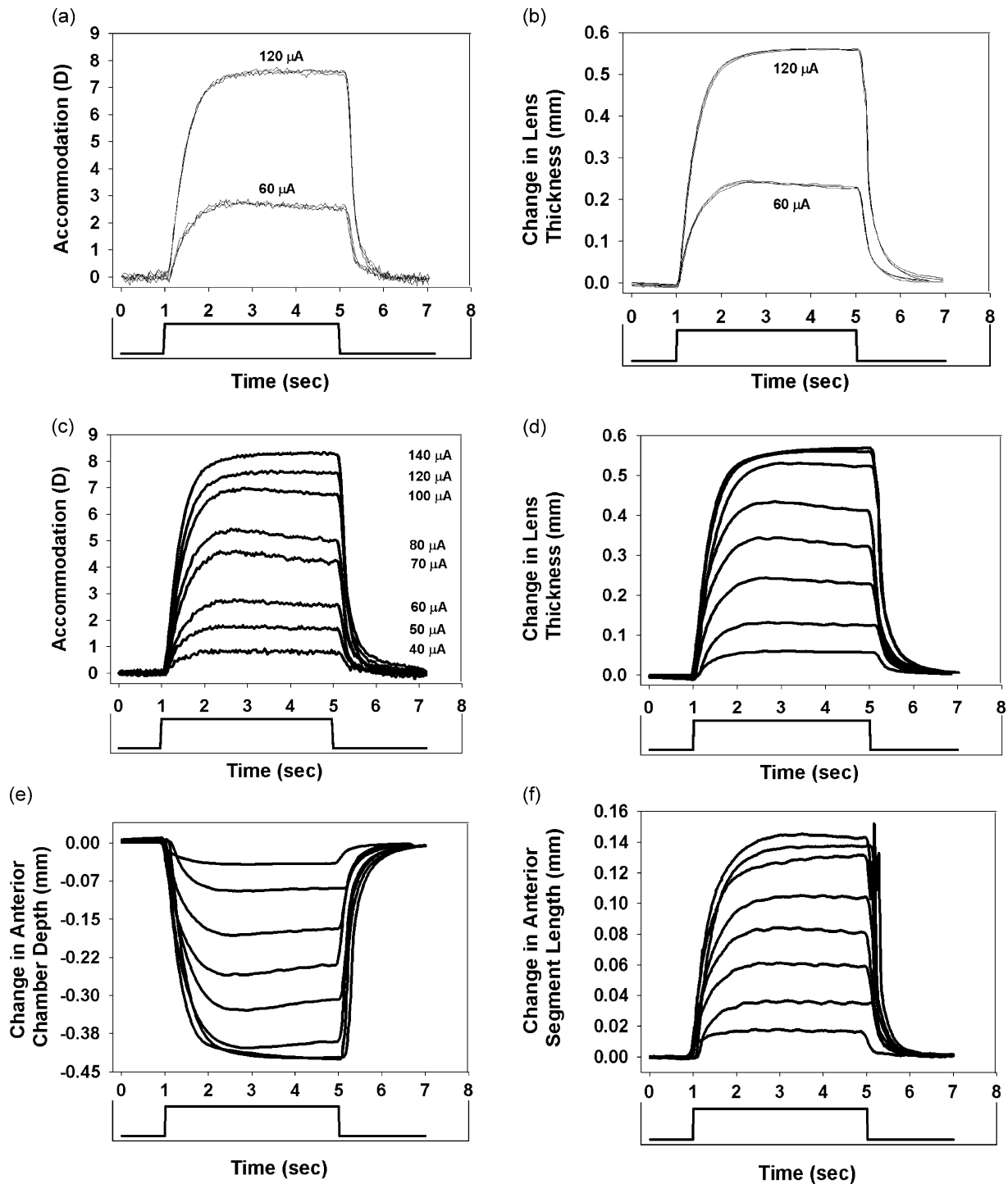
Fig. 1. Three individual raw accommodative refractive (a) and biometric (b) responses to 60 and 120 μA stimulus amplitudes from the left eye of monkey #4. The three individual traces shown for each response amplitude are essentially identical. In the subsequent graphs (c-f) each data trace is the average of three individual responses. Accommodative refractive (c) and biometric (d-f) changes during EW stimulated accommodation to a range of stimulus current amplitudes from the left eye of monkey #4 are shown. The solid black line below each graph indicates the start, duration (4 seconds) and termination of the stimulus. Dynamic refractive responses were measured with photorefraction and dynamic biometric responses were measured with high resolution continuous ultrasound biometry (CUB). The same current amplitudes were used to record the refractive and subsequently the biometric responses.

disaccommodative phases of the responses were fitted with the same equations as used for the refraction data. The maximum value of the derivatives of the fitted equations provided peak velocities of accommodation and

disaccommodation for both refractive and biometric responses. Main sequence relationships (peak velocity of a response vs response amplitude) were established for accommodative and disaccommodative phases for both

refraction and biometry (Vilupuru and Glasser, 2002, 2003).

6. Results

The three individual accommodative refractive and biometric responses averaged for each stimulus amplitude were virtually superimposable. Three individual traces each for refractive and lens thickness measurements for two stimulus amplitudes are shown in Fig. 1a and b. Examples of accommodative refractive changes (Fig. 1c), measured first and biometric (Fig. 1d–f) response measured subsequently from the left eye of monkey #4 at the same eight stimulus current amplitudes are shown. Dynamic accommodative changes in LT are compared with refraction in two eyes of two different monkeys for increasing amplitudes (Fig. 2a). The data for the two monkeys are separated along the abscissa to distinguish the individual responses of increasing amplitudes. The dynamic relationship between accommodative refractive change and change in LT is relatively constant with increasing amplitude. The dynamic biometric accommodative changes (LT, ACD and ASL) are compared to the refractive changes for all amplitudes for both eyes of each monkey (Fig. 2b, d and f). In Fig. 2c, e and g, the same data from each eye is plotted, separated along the abscissa, for visibility. The relationship between accommodative refractive change and LT, ACD and ASL is relatively linear for each eye of each monkey with slightly differing slopes between the monkeys and within a given monkey (#4 left eye (OS) vs right eye (OD), for example) (Fig. 2c, e and g). To compare the relationships between different eyes, the data for all amplitudes of each eye were fitted with a single linear regression line. Slopes of these regression lines for the relationships between ACD, LT and ASL and the accommodative refractive changes are shown in Table 1. The mean of the slopes of these relationships for all eyes show that with accommodation, on average, lens thickness increases by $0 \cdot 063 \, \mathrm{mm \, D^{-1}}$, anterior chamber depth decreases by $0 \cdot 046 \, \mathrm{mm \, D^{-1}}$ and anterior segment length increases by $0 \cdot 017 \, \mathrm{mm \, D^{-1}}$. The relationship between refraction and biometry differed slightly, although non-systematically between eyes (Fig. 2a, c, e and g).

The biometric changes occurring with accommodation were compared with each other to understand the accommodative lens movements. Dynamic biometric relationships do not change systematically with increasing response amplitude (Fig. 3a). Dynamic changes in ACD and ASL were compared with dynamic changes in LT (Fig. 3b and d) and dynamic changes in ASL were compared with dynamic changes in ACD (Fig. 3f). The same data from each eye are replotted separated along the abscissa for visibility (Fig. 3c, e and g). In each eye, the slopes of the interrelationships between LT, ACD and ASL are relatively consistent with increasing amplitude although with some variability (Fig. 3a, c, e and g). The relationships between LT, ACD

and ASL are similar for all six eyes of the three monkeys (Fig. 3b, d and f). To compare the relationships between different eyes, the data for all amplitudes of each eye were fitted with a single linear regression line. Slopes of these regression lines for the biometric relationships are shown in Table 1. The slopes of the relationships between ACD, ASL and LT are shown in Table 2 with an overall decrease in ACD of $0 \cdot 715$ mm per mm increase in LT and an increase in ASL of $0 \cdot 285$ mm per mm increase in LT. The difference between the eyes of different monkeys is no greater that the interocular difference between two eyes of the same monkey (#70).

The data for refraction vs biometry and biometry vs biometry for disaccommodation (not shown) are qualitatively and quantitatively similar to the accommodative data shown.

The cumulative data from both eyes of each of the three monkeys shows that there is a linear relationship between the extent of change in lens thickness and the peak velocity of the change in lens thickness (the main sequence) for accommodation and disaccommodation (Fig. 4a and b). This is also true for the main sequence for accommodative refractive changes (Fig. 4c and d). Peak velocities for disaccommodation (Fig. 4b and d) are greater than for accommodation (Fig. 4a and c). Accommodative and disaccommodative main sequence slopes are not statistically different for refraction and biometry (accommodative phase $p = 0 \cdot 78$ and disaccommodative phase $p = 0 \cdot 52$).

7. Discussion

Besides the prior preliminary study (Vilupuru and Glasser, 2003), dynamically recorded biometric and refractive accommodative responses have not been compared. Prior experiments in humans compared static biometric changes to accommodative stimulus demands rather than accommodative responses (Drexler et al., 1997). A replot of the data from Fig. 5a from that study (Drexler et al., 1997; with permission from the authors) is compared with a similar plot from two monkey eyes from the current study (Fig. 5). The graphs show anterior movement of the anterior lens surface and a posterior movement of the posterior lens surface in both humans and monkeys, with larger movements for smaller monkey eyes. In the human data ACD and ASL appear to change non-linearly when biometry is compared to accommodative stimulus demand as presented by Drexler et al. However, in the monkey data, where biometric and *actual* refractive changes are compared, there is a linear change. The difference emphasizes the importance of considering the actual refractive change of the eye to understand how accommodation occurs. The ideal approach to determine the relationship between the refractive and biometric changes would be to record them simultaneously in the same eye during accommodation. However, this may not yet be possible with existing technology. Fig. 5 also
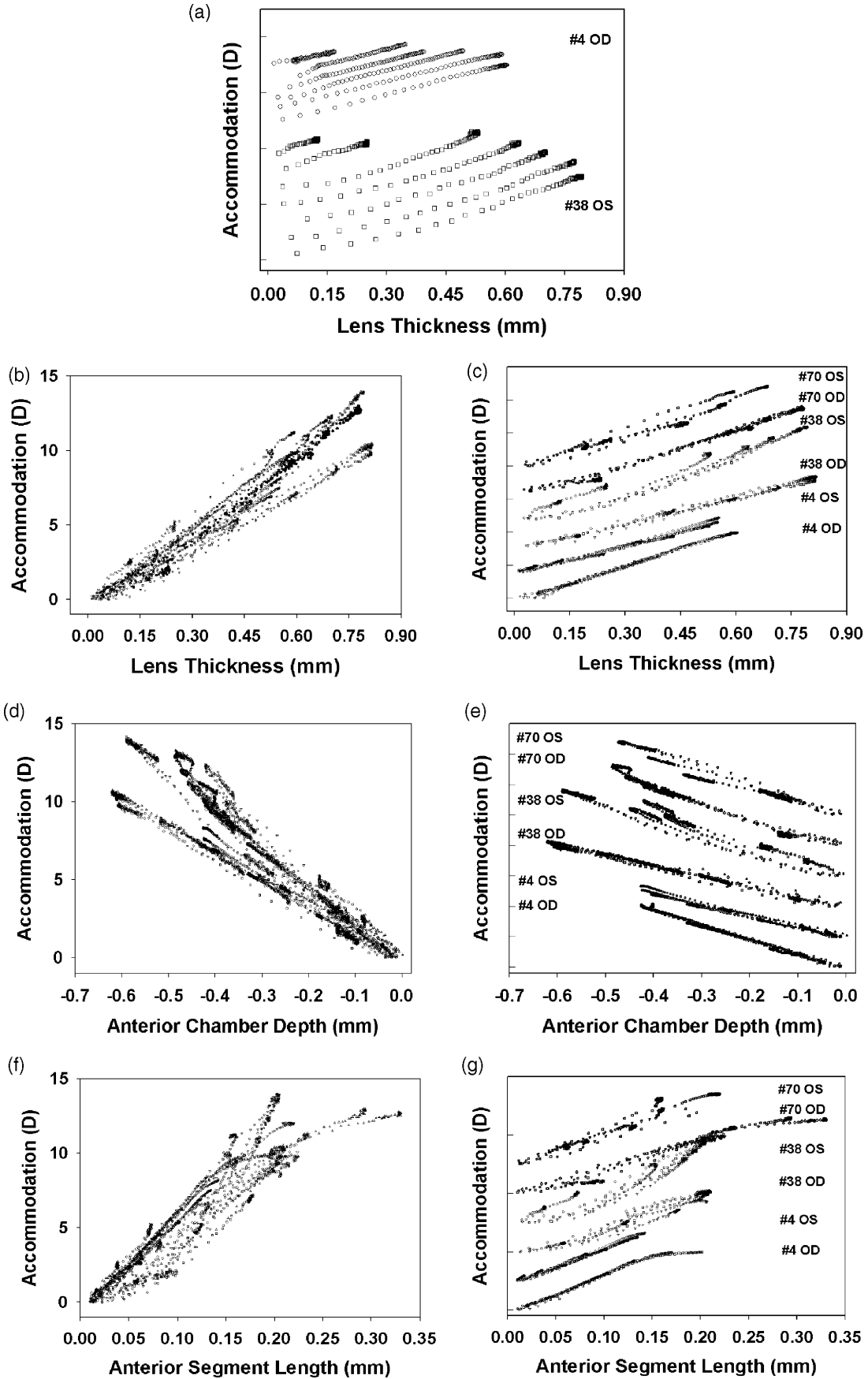
Table 1
Biometric changes in mm per diopter of accommodation in each eye of each monkey

Eye	ACD	LT	ASL
4 OD	−0·041	0·059	0·016
4 OS	−0·054	0·072	0·016
38 OD	−0·057	0·074	0·018
38 OS	−0·046	0·058	0·015
70 OD	−0·039	0·059	0·021
70 OS	−0·039	0·056	0·015
Mean	−0·046	0·063	0·017
±SD	±0·008	±0·008	±0·002

For each eye, a single linear regression line was fitted to the combined responses for all amplitudes. Range of r^2 values: 0·937–0·996.

shows the calculated anterior movement of the center of the lens, calculated as half-way between the anterior and posterior lens surfaces. Since the primate lens anterior surface is flatter than the posterior surface, this center does not correspond to the equatorial plane of the lens, but it does show a modest anterior movement of the center of the adolescent human and monkey lens during accommodation.

A prior study using pharmacological and EW stimulated accommodation in rhesus monkeys compared static Scheimpflug and A-scan measured biometric changes at different accommodative amplitudes to static Hartinger coincidence refractometer measured refractive changes (Koretz et al., 1987). Data relating biometric and refractive changes from only two eyes of one 7-year-old monkey are shown but without regression slopes and intercepts. Lens thickness increase linearly, evidently by about 0·041 mm D^{-1} and Koretz et al. (1987) report that the position of the posterior lens surface remains roughly constant with accommodation. The data shown are averaged from several experiments using several different approaches. Previous dynamic comparison between biometry and refraction in one rhesus monkey yielded an increase in LT of 0·023–0·045 mm D^{-1} (Vilupuru and Glasser, 2003), comparable to the Koretz et al. (1987) result. These two prior studies used relatively low resolution techniques. The clinical A-scan ultrasound transducers used have relatively large diameter tips which could lead to misalignment of the transducer with the optical axis of the eye, thereby possibly underestimating the true lens biometric changes.

The CUB affords improved resolution and has a 4 mm diameter transducer allowing more accurate alignment along the optical axis. The CUB has been reported to resolve ±2 μm movements of an interface between media

of differing sound velocities (Beers and Van der Heijde, 1994b). This was tested and verified to be true in the present study by measuring movements of the end of the spindle of a digital micrometer capable of 1 μm movements (MDD-25 Titan digital micrometer, Tital Tool Supply Co., Inc., Buffalo, NY). Movements as small as 1 μm could readily be detected and 2 μm movements were clearly discernable and were well above the noise level of the instrument. Measuring such small movements in a non-physiological, mechanical apparatus offers definitive proof of ability to detect small movements. While recording microfluctuations (Van der Heijde et al., 1996) may offer another such method, prior experiments aimed at completely eliminating other variables such as eye movements under anesthesia in monkeys (Glasser and Kaufman, 1999) show that it is not possible to completely eliminate external physiological influences.

The CUB recordings show small changes in axial length with accommodation. In some eyes these were increases in axial length and in some eyes these were decreases in axial length. These axial length changes may be real axial length changes, may be artefacts due to eye movements, or may be due to changes in choroidal blood flow as has previously been demonstrated with EW stimulation in birds (Fitzgerald et al., 1990). Van der Heijde and colleagues (Van der Heijde and Weber, 1989) have previously shown the absence of axial length changes during accommodation with the CUB in human eyes, however, other studies have shown systematic change in axial length during accommodation in humans (Drexler et al., 1998). No other studies have looked at axial length changes with accommodation in monkeys, so, contradictory results aside, neither of the two human studies provide any clear indication of whether or not there are axial length changes with accommodation in monkeys. The anatomy of the monkey eye, the extent of the ciliary muscle contraction, and the thickness of the sclera of the monkey eye are all quite different from that of human eyes, so no conclusions about axial length changes in monkey eyes can be made from human studies. Even clamping the CUB transducer to the cornea with negative vacuum pressure as Van der Heijde and colleagues have done in humans (Van der Heijde and Weber, 1989) would not offer a resolution to this question, unless it could be shown that there was no change in axial length in aphakic monkeys. Since we have no aphakic monkeys, we have not done this testing.

Because change in axial length with accommodation were recorded, the method previously used to calculate

Fig. 2. Individual responses for two eyes comparing refraction and LT changes for increasing amplitudes (a). For this comparison the 100 Hz biometry data were resampled at 30 Hz to match the lower frequency photorefraction data. Accommodative responses of increasing amplitude in two eyes (#4 OD, circles and #38 OS, squares) have been separated along the abscissa for visibility. Dynamic comparisons between refraction (accommodation) and biometry (LT, ACD & ASL) during the accommodative phases at increasing amplitudes in each eye of the three monkeys (b, d & f) are shown. To visually resolve the individual responses for different eyes, the data is re-plotted, separated along the abscissa (c, e & g). For each eye, all the increasing responses for increasing amplitudes are shown as different symbols (although these are often superimposed because the data for different amplitudes follows a similar path). Over most of the accommodative range, there is a roughly linear relationship between LT, ACD and ASL and accommodation (b, d & f). In some eyes, slight nonlinearities occur near the maximally accommodated state at the highest amplitudes especially for the ASL-accommodation relationships (e.g., g, #4 OD).
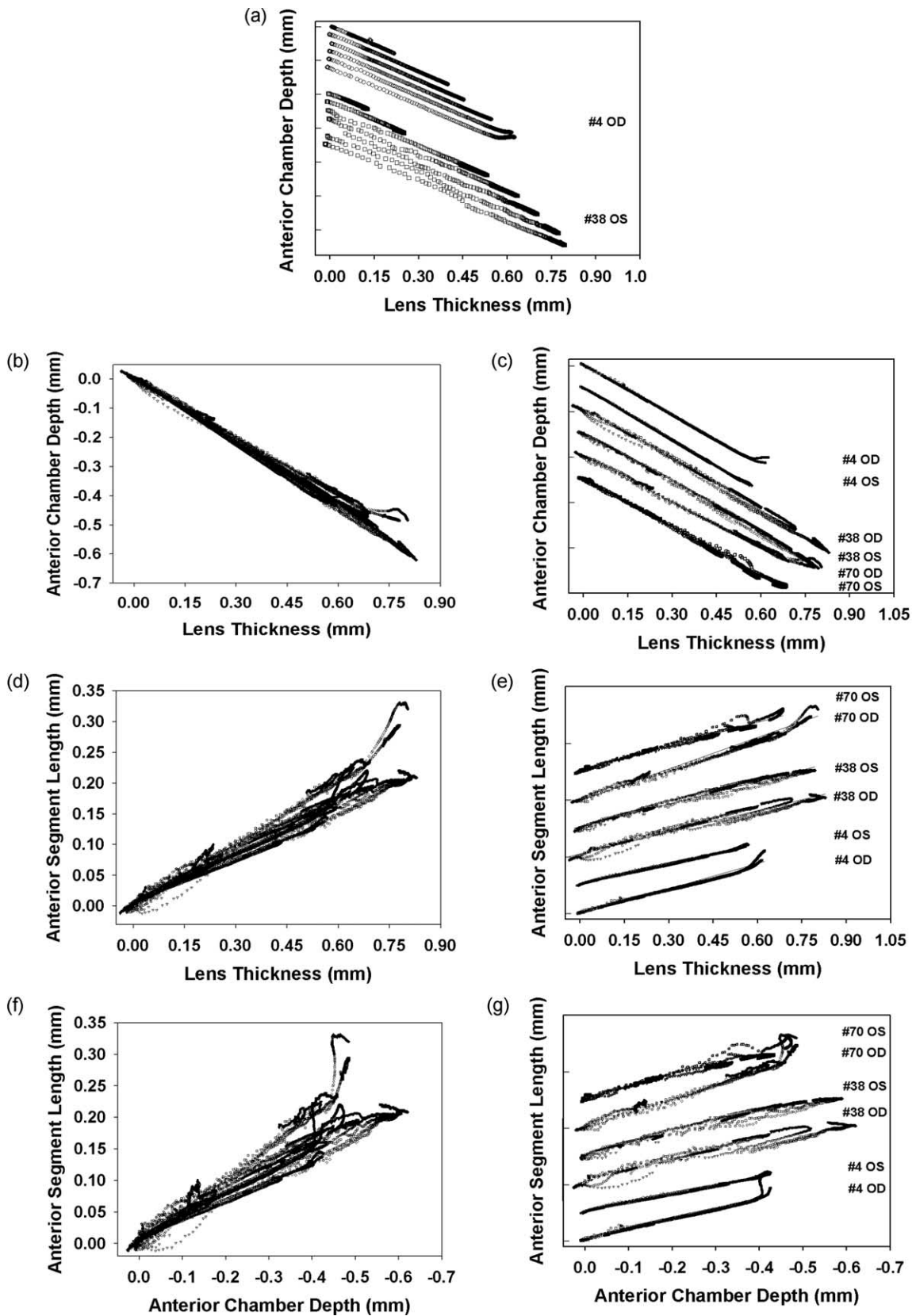
Fig. 3. Dynamic interrelationship between LT, ACD and ASL during the accommodative phase for each increasing amplitude in each eye of the three monkeys (a, b, d & f). To show variability with increasing amplitudes, increasing responses in two eyes (#4 OD, circles and #38 OS, squares) have been separated along the abscissa (a). The data from each eye are comparisons at all amplitudes. Plots for the different eyes have been separated vertically along the abscissa for visibility (c, e & g). Different symbols represent different response amplitudes. In any given eye the relationship between ACD and LT (a, c) and ASL and LT (e) follows the same general linear path with increasing amplitudes until near the maximally accommodated state for the highest amplitude when some non-linearities are observed.

Table 2
Change in ACD and ASL in units of mm per mm change in LT in each eye of each monkey

Eye	ACD	ASL
4 OD	−0·702	0·298
4 OS	−0·759	0·241
38 OD	−0·746	0·254
38 OS	−0·734	0·266
70 OD	−0·629	0·371
70 OS	−0·721	0·278
Mean	−0·715	0·285
±SD	±0·047	±0·047

For each eye, a single linear regression line was fitted to the combined responses for all amplitudes. Range of r^2 values: 0·969–0·999.

the ultrasound velocity in the human lens (Van der Heijde and Weber, 1989) cannot be used here in this monkey study. That approach relies on there being no change in axial length. A plot of the relationship between change in anterior chamber + vitreous chamber vs that for the lens (the slope of which would provide the ultrasound velocity for the lens) showed distinct and inconsistent non-linearities. Thus, it is not possible to attempt to determine the ultrasound velocity in the human lens from that data in the way reported previously.

8. Biometric and refractive changes: dynamic comparison

Relatively systematic relationships exists between changes in LT, ACD, ASL and refraction. The data indicates that, on average, lens thickness increases by 0·063 mm D^{-1}, ACD decreases by 0·046 mm D^{-1} and ASL increases by 0·017 mm D^{-1}. This implies that about 72% of the increase in LT occurs as an anterior movement of anterior pole of the lens and 28% due to a posterior movement of posterior lens pole (Fig. 5). Prior data from rhesus monkeys and humans shows that about 75% of the increase in lens thickness occurs as an anterior movement of the anterior lens surface, the remainder being due to a posterior movement of the posterior lens surface (Drexler et al., 1997; Vilupuru and Glasser, 2003). A posterior movement of the posterior lens surface is likely to be a real component of the accommodative mechanism in both humans and rhesus monkeys. The maximum change in LT and ACD for the smaller rhesus monkey eye is approximately twice that of human eyes, although, within the limits of the approaches used, the responses appear qualitatively similar.

Since refraction and biometry cannot be measured simultaneously in the same eye, they were measured
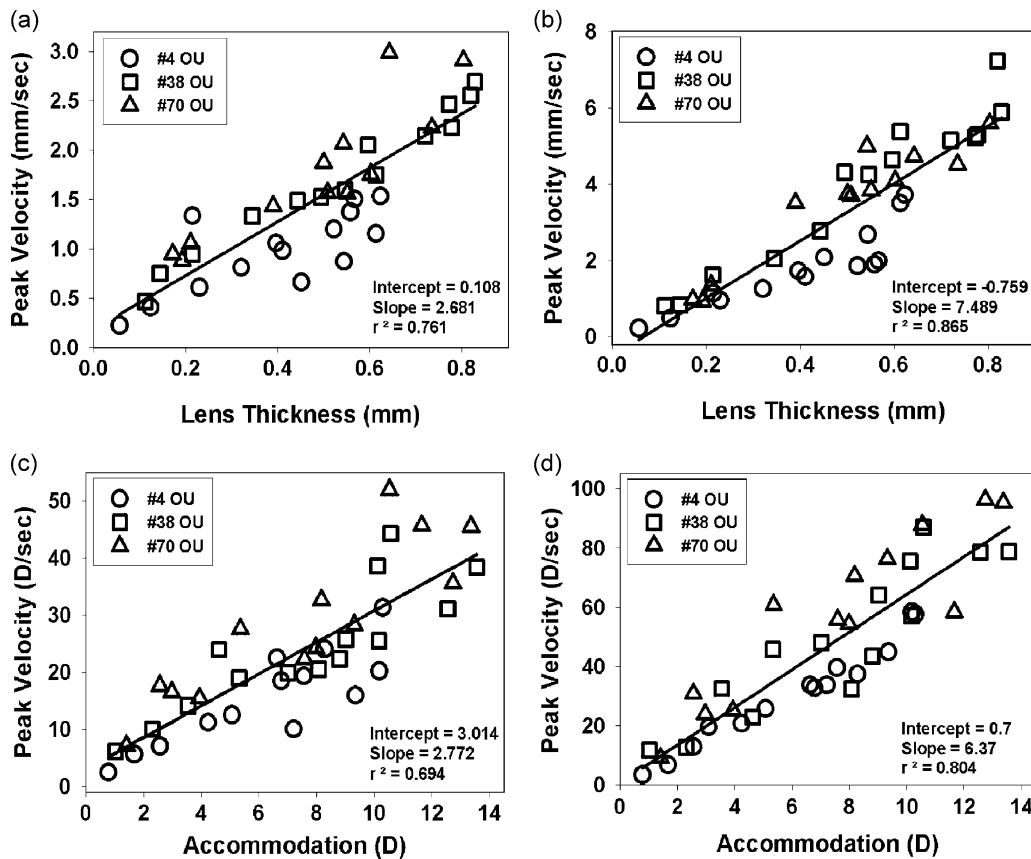

Fig. 4. Main sequence relationships during accommodative and disaccommodative phases of lens thickness and refraction (a-d). Accommodative and disaccommodative main sequence slopes are not statistically different between biometric and refractive measures (accommodative phase p=0.78 & disaccommodative phase p=0.52).
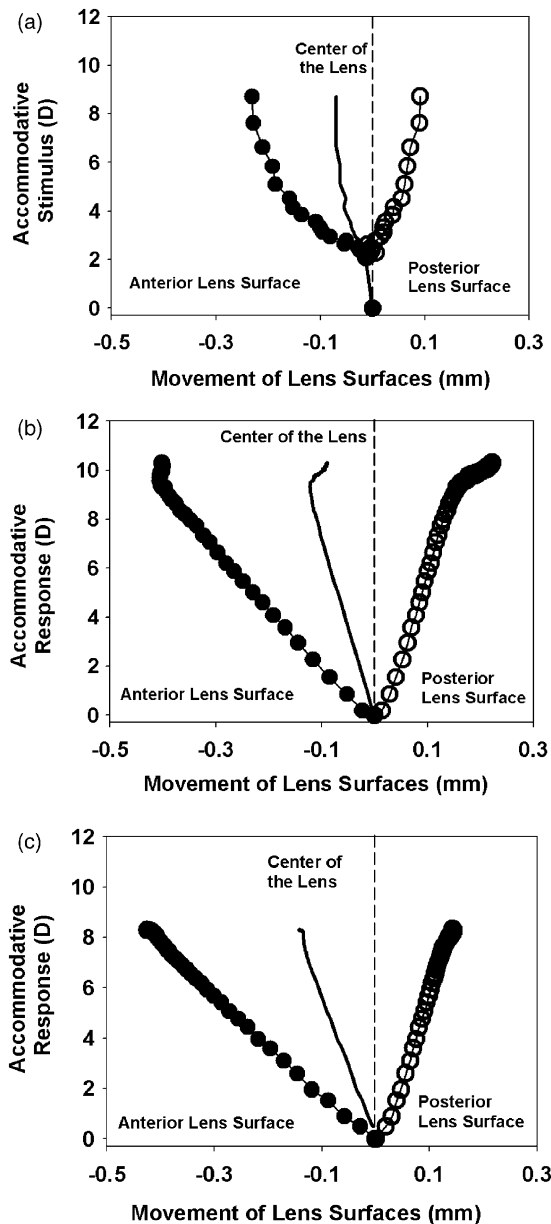
Fig. 5. Changes in ACD and ASL as a function of accommodative stimulus demand for accommodation in the eye of an 27 year old human emmetrope (a) from Drexler et al, (Drexler et al., 1997) replotted from their published figure 5a with permission from the authors. ACD and ASL as a function of accommodative response from the left (b) and right (c) eyes from rhesus monkey #4 from the present study. The human data, plotted as a function of stimulus amplitude, suggest there are non-linear biometric changes with accommodation. When biometric changes are compared with actual accommodative response in the monkey data, a more linear relationship is observed. The accommodative response and the absolute biometric changes are larger in the relatively smaller monkey eye. The data show a forward movement of the center of lens of the human and monkey lens (solid lines) with accommodation of ~50 μm for the human and ~150 μm for the monkey.

sequentially. EW stimulated accommodation allows repeated and reliable accommodative responses (Fig. 1a and b). However, the response characteristics for a given current amplitude vary slightly with time, resulting in slight

mismatches between the CUB and photorefraction measured responses (Fig. 2b, d and f). The rigorous control over the duration and amplitude of the response afforded by EW stimulated accommodation reduces, but does not eliminate, this source of variability. To reduce the variability between the refractive and biometric changes in an eye, the measurements are performed as close in time as possible. In the prior study in which this comparison was made (Vilupuru and Glasser, 2003), a longer time elapsed between the biometry and refraction measurements as other procedures were performed which may have resulted in greater variability in the results.

9. Biometric changes

Lens accommodative axial changes can be understood by comparing ACD and ASL with LT (Figs. 3 and 5b and c). Because ACD and LT are measured simultaneously with the CUB in the same accommodative response, the variability is relatively low. The biometric accommodative relationships in the eye follow relatively linear paths for increasing accommodative amplitudes. Data from all six eyes shows that lens biometric changes are relatively consistent between different eyes of different monkeys with different maximum accommodative amplitudes. Monkey #4, the oldest monkey with the lowest accommodative amplitude had response characteristics not systematically difference from the two younger monkeys.

Non-linearities occur near the maximum accommodative state at the highest amplitudes in some eyes (#4 OD and #70 OD). These effects are small (less than 50 μm) relative to the overall biometric accommodative changes and are likely to be non-systematic responses that may occur at the extreme states of accommodation in some monkeys. The non-linearities could be due to small eye movements or a downward sag of the lens under the influence of gravity at maximum accommodation as zonular tension is released (Glasser and Kaufman, 1999).

10. Main sequence relationships

Main sequence relationships have been established for EW stimulated accommodative and disaccommodative phases of LT and refractive changes. Main sequence relationships for refraction and biometry are similar for accommodation (Fig. 4a and c) and are also similar for disaccommodation (Fig. 4b and d), although the relationships between accommodation and disaccommodation differ. The refractive changes are a consequence of the lens biometric changes, therefore the first order dynamics of the accommodative system during EW stimulation in monkeys can be studied using either dynamic refractive or biometric measurements. The results show that disaccommodation is faster than accommodation and the main

sequence relationships agree well with those reported previously (Vilupuru and Glasser, 2002, 2003).

Although the ocular refractive change is primarily brought about by changes in lens surface curvature, relatively systematic linear relationships exist for increasing accommodative amplitudes between LT, ACD and ASL and refraction. Although this data do not suggest any age related differences, the comparisons between biometric and refractive responses (Fig. 3) and main sequence relationships (Fig. 4) shown here for adolescent monkeys will ultimately be compared with results from older monkeys with lower maximum accommodative amplitudes to understand if systematic age related changes occur.

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