

# The Zonula, Lens, and Circumferential Space in the Normal Iridectomized Rhesus Monkey Eye

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**PURPOSE.** To document zonular orientation and suspension of the lens during accommodation, and age-related changes of the circumferential space (CLS) at rest and during accommodation, in living iridectomized rhesus monkey eyes.

**METHODS.** The CLS was measured in 34 iridectomized eyes of 24 living rhesus monkeys, age 5.7 to 26 years, in the resting and accommodated state, and the orientation of the zonula and suspension of the lens during accommodation was assessed qualitatively.

**RESULTS.** The nonaccommodated CLS decreased significantly with age in both the nasal and temporal quadrants and tended to do so at a slightly faster rate in the temporal quadrant. The CLS correlated significantly with the accommodative amplitude: the greater the CLS the greater the accommodative amplitude. Multiple regression analysis indicated that age and CLS together are better predictors of accommodative amplitude than is age alone. The zonula appeared taut in the nonaccommodated eye throughout the age range despite the age-related decline in CLS.

**CONCLUSIONS.** Characterization of age-related changes in the accommodative apparatus may help to model the system for hypothesis testing. The CLS may be an indicator of presbyopia-related processes in surrounding tissues. However, these results do not prove that the width of the CLS, in and of itself, has a causal relationship with accommodative amplitude, or that changes in the CLS play a pathophysiological role in presbyopia. (*Invest Ophthalmol Vis Sci.* 2006;47:1087-1095) DOI:10.1167/iovs.04-1524

It is generally accepted that with accommodation, the ciliary muscle moves forward and inward, releasing tension on the zonular fibers, allowing the lens capsule to mold the lens and the equator to move away from the sclera.<sup>1</sup> Presbyopia (age-related loss of accommodative ability) has been attributed to increased hardness of the lens with age,<sup>2-8</sup> lens growth,<sup>7,9-15</sup>

and loss of elasticity of the ciliary muscle's posterior attachments.<sup>16,17</sup>

The crystalline lens grows throughout life through proliferation of epithelial cells near the lens equator; the cells elongate toward the anterior and posterior poles of the lens and become lens fibers. The mass of the lens increases, and the axial lens thickness increases anteroposteriorly.<sup>7,18-20</sup> In vivo human data, gathered using magnetic resonance imaging (MRI), demonstrates that the lens equatorial diameter in the nonaccommodated eye does not change systematically with age and that the anteroposterior (A-P) thickness increases with age.<sup>21</sup> Although further research is needed because of the limitations of MRI, the MRI data provide the strongest available evidence against suggested age changes in lens diameter in vivo, especially absent any contravening in vivo data. In vitro data from excised lenses show increased equatorial diameter with age.<sup>22</sup> However, young excised lenses are accommodated (diminishing the equatorial diameter) whereas old, presbyopic, and hardened lenses are not.<sup>3,18,23</sup>

Studies in which the ciliary ring diameter was directly measured in vivo in the human eye, by using MRI<sup>21</sup> and histologic studies of human ciliary muscle<sup>24</sup> show an age-related decrease in nonaccommodated ciliary muscle ring diameter. Scanning electron microscopy studies show no age-related change in zonular length, but show an anterior shift of the zonular insertion onto the lens anterior surface.<sup>9</sup> This is suggested to be a factor in the loss of accommodation with increasing age.<sup>25-27</sup>

Whether the age-related decrease in ciliary ring diameter is the initial, middle, or end link in the chain of events that lead to presbyopia, it may affect the forces applied to the lens during accommodation and disaccommodation. The width of the circumferential space (CLS) may reflect the diminished ciliary ring diameter and therefore may be an indicator of age-related changes in the zonular forces applied to the lens.

The present studies were undertaken in living iridectomized rhesus monkeys to document the zonular orientation and suspension of the lens during accommodation and to quantify age-related changes of the CLS in the resting and accommodated eye.

## MATERIALS AND METHODS

Measurement of accommodation, goniovideography, image calibration, prismatic distortion, animal handling, electrode placement, and anesthesia have been described.<sup>28</sup> Thirty-four eyes of 24 rhesus monkeys (*Macaca mulatta*; age, 5.7-24 years at entry) were included in the study. In 28 eyes (21 monkeys), the data were collected during the same experimental sessions as in Croft et al.,<sup>28</sup> and all eyes were analyzed by using the same procedures. Experiments were performed between 2 weeks and 5 years after study entry. Ages given in the Results section refer to the time at which the experiment was performed. Therefore, the youngest animals are reported as 5.7 or 5.8 years, and the oldest up to 26 years. Longitudinal comparisons were not performed in any monkeys.<sup>28</sup>

Goniovideography allowed a determination of age-related changes in the nonaccommodated and accommodated circumferential space (CLS) in the nasal and temporal quadrants. The CLS is the average

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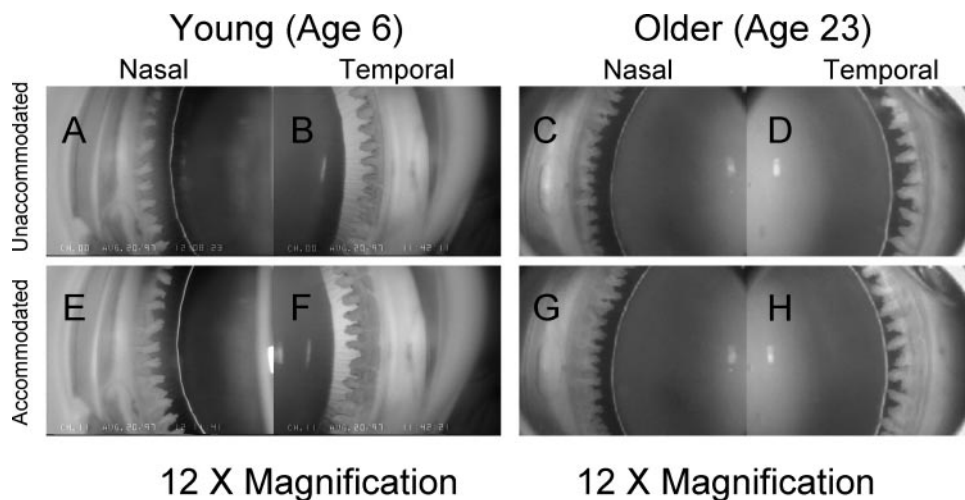
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**FIGURE 1.** Goniovideography of the (A, C, E, G) nasal and temporal (B, D, F, H) quadrants of a young and older monkey in the accommodated and nonaccommodated states. The CLS is reduced in the old eye compared with the young eye.

closest distance from the tips of four to five ciliary processes (CPs) in the midregion of the nasal and temporal quadrants (i.e., 3 or 9 o'clock) to the equatorial edge of the lens. Relaxation or bending of the zonular fibers anywhere within the field of view was recorded.

After total iridectomy was performed<sup>29</sup> in both eyes, a bipolar stimulating electrode was implanted into the Edinger-Westphal (E-W) nucleus.<sup>30</sup> Surgical depth anesthesia was achieved before all procedures. A Hartinger coincidence refractometer (Aus Jena, Jena, Germany) was used to measure resting refractive error and accommodation.

Goniovideography images (Swan-Jacob gonioscopy lens) were recorded during E-W stimulation. Extreme care was taken to align the slit lamp observation tube with the A-P axis of the eye so that the ciliary processes, lens, and CLS could be visualized through the gonioscopy lens. In the resting eye, there were no convergence eye movements. Convergence eye movements during stimulation were minimized and measured (0.17 mm;  $n = 27$ ).<sup>28</sup> The effect of eye movement alone on CLS was determined by inducing  $\sim 0.17$  mm of convergence eye movements without accommodation in four eyes<sup>28</sup> and comparing the CLS measurements to baseline.

Goniovideography recordings of the ciliary body, zonule and lens equator accommodative movements were made at several different current amplitudes, as described.<sup>28</sup> Beginning at minimum accommodation, the stimulus was increased by consistent increments available on the stimulus isolation unit up to maximum accommodation (maximal stimulus). The stimulus level was then increased again by the same increment (supramaximal stimulus). The supramaximal stimulus was retrospectively calculated from all monkeys to be between 0.1 to 0.2 mA or  $26.2\% \pm 3.9\%$  above that necessary to induce maximum accommodation. This ensured that maximum accommodation had been achieved as measured refractometrically, and allowed determination of whether the CP and lens accommodative movement had plateaued. The goal was to stimulate the muscle beyond the point at which dioptric accommodation plateaued, to determine the limiting factors in the accommodative response (i.e., CP or lens movement, and the impact on CLS). Images recorded during higher than supramaximal stimulation are also shown for comparison and indicated by the level of current provided with the image. Qualitative assessment of movements at other, submaximal stimulus levels is included, and the stimulus level is given for each case.

The CLS was measured from digitized images (Optimas software; Media Cybernetics Inc, Silver Spring, MD) taken from SVHS videotape before, during and after a  $\sim 2.2$ -second stimulus duration.

Scheimpflug images were collected in phakic eyes.<sup>31,32</sup>

A 50-mHz ultrasound biomicroscopy (UBM) instrument (Humphrey model 840; Carl Zeiss Meditec, Dublin, CA) was used to image the lens, zonule and ciliary body configuration of the eye at rest.<sup>28,33</sup> In addition to the 34 iridectomized eyes, five noniridectomized rhesus monkey

eyes (6–8 years old) were imaged by UBM to determine the effect of the iris on the CLS.

### Definitions

The maximal stimulus is the level of E-W stimulation necessary to induce maximum accommodation. The supramaximal stimulus is a level of E-W stimulus current  $26.2\% \pm 3.9\%$  (or  $\sim 0.10$ – $0.20$  mA) above maximal stimulation.

### Statistical Analysis

Simple linear regression (i.e., CLS versus age; CLS versus accommodation) and multiple regression analysis (i.e., accommodation versus age and CLS) were undertaken in all monkeys. The multiple regression analysis adjusts for the relatedness between two observations (i.e., instances in which there were two eyes from the same monkey) and has no associated correlation coefficient.

## RESULTS

### Average CLS

**Young Eye.** In the nonaccommodated young eye (ages, 5.8–9.5 years;  $n = 7$ ), the CLS was similar in the nasal ( $0.59 \pm 0.04$  mm) and temporal ( $0.55 \pm 0.03$  mm) quadrants (Figs. 1A, 1B; Table 1). With accommodation, the CLS diminished only by 0.09 mm (nasal,  $P < 0.01$ ) and 0.11 mm (temporal,  $P < 0.001$ ), even during supramaximal stimulation (Figs. 1E, 1F; Table 1). In six of the seven young eyes, the nasal and/or temporal zonular fibers began to relax or bend at the supramaximal stimulus level.

**Older Eye.** In the nonaccommodated older eye (ages, 17–26 years;  $n = 18$ ), the CLS averaged  $0.42 \pm 0.03$  mm in the nasal and  $0.29 \pm 0.03$  mm in the temporal quadrant (Table 1), significantly less than in the young eye by 0.17 mm (nasal,  $P < 0.02$ ) and 0.26 mm (temporal,  $P < 0.0001$ ). The nonaccommodated temporal CLS was significantly less than the nasal CLS (Figs. 1C, 1D) by  $0.13 \pm 0.02$  mm ( $P < 0.001$ ). The CLS diminished more during maximal stimulation in the older eye ( $0.11 \pm 0.01$  mm nasal;  $0.13 \pm 0.02$  mm temporal) than in the young eye ( $0.07 \pm 0.02$  mm nasal;  $0.09 \pm 0.01$  mm temporal; Table 1), and the difference was greater still with supramaximal stimulation (older eye:  $0.18 \pm 0.02$  mm nasal,  $0.17 \pm 0.02$  mm temporal; young eye:  $0.09 \pm 0.02$  mm nasal,  $0.11 \pm 0.01$  mm temporal). This was due to diminished centripetal lens accommodative movement with age and dramatically increased CP centripetal movement at the supramaximal (vs. maximal) stimulus in the older eyes.<sup>28</sup> At times, the temporal

TABLE 1. The Average CLS and the Mean Differences

	Circumlental Space (mm)						CLS Mean Difference (mm)			
	Unaccommodated		Maximal		Supramaximal		Unaccommodated Minus Maximal		Unaccommodated Minus Supramaximal	
	Nasal	Temporal	Nasal	Temporal	Nasal	Temporal	Nasal	Temporal	Nasal	Temporal
Young										
Mean	0.59	0.55	0.52	0.46	0.50	0.44	0.07	0.09	0.09	0.11
SEM	0.04	0.03	0.05	0.04	0.05	0.05	0.02	0.01	0.02	0.02
P	na	na	na	na	na	na	<0.01	<0.0001	<0.01	<0.0001
Older										
Mean	0.42	0.29	0.31	0.16	0.24	0.12	0.11	0.13	0.18	0.17
SEM	0.03	0.03	0.02	0.03	0.02	0.03	0.01	0.02	0.02	0.02
P	na	na	na	na	na	na	<0.0001	<0.0001	<0.0001	<0.0001
Mean CLS Young minus Mean CLS Older										
Difference	0.17	0.26	0.21	0.30	0.26	0.32	0.04	0.04	0.09	0.06
P	<0.02	<0.0001	<0.01	<0.0001	<0.02	<0.0001	<0.14	<0.05	<0.01	<0.05

Data show the mean ± SEM CLS in the young (6-9.5 y; n = 7) and older (17-24 y; n = 18) monkey eyes and the difference between the means. The probabilities are for the difference between the means by the two-tailed, two-sample t-test. Also shown are the mean differences of resting CLS minus accommodated CLS. Probabilities are for the mean difference by the two-tailed, paired t-test.

CPs were seen to bend as they came in contact with the lens during accommodation in the older eye (Fig. 1H).

**Lens Equator and Anterior Zonula**

In the nonaccommodated state, the zonular fibers, as visualized goniovideographically, appeared to be taut in both eyes in both the nasal and temporal quadrants of all 24 monkeys, regardless of age (Figs. 1B; 2B; 3A, 3B; Movies 1, 2, available online at <http://www.iovs.org/cgi/content/full/47/3/1087/DC1>).

**Young Eye.** At the supramaximal stimulus level, zonular fibers began to relax or bend in five of seven eyes in both quadrants; and in one of seven eyes, the zonular fibers began to relax or bend in the temporal but not the nasal quadrant. In one eye, the zonular fibers did not bend in either quadrant.

**Older Eye.** During supramaximal stimulation, in older eyes in which the zonular fibers were clearly visualized in the goniovideography images, the temporal and nasal zonular fi-

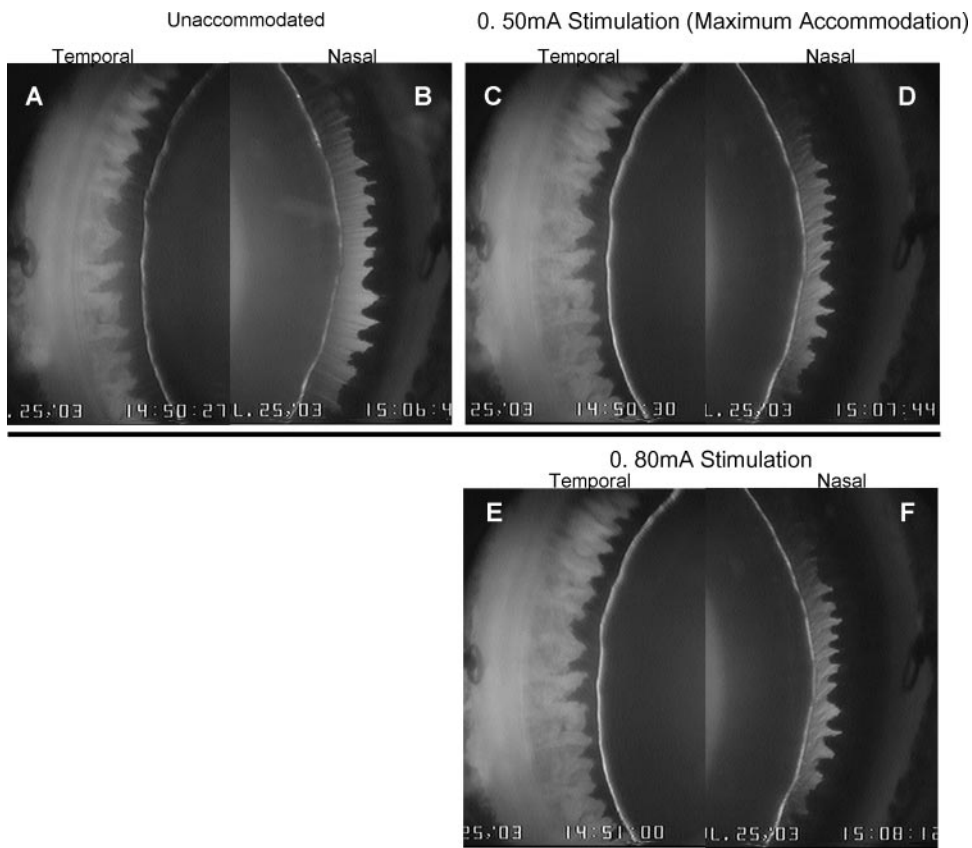
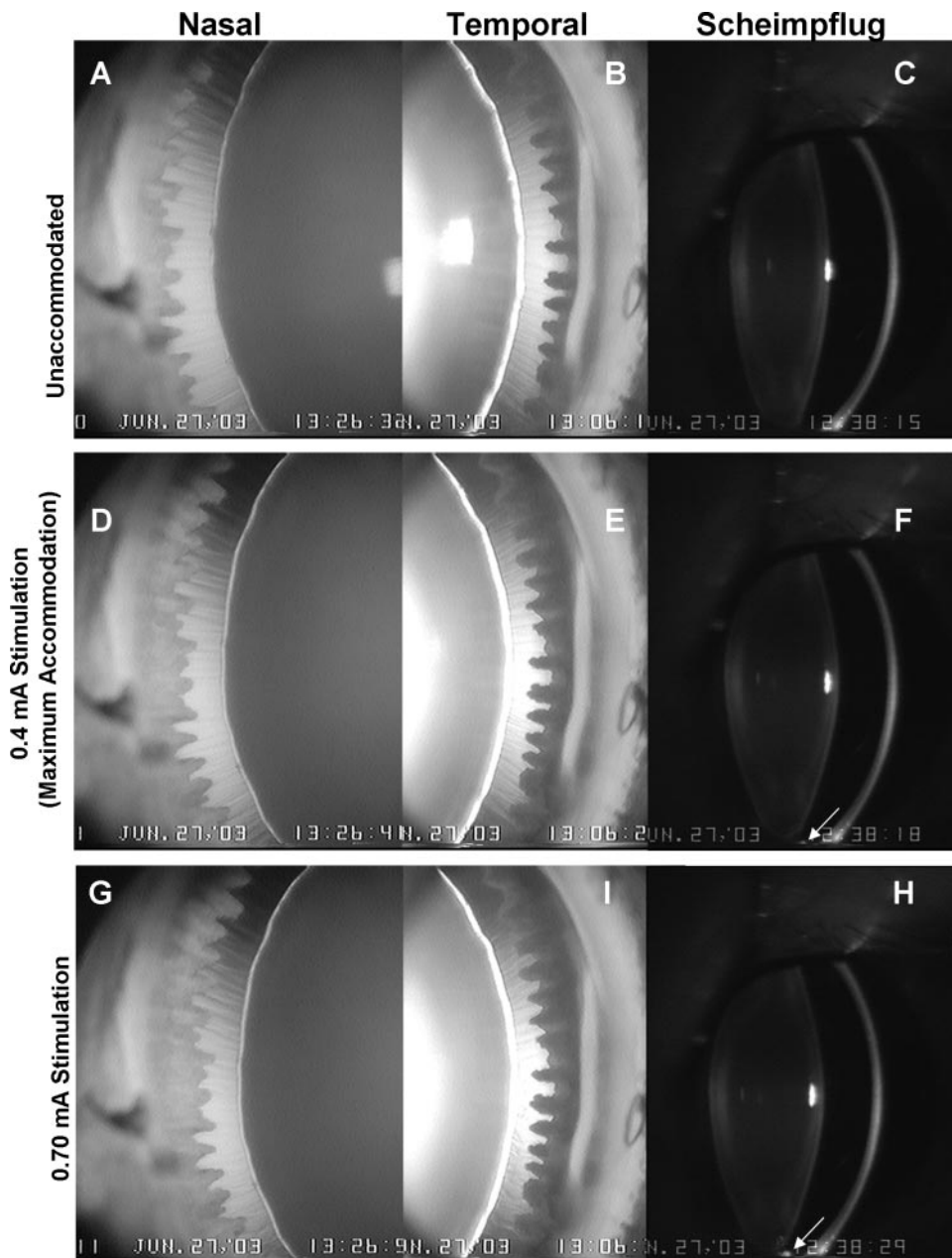


FIGURE 2. Goniovideography images showing the nasal and temporal quadrants of a 16.5-year-old rhesus monkey eye in the nonaccommodated state (A, B) and during 0.05 mA (maximal; C, D) and 0.80 mA (E, F) of central stimulation. The numbers represent the stimulus current in milliamperes (mA). The eye accommodated to a maximum of 9.25 D. The lens moved downward within the eye during 0.8 mA stimulation (see Movie 1, <http://www.iovs.org/cgi/content/full/47/3/1087/DC1>). Note that the CLS in both quadrants in the nonaccommodated state is similar superiorly and inferiorly. In the accommodated state the CLS is smaller inferiorly than superiorly (E, F). Also note that the zonular fibers in the accommodated state are oriented in a downward direction, more clearly visualized in the nasal quadrant (D, F).





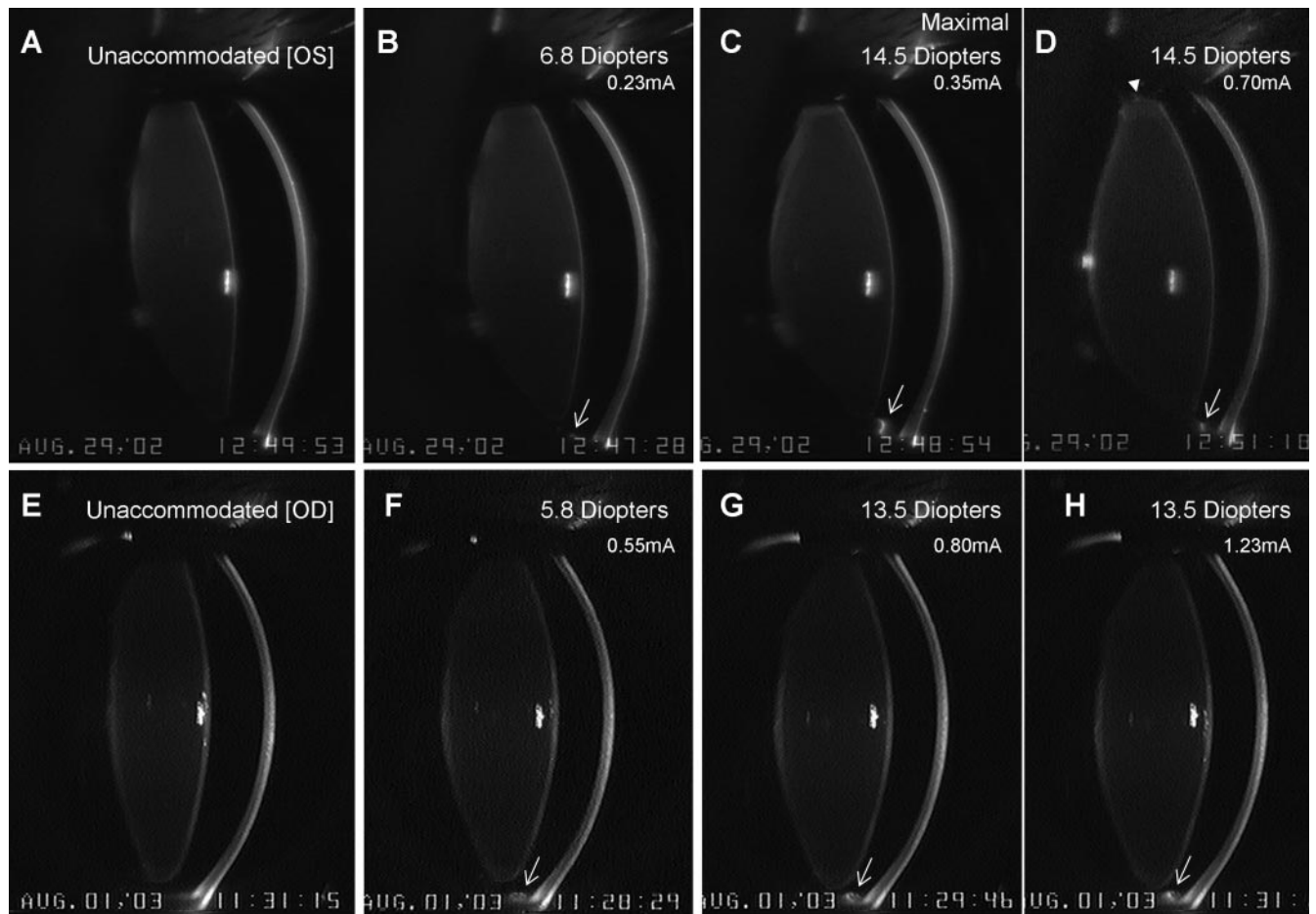
**FIGURE 3.** Goniovideography images showing the nasal and temporal quadrants of a 14-year-old rhesus monkey eye in the nonaccommodated state (**A**, **B**) and during maximal (**D**, **E**) and 0.70 mA (**G**, **I**) stimulation. The numbers represent the stimulus current in milliamperes (mA). The zonular fibers appeared taut when the eye was nonaccommodated (**A**, **B**). The lens did not move downward pronouncedly within the eye during accommodation. The CLS in both quadrants in the nonaccommodated state was similar superiorly and inferiorly and remained fairly uniform during maximum accommodation. During supramaximal stimulation, the zonular fibers in the accommodated state were more relaxed inferiorly than superiorly but were not oriented predominantly in a downward direction, as in Figure 2F (Movie 1, <http://www.iovs.org/cgi/content/full/47/3/1087/DC1>). Scheimpflug images show the anterior segment in the nonaccommodated (**C**) state and during maximal (**F**) and 0.70-mA (**H**) stimulation. The inferior CPs (*arrow*) came into view during maximal stimulation (**F**) and touched the inferior lens during the 0.70-mA stimulation (**H**).

bers began to relax or bend in 9 of 9 and 9 of 10 eyes, respectively (Fig. 2). Zonular relaxation and bending was observed, but less consistently, in these eyes at maximal (as opposed to supramaximal) stimulus currents. The zonular fibers were not readily visualized in six other older monkey eyes because of the illumination level required.

The lens fell with gravity in six eyes of four rhesus monkeys (ages, 6, 14, 16.5, and 26 years) after pronounced zonular relaxation was achieved (Figs. 2, Movies 1, 2). The determination of whether the lens fell with gravity or not during stimulation was based on examination of the goniovideography recordings, using both qualitative assessment of the orientation of the zonular fibers (Fig. 2, Movie 2) and quantitative measurements of specific points on the lens (Fig. 2, Movies 1, 2). In two eyes (age, 26 years), the lens fell with gravity at the maximal stimulus level. In two other eyes (ages, 14 and 16.5 years), the lens did not fall until a supramaximal stimulus was applied; in one case (age, 6 years), a much higher stimulus was required ( $\sim 0.35$  mA above the maximal stimulus). In six other

eyes, the lens did not fall with gravity (Figs. 1E, 1F, 3). In one of these eyes, Scheimpflug images showed inferior CPs contacting the inferior lens equator (Fig. 3). In the remaining 15 eyes, an unequivocal determination of whether the lens fell could not be made. Eight of these 15 were older eyes in which the CPs touched the lens during accommodation (Fig. S1, <http://www.iovs.org/cgi/content/full/47/3/1087/DC1>). In no case did the lens position ever move upward in the eye at any stimulus level compared with the resting state.

Typically, Scheimpflug imaging does not allow visualization of the superior/inferior CPs or lens equator due to the presence of the eyelids. However, in five eyes of four monkeys (ages, 6 [2 eyes] 13, 14, and 16 years), it was possible to observe the inferior CP or lens equator. In all five of these eyes, the Scheimpflug images showed that the inferior CPs came in close proximity to or touched the lens equator during accommodation (Figs. 3F, 3H, 4C, 4D, 4G, 4H). In one of the 6-year-old eyes (the only eye in which the superior lens equator was



**FIGURE 4.** Scheimpflug images at rest and during increasing stimulus amplitudes in the left (A–D) and right (E–H) eyes of a 5.8-year-old monkey. Numbers in the *top* and *lower portion* of the panels represent diopters of accommodation and stimulus current in milliamperes (mA), respectively. Maximum accommodation was 14.5 diopters in the left eye and 13.5 diopters in the right eye. The top of the lens (*arrowhead*) of the left eye was seen during the 0.70 mA stimulus (D) but not at rest, indicating that the superior lens equator moved away from the sclera during accommodation. In both eyes, the inferior ciliary processes (*arrows*) came in contact with the lens.

observed), Scheimpflug images showed that the superior lens equator moved away from the sclera (Figs. 4A–D) during accommodation; the inferior lens equator was visible at rest (Fig. 4A) but not at maximum accommodation (Fig. 4C). The inferior lens equator of the right eye moved away from the sclera at half maximum accommodation, but seemed to move back toward the inferior sclera during maximal and supramaximal stimulation (see the Discussion section).

### Prismatic Distortion, Residual Eye Movements, and Variance

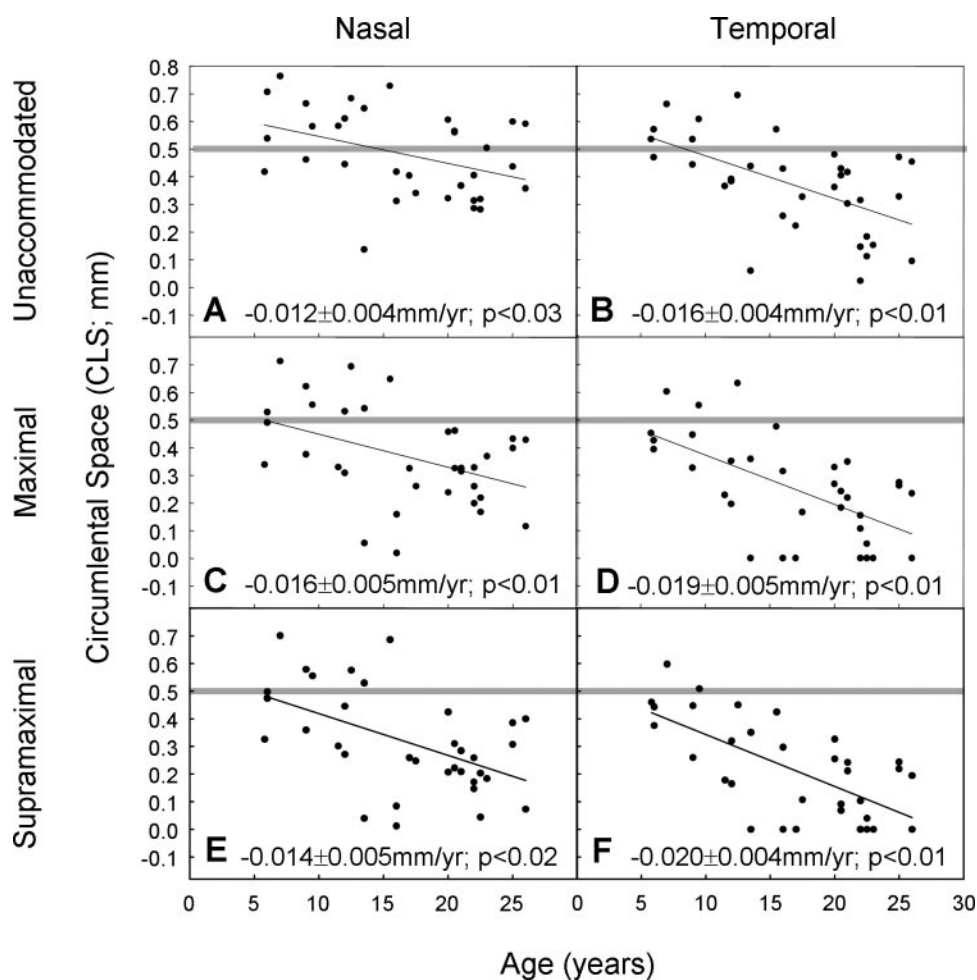
The mean  $\pm$  SEM convergence eye movement during supramaximal stimulation was  $0.17 \pm 0.03$  mm in 27 eyes.<sup>28</sup>

Artificial convergence eye movements  $\approx 0.17$  mm induced by pulling on extraocular muscle sutures (without accommodation) were analyzed, and averaged in the nasal quadrant ( $0.19 \pm 0.01$  mm;  $n = 17$  image frames) and in the temporal quadrant ( $0.17 \pm 0.01$  mm;  $n = 24$  image frames).<sup>28</sup> The CLS decreased during convergent eye movement by  $0.01 \pm 0.01$  mm ( $n = 8$ ) in the nasal quadrant and increased by  $0.003 \pm 0.004$  mm ( $n = 8$ ) in the temporal quadrant, neither being significantly different from 0.0. Thus, variability was introduced by convergence eye movement, but of a magnitude insufficient to impact the overall results or conclusions.

Imaging through the gonioscopy lens introduced some prismatic distortion<sup>28</sup> but any consequent variability due to variability in placement of the lens on the eye was random, small, and similar in all monkeys, and not enough to affect the overall results or conclusions. Evidence for this is that the SEM was small (Table 1) in both the young and old eyes and that the nasal and temporal CLS of the young eye were not significantly different from each other. Therefore, although nonsystematic variability may be introduced by slight prismatic distortion or eye movement, the data are reliable and the comparisons between young and older are valid. In addition, measurements analogous to the gonioscopically measured CLS width were taken using UBM.

### Ultrasound Biomicroscopy

UBM also allowed visualization and measurement of the CLS (CLS-UBM), analogous to that measured by goniovideography, in five young noniridectomized and five young iridectomized monkey eyes. The presence or absence of the iris did not affect the width of the CLS-UBM significantly in either the nasal (noniridectomized  $0.58 \pm 0.02$  mm versus iridectomized  $0.59 \pm 0.02$  mm) or the temporal (noniridectomized  $0.50 \pm 0.02$  mm versus iridectomized  $0.53 \pm 0.02$  mm) quadrants. Further, the CLS-UBM and gonioscopically measured CLS were



**FIGURE 5.** CLS versus age in the nonaccommodated and maximally accommodated states and during supramaximal stimulation to induce accommodation in 34 eyes of 24 monkeys ranging in age from 5.8 to 26 years. The supramaximal stimulus was  $\sim 0.1$  to  $0.2$  mA above the maximal stimulus. *Solid line*: least-squares regression of CLS versus age (adjusted for relatedness where two eyes are from the same monkey). The CLS significantly decreased with age at rest and in the accommodated state. *Shaded line*: a slope of 0.0. Slopes are coefficients  $\pm$  SE; *P*, probability that the slope = 0.0.

not significantly different (see the nonaccommodated young monkey eye; Table 1), validating the technique used to calibrate the goniovideography images. All references to CLS width outside the current section are based on the goniovideography images.

### Regression Analysis: Goniovideography of Iridectomized Eyes

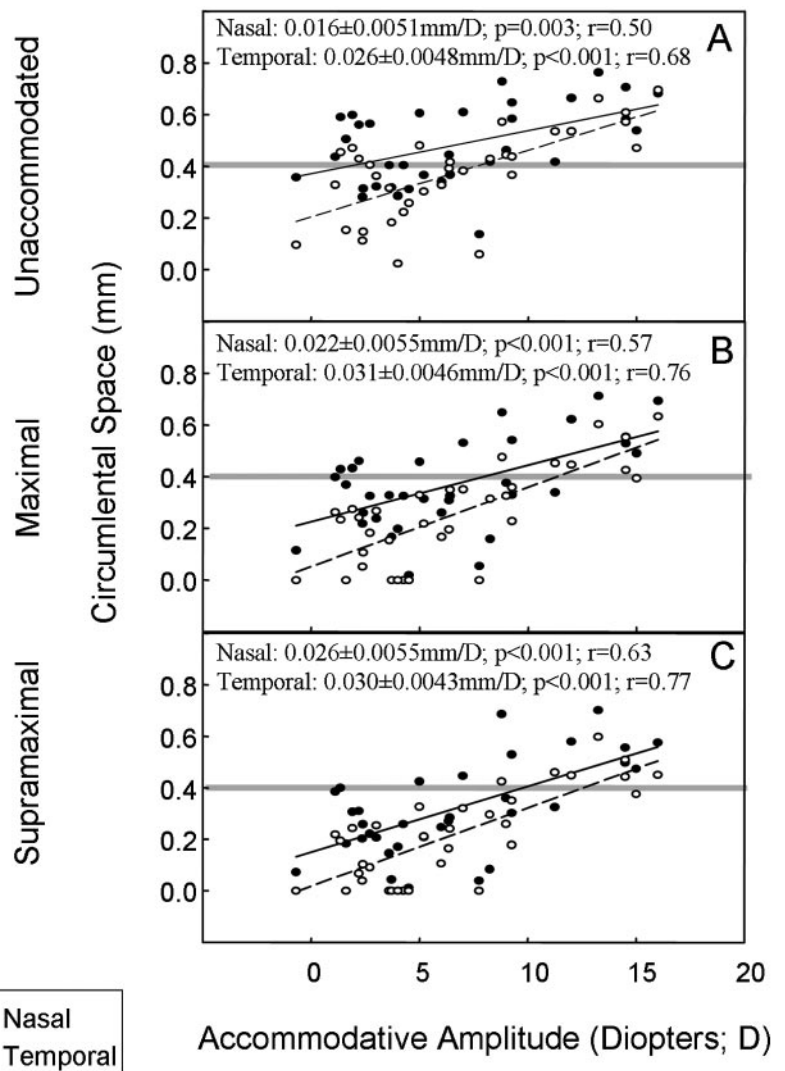
There was no correlation between the width of the CLS in the resting eye and the elapsed time between iridectomy and the imaging session in either quadrant ( $n = 30$  eyes). The same was true at the maximal and supramaximal stimulus currents (data not shown).

**Circumferential Space (CLS; 34 eyes, 24 monkeys).** The nonaccommodated CLS decreased significantly with age in both the nasal ( $-0.012 \pm 0.004$  mm/y;  $P < 0.03$ ) and temporal ( $-0.016 \pm 0.004$  mm/y;  $P < 0.01$ ) quadrants and tended to do so at a slightly faster rate in the temporal quadrant (Figs. 5A, 5B). The nonaccommodated nasal and temporal CLS was significantly correlated with the accommodative amplitude of each monkey (Fig. 6A); the greater the CLS the greater the accommodative amplitude. Similar results were seen in the maximally (Fig. 6B) and supramaximally (Fig. 6C) stimulated states. Because CLS and accommodative amplitude covaried with age, a multiple regression analysis that models accommodation as a linear function of age and nonaccommodated CLS was undertaken. A mixed model (using SAS Proc Mixed; SAS, Cary, NC) that recognizes that measurements taken from two eyes of the same monkey may correlate, was used, with the

thought that the decrease in nonaccommodated CLS with age might explain the decrease in accommodative amplitude over and above what age could do alone. The multiple regression coefficient of nonaccommodated temporal (but not nasal) CLS was significantly different from 0.0 ( $P < 0.03$ ), indicating that age and nonaccommodated temporal CLS together are better predictors of accommodative amplitude than is age alone (Table S1, <http://www.iovs.org/cgi/content/full/47/3/1087/DC1>). A similar multiple regression analysis using CLS measured during maximal stimulation showed significance in both quadrants, indicating that age and CLS during maximal stimulation together are better predictors of accommodative amplitude than is age alone (Table S1). Similar results were seen at the supramaximal stimulus level. The difference between the CLS in the nonaccommodated state and during maximal and supramaximal stimulation did not decline significantly with age in either quadrant. However, in the nasal quadrant, the supramaximally accommodated CLS minus the maximally accommodated CLS tended to decline with age ( $P = 0.053$ ). The results of the multiple regression analysis and the corresponding F-statistic show that age (which typically has much larger F-statistics than CLS) explains nearly all of the variation in accommodative amplitude. However, as stated earlier, CLS was important in predicting accommodative amplitude over and above what age could do alone.

The model diagnostics were performed and, based on the residual plots, the proposed models are not unduly affected by variance fluctuations.<sup>28</sup> Thus, these models would be reasonable for the underlying data. Because these regression models





**FIGURE 6.** Data represent the mean CLS in nonaccommodated (A), maximally accommodated (B), and supramaximally stimulated (C) eyes, plotted versus maximum accommodation in 34 eyes of 24 rhesus monkeys ranging in age from 6 to 26 years. Negative accommodation occurred in one rhesus monkey. In this one monkey eye, the CPs touched the periphery of the anterior lens surface, and the anterior chamber deepened during accommodation (data not shown), but the CP and lens equator moved away from the sclera, as is normal.

take the relatedness of the eyes into account, it is not possible to divide the total model variance into components based on individual independent variables. However, the more significant the probability for the individual independent variable, the more it would contribute to the explanation of the variance.

**DISCUSSION**

Prior gonioscopy studies of accommodation in the monkey<sup>31</sup> used a viewing angle set to 35° from the A-P axis of the eye. In the present study, the viewing angle was along the A-P axis of the eye. Viewing the CLS across the anterior face of the lens at a 35° viewing angle could give the impression of closure of the CLS as the anterior lens surface moves forward with accommodation in the young eye. A consistent observation angle (0° from the A-P axis) for all eyes is important for quantitative comparisons. A supramaximal dose of carbachol<sup>30,34</sup> also results in closure of the circumlental space in the young monkey (Croft MA, Kaufman PL, unpublished observation, 2004). This did not happen with centrally stimulated accommodation in the young monkey eye. Closure of the circumlental space was observed in the older eye at the supramaximal stimulus, more so in the temporal quadrant than in the nasal quadrant.

Reporting only the results of the maximal stimulus level would not have identified the fact that the CP can move more than required to induce maximum accommodation. Therefore, the results of both the maximal and supramaximal stimulus levels are reported. The CLS diminished by 0.09 to 0.11 mm during supramaximal stimulation in the young eye but diminished to a greater extent during accommodation in the older eye, due to the loss of lens centripetal accommodative movement with age, as shown from an analysis of the same goniovideography images presented elsewhere.<sup>28</sup> Age and resting temporal CLS (but not nasal), together are better predictors of accommodative amplitude than age alone, suggesting that there is some presbyopia-related process that impacts the temporal CLS more dramatically than the nasal CLS. In vivo MRI data from the nonaccommodated human eye demonstrated that, with age, the ciliary ring diameter decreases, lens equatorial diameter does not change systematically, whereas lens A-P thickness increases.<sup>21</sup> In excised partially dissected human eyes<sup>9</sup> it was reported that there is an anterior zonular shift with increasing age, but “[t]he loss of zonular tension due to a decreased circumlental space does not occur since the insertion-ciliary body distance remains constant.” The zonular insertion point onto the capsule is fixed for life, but with age the capsule stretches (to compensate for the increased lens thick-

ness), possibly pulling the zonule-capsule insertion point farther onto the front surface of the lens.

The decrease in resting CLS with age is most likely a product of diminished ciliary ring diameter<sup>21,24</sup> and increased A-P thickness<sup>21</sup> and not due to increased lens equatorial diameter.<sup>15</sup> To achieve zonular relaxation with accommodation in the young eye, the CLS need only be diminished by ~0.09 (nasal) and 0.11 (temporal) mm. Also, the CLS in the older eye was significantly narrower than that in the young eye by 0.17 (nasal) and 0.26 (temporal) mm. If the nonaccommodated CLS diminished with age, either due to diminished ciliary ring diameter alone or increased lens equatorial diameter alone (without anterior zonular shift), a relaxed zonula would have been observed in the nonaccommodated older eye. Instead, the zonular fibers clearly appeared taut in the nonaccommodated older eye.

Previous reports have postulated that an age-related overall steepening of lens curvature occurs, to counteract the concomitant reduction in the gradient refractive index of the lens<sup>35</sup> and that the age-related remodeling of the ciliary muscle may be important to maintain emmetropia.<sup>24</sup> The geometric theory suggests that the geometry of the lens/zonular fibers and thereby the direction of the zonular force changes with age. The ciliary ring diameter diminishes with age, zonular fiber length remains constant, the lens thickens, but the lens equatorial diameter does not change. An increase in A-P lens thickness, which in turn places increased tension on the anterior zonular fibers, could pull centripetally on the ciliary ring causing, over a long period, the ciliary ring diameter to diminish. In this scenario, the zonular fibers would remain taut, possibly becoming increasingly taut with increasing age. Surgical manipulations of the eye show that the capsule supplies centripetal force to aid centripetal accommodative velocity and amplitude of movement of the ciliary body (Croft MA, et al. *IOVS* 1999;40:ARVO Abstract 1918). The fact that the CLS is narrower in the temporal versus the nasal quadrant of the older resting eye suggests that there may be more zonular tension pulling the lens toward the temporal quadrant in the resting older eye.

In one 6-year-old monkey eye (Scheimpflug; Fig. 4) the inferior lens equator moved away from the inferior sclera at half maximal accommodation but seemed to move back toward it during maximal and supramaximal stimulation. During the half-maximum accommodative response, sufficient zonular tension is still present, but as the zonular fibers relax at the maximal and supramaximal stimulus, the lens falls with gravity.

That the lens falls with gravity is in opposition to the Schachar theory of accommodation. Schachar et al.<sup>15</sup> posited that the lens equator moves toward, rather than away from, the sclera during accommodation due to increased equatorial zonular tension and that presbyopia occurs because the lens increases in diameter with increasing age.<sup>15</sup> If Schachar were correct (i.e., equatorial zonular tension increases during accommodation), the lens should be held in position during accommodation and should not move inferiorly due to gravitational pull. The lens fall with gravity that we report herein is documented by evidence of both positional change and zonular reorientation.

Inferior CPs that contact the lens equator during accommodation may inhibit a pronounced downward movement of the lens, and this may be why the sagging of the lens under the influence of gravity is not seen in all eyes. The movement of the inferior lens equator toward the sclera during accommodation (before coming in contact with the inferior CPs) cannot be interpreted as corroboration of the Schachar theory of accommodation,<sup>15</sup> because the zonular fibers relax with accommodation, and the lens equator

moves away from the sclera in the nasal, temporal, and superior (Fig. 4D) quadrants.

Characterization of any ocular parameters related to the accommodative apparatus that change with age may help to model the system for hypothesis testing. The CLS may be an indicator of a presbyopia-related process or processes that affect accommodation, such as the age-related loss of lens equator accommodative movement, diminished ciliary ring diameter, and lens A-P thickening. However, these results do not prove that the width of the CLS in and of itself has a causal relationship to accommodative amplitude, or that changes in the CLS play a pathophysiological role in presbyopia.

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