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Accommodative Changes in Lens Diameter in Rhesus Monkeys

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Abstract

Purpose—Some debate surrounds the accommodative mechanism in primates, particularly whether the lens equatorial diameter increases or decreases during accommodation. This study has been undertaken to measure the relationship between changes in lens diameter and refraction during accommodation in rhesus monkeys.

Methods—Photorefractive was used to measure accommodation, and goniovideography was used to measure accommodative changes in lens diameter in the iridectomized eyes of two rhesus monkeys. Accommodation was stimulated through the full amplitude available to each eye by stimulation of the Edinger-Westphal nucleus of the brain. Dynamic measurement of refractive changes followed by dynamic measurements of changes in lens diameter for the same stimulus current amplitudes allow the relationship between refraction and lens diameter to be determined.

Results—Lens diameter decreased relatively linearly during accommodation by 0.055 mm/diopter (D), resulting in an overall decrease in lens diameter of approximately 7% of the unaccommodated lens diameter for approximately 12 D of accommodation.

Conclusions—The rhesus monkey lens diameter decreases systematically with the refractive change during accommodation in accordance with the Helmholtz accommodative mechanism and in contrast to the accommodative mechanism originally proposed by Tscherning.

It is well established that accommodation is a dioptric change in power of the eye to allow the eye to focus at near distances. Several aspects regarding how this optical change occurs are undisputed. The increase in optical power of the eye is attributed to an increase in power of the lens. The optical change in the lens occurs as a consequence of ciliary muscle contraction and results in an increase in the central lens surface curvatures and thickness.

It is less well established exactly how the accommodative increase in lens thickness and surface curvatures occur. The accommodative mechanism proposed by Helmholtz¹ suggests that in the unaccommodated state, resting tension on zonular fibers extends from the ciliary body to the capsule around the lens equator. This resting zonular tension and the capsular molding forces hold the lens in a relatively flattened and unaccommodated state. With a contraction of the ciliary muscle, the apex of the ciliary body moves toward the lens equator to release tension on the zonular fibers. Gullstrand² and Fincham³ suggest that when zonular tension is released, the elasticity of the capsule molds the lens into an accommodated form. Fincham³ suggests that the capsular molding forces cause a decrease in the lens equatorial diameter, an increase in lens axial thickness, and an increase in the lens anterior and posterior surface curvatures.

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Many studies address the accommodative changes in the ciliary body, lens thickness, and lens surface curvatures. Few of the basic changes that occur in these aspects of the accommodative mechanism are disputed. Because the lens periphery and the equator are generally hidden behind the iris and are relatively inaccessible, it has been more difficult to observe accommodative changes at the lens equator or to study accommodative changes in lens diameter. However, several studies have considered these.

Helmholtz¹ infers that because lens axial thickness increases and the lens volume cannot change, the lens equatorial diameter must decrease during accommodation. Grossmann observes in a 26-year-old patient with congenital aniridia that a lens diameter of 11.25 mm in the untreated eye increased to 12.25 mm when subjected to cycloplegia with homatropine and decreased to 10.25 mm with eserine stimulated accommodation.^{4,5} This is an 8.8% decrease in lens diameter from unaccommodated to accommodated, as measured through the cornea.

Fincham³ observed accommodative changes in lens diameter in a 22-year-old patient who sustained traumatic aniridia. Retroilluminated photographs were taken through the cornea of the unaccommodated and accommodated aniridic eye while the contralateral eye viewed far and near (12.5 cm) fixation targets. Superimposed images consistently showed a decrease in lens diameter of 0.45 mm from 10.2 mm to 9.75 mm with accommodation. The upper edge of the lens was covered by the eyelid, but the remaining two thirds of the lens diameter was clearly visible and showed a concentric decrease with accommodation.

Wilson⁶ used retroillumination infrared videophotography to observe accommodative changes in the lens diameter during accommodation in a 27-year-old patient with ocular albinism. The lens diameter was measured at rest, during voluntary accommodation, and during pharmacologic cycloplegia and showed a 7.44% decrease in lens diameter with accommodation and an increase in lens diameter during cycloplegia. No indication is provided regarding the extent of the accommodative response achieved. Magnetic resonance imaging was used to measure lens diameters in 25 patients and showed that lens diameter decreased by 604 μm (6.57%) with accommodation to an 8 D stimulus in the eight youngest subjects (age range, 22–29.2 years; mean age, 25.2 years).⁷

Rhesus (*Macaca mulatta*) and cynomolgus (*Macaca fascicularis*) monkeys have been widely used to study the primate accommodative mechanism and the progression of presbyopia. The anatomy of the rhesus monkey accommodative structures and the accommodative mechanism are similar to that of humans.^{8–12} Despite quantitative differences that exist in the accommodation, the eyes and ocular age changes between monkeys and humans (including eye size and accommodative amplitude, for example), qualitatively the two species are remarkably similar. Rhesus monkeys are widely regarded as an excellent animal model for studies of human accommodation and presbyopia,^{13–17} even among investigators proposing alternative theories of accommodation and presbyopia.^{18,19}

Studies in rhesus monkeys that have undergone iridectomy, in which accommodation was stimulated through an electrode in the Edinger-Westphal (EW) nucleus of the brain, have used slit lamp goniovideography to observe and quantify accommodative movements of the lens equator.^{11,20} In monkeys in which only one side of the eye was imaged, the lens equator moved away from the sclera during accommodation. When the entire lens diameter was imaged, a decrease in lens diameter with both EW-stimulated accommodation and pharmacologically stimulated accommodation was observed.^{21,22} The lens equator was also observed to move away from the sclera with ultrasound biomicroscopy (UBM) during EW-stimulated accommodation in monkeys.²¹

In opposition to the Helmholtz theory, Tscherning²³ proposed that accommodation occurs through an increase in zonular tension at the lens equator with ciliary muscle contraction. Tscherning²³ suggested this could be caused by a vitreous force against the posterior lens surface or directly through a contraction of the ciliary muscle to flatten the peripheral anterior lens surface and to increase the curvature of the central anterior lens surface. Tscherning²³ did not directly address what happens to the lens equatorial diameter during accommodation. This theory of accommodation has received renewed attention with the suggestion that the lens equator moves toward the sclera and that, therefore, the lens diameter increases during accommodation.^{18,24,25} These studies used UBM imaging of the lens equator during pharmacologically stimulated accommodation in monkeys and humans and report that the lens equator moves toward the sclera (monkeys, 20–60 μm ; humans, 40–66 μm) for the full range of accommodation (monkeys, 9.5–35.5 D; humans, 5.5–11 D). Tabled data show this to be a movement of 1.9 $\mu\text{m}/\text{D}$ in monkeys and 6.8 $\mu\text{m}/\text{D}$ in humans, corresponding to an average calculated increase in lens diameter of 3.8 $\mu\text{m}/\text{D}$ in monkeys and 13.7 $\mu\text{m}/\text{D}$ in humans.^{18,25}

Although the general consensus is that the lens diameter decreases during accommodation, there is greater uncertainty as to exactly how the lens undergoes these accommodative changes in shape. Certainly, the lens optical power must increase with accommodation, and this occurs through an increase in lens surface curvatures, but the optical changes occur as a result of physical changes in lens shape. Understanding the relationships between the accommodative optical and physical changes will provide a clearer picture of the accommodative mechanism and of the relationships between biophysical and biomechanical changes in the lens that must occur to produce the lens optical changes. This has implications not only for understanding how the natural lens accommodates and how aging affects the accommodative performance of the lens but also for understanding whether accommodation can be restored in patients with presbyopia through scleral expansion surgical techniques or with accommodative intraocular lenses. The Tscherning theory of accommodation serves as the basis on which scleral expansion restoration of accommodation is founded.^{18,26–28} Many new kinds of accommodative intraocular lenses (IOLs) under development rely on forces or movements generated by the accommodative structures.^{29–32} Knowledge of the forces, the directions, and the extents of movement may be important for optimizing performance of this new generation of IOLs. Direct measurement of the forces in the living eye may be beyond current technical capabilities, but measurements relating the physical and optical changes are certainly possible and long overdue. Much remains to be learned about presbyopia. Understanding how the young eye accommodates and comparing it with older eyes with lower accommodative amplitudes may provide a clearer understanding of presbyopia.

The aims of this study were to document, in rhesus monkeys, how the lens diameter changes during accommodation and to relate the physical changes in lens diameter to the accommodative optical changes. The study was performed in anesthetized, iridectomized rhesus monkeys in which accommodation was stimulated through an electrode implanted in the EW nucleus of the brain. This allows for rigorous control of the amplitude and duration of the accommodative response^{33,34} and the recording conditions to correlate changes in lens diameter with refractive changes.

Methods

All experiments conformed to the ARVO Statement for the Use of Animals in Ophthalmic and Vision Research and were conducted in accordance with institutionally approved animal protocols. Five experiments were performed, one for each eye of rhesus monkeys (*Macaca mulatta*) 111 and 38, aged 5 and 6 years, respectively, and one repeated on the left eye of

monkey 111. Experiments were performed on only one eye during each experimental session. The monkeys had previously undergone bilateral iridectomy and implantation of a stimulating electrode into the EW nucleus of the brain.^{21,33–37} Monkeys were initially anesthetized with intramuscular 15 mg/kg ketamine and 0.5 mg/kg acepromazine (Phoenix Pharmaceutical, St. Joseph, MO), and the experiments were performed under intravenous propofol (Propofol; Abbott Laboratories, North Chicago, IL) anesthesia with an initial bolus of 1.5 mg/kg and a continuous infusion at a rate of 0.5 mg/kg/min. Throughout the experiment, pulse rate and PO₂ were monitored, and each monkey was wrapped in a 37°C water-heated pad to maintain body temperature. The monkey lay prone on a table with its head in a head holder, upright and facing forward. The eyelid was held open with a speculum, and 4-0 silk sutures were tied beneath the medial and lateral rectus muscles with slight tension to reduce eye movements. A clear, plano contact lens (Metro Optics, Dallas, TX) was initially placed on the cornea for refraction measurements to prevent the cornea from drying and to maintain optical quality.

Static Accommodative Stimulus Response Functions

At the start of each experiment, a static EW-stimulated accommodative response function was recorded. A static coincidence refractometer (Hartinger; Zeiss, Jena, Germany) was used to measure the refraction of the eye at rest and for a range of approximately 10 increasing stimulus amplitudes, including supramaximal stimulus amplitudes, delivered to the EW nucleus. Supramaximal stimulus amplitudes were current amplitudes greater than those required to elicit the maximum response. Accommodation was stimulated with trains of square wave pulses, 0.6 ms in duration, at 72 Hz. Maximum current amplitudes were 700 μ A in both eyes of monkey 38 and 650 μ A in the left eye and 1.3 mA in the right eye of monkey 111. A range of stimulus amplitudes was delivered producing accommodative responses spanning the full accommodative range available to each eye, and three successive response amplitudes were measured with the static refractometer (Hartinger) for each stimulus amplitude.

Dynamic Recordings of Accommodative Responses

After recording the static accommodative stimulus response function, the same stimulus amplitudes were used to record refractive responses with dynamic video-based infrared photorefractometry and changes in lens diameter with gonioscopic slit lamp videography to videotape at 30 Hz. A text overlay was recorded on each frame of the videotape to indicate the stimulus status (on or off). For each stimulus amplitude, five 4-second stimulus trains were delivered, each with a 4-second interstimulus interval. Only the last three of the five recorded responses were analyzed for the far-to-near (accommodative) and the near-to-far (disaccommodative) phases of the responses.

Dynamic Infrared Photorefractometry

Infrared photorefractometry was recorded with a charge-coupled device videocamera with 20 infrared (IR) light-emitting diodes mounted in front of a knife-edge aperture on a 55-mm lens.^{33,38,39} Each frame of the recorded video was analyzed using a macro written for Optimas 6.5 image analysis software (MediaCybernetics, Inc., Silver Spring, MD). Two vertical lines in the central 40% of the iridectomized pupil diameter were drawn on either side of the corneal Purkinje image. Luminance profiles were extracted from each line, averaged, and fitted with linear regression lines (Figs. 1A, 1B). For each experiment, a unique calibration curve relating refractive state to the slope of the luminance profiles was generated using the static refraction measurements (Hartinger) and the photorefractometry luminance slope measurements for a range of stimulus amplitudes.³³ From these calibration curves, the photorefractometry slope values were subsequently converted to refraction in diopters (D).

Dynamic Videography of Changes in Lens Diameter

Immediately after photorefractive, the contact lens and the lid speculum were removed. A custom-designed polymethylmethacrylate gonioscopic lens (Glasser Monkey Lens; Ocular Instruments, Bellevue, WA) with a base curve to match the monkey corneal radius of curvature with a 1.5-cm center thickness and a plano face was used to image the crystalline lens diameter. The base of the gonioscopy lens was filled with methylcellulose, and the scleral lip of the gonioscopy lens was inserted beneath the monkey's eyelids with a muscle hook. The gonioscopy lens was clamped in front of the eye with holder.

A slit lamp (Zeiss, Oberkochen, Germany) with a black-and-white videocamera (Cohu, San Diego, CA) attached was then positioned in front of the monkey. The slit lamp was aligned with the optical axis of the eye and the gonioscopy lens. Slit lamp illumination was adjusted to a circle smaller than the monkey crystalline lens diameter and was adjusted slightly off axis so that the perimeter of the crystalline lens was clearly visible in the video image through the face of the gonioscopy lens (Figs. 1C, 1D). The video image was recorded to videotape at 30 Hz. The same stimulus parameters and amplitudes as those used for photorefractive were then delivered to the EW nucleus while the changes in crystalline lens diameter were recorded. Only the last three of five responses at each stimulus amplitude were analyzed. A macro written in Optimas 6.5 found 24 evenly spaced points around the monkey crystalline lens perimeter, from frame to frame of the videotape, off line. From these points, an average diameter and x and y coordinates of the lens center, in arbitrary Optimas units, were saved to a file from each video frame.

To convert these measurements to millimeters, an artificial anterior chamber was constructed. The end was cut off the tip of a 20-mL syringe. A rigid PMMA monkey contact lens was adhered to the open end of the syringe, and a vent hole was drilled through the syringe wall near the end of the syringe. The syringe was filled with saline, and a piece of graph paper was glued to the end of the rubber plunger. The plunger was depressed to within approximately 5 mm of the contact lens to create an artificial anterior chamber. The syringe was clamped in front of the slit lamp, and the gonioscopy lens was applied to the contact lens with methylcellulose as it was to the monkey eye. The graph paper on the end of the plunger was imaged through the gonioscopy lens with the slit lamp in the same way the monkey crystalline lens diameter was imaged. Images of the graph paper were captured for a range of artificial anterior chamber depths comparable to monkey anterior chamber depths. Artificial anterior chamber depths in the syringe (graph paper to contact lens) were then subsequently measured with an ultrasound biomicroscope (P40 UBM; Humphries, San Leandro, CA). Slit lamp gonioscopy image magnifications from this artificial eye were related to the UBM-measured artificial anterior chamber depths to obtain a calibration curve. At the end of each monkey experiment, the actual anterior chamber depth of each monkey eye was measured five times in succession with A-scan ultrasound (A-5500; Sonomed, Lake Success, NY), and the mean measured anterior chamber depth and calibration curve were used to convert the measured monkey crystalline lens diameter and the x , y center coordinates from Optimas units to millimeters.

Once the dynamic accommodative refractive and lens diameter responses were analyzed from the videotape for the same range of stimulus amplitudes, accommodative refractive and lens diameter data were plotted against each other in relation to the time of initiation of the stimulus. For this analysis, preaccommodation baseline was considered to be 20 video frames before the stimulus onset, accommodation proceeded from stimulus onset until maximum accommodative amplitude (refraction and diameter) was achieved, and disaccommodation started when the stimulus terminated and proceeded until no further change in refraction or diameter occurred.

Eye Movement Analysis

Despite the use of extraocular muscle sutures to minimize eye movements, micro-eye movements still occurred during and between stimulations. An analysis was undertaken to determine the extent to which eye movements might influence the crystalline lens diameter measurements. Measured lens diameters, during stimulation and in the unstimulated state when micro-eye movements occurred, were plotted against the extent of movement of the x,y center of the lens.

Results

The last three of the five stimulus trains analyzed showed highly reliable, repeatable responses for refraction and lens diameters. Figures 2A and 2B each show three raw traces of refraction and lens diameter for two stimulus amplitudes (250 and 650 μ A) in the left eye of monkey 111. The three individual responses are essentially identical and are superimposed. The full range of stimulus amplitudes applied yielded increasing response amplitudes covering the full range of accommodation (refraction and lens diameter) available to each eye (Figs. 2C, 2D). Several supramaximal stimulus amplitudes (550, 600, and 650 μ A) verified that the maximum response amplitude was achieved. Figures 2C and 2D show, for each stimulus amplitude, a single average trace from the three responses analyzed.

Lens diameter decreased systematically with refraction for responses of all amplitudes during accommodation (Figs. 3A–C) and increased systematically with refraction during disaccommodation (Figs. 3D–F). Because neither accommodation nor lens diameter can be considered the dependent variable, the data were fitted with orthogonal regressions. Orthogonal regressions fitted through the maximum amplitude accommodative responses from all eyes tested (together with the 95% confidence intervals) show that refraction changed by 18.16 D/mm decrease in lens diameter, or lens diameter decreased by 0.055 mm/D. During disaccommodation, refraction changed by 17.67 D/mm increase in lens diameter, or lens diameter increased by 0.057 mm/D. Orthogonal regression lines for each graph fall within the 95% confidence intervals of the other regression line, rendering them not significantly different from each other. Table 1 shows the accommodative amplitudes, resting lens diameters, accommodated lens diameters, and changes in lens diameter for each of the eyes. Average values are shown in the table for all eyes, though measurements were repeated twice on one eye. Lens diameter decreased by 7.04% of the unaccommodated lens diameter for maximum accommodation. Table 2 shows the A-scan data measured in the unaccommodated eye of each monkey.

Accommodative eye movements occurred during stimulation, and, on occasion, wandering eye movements occurred in the absence of stimulation. These movements were in various directions; generally, the x,y center of the lens moved by $<1000\ \mu$ m. Eye movements larger than this would result in the lens edge moving out of the video field of view (Fig. 1). Although stimulation of accommodation caused eye movements and systematic changes in lens diameter, wandering eye movements in various directions that occurred without stimulation caused no significant change in the measured lens diameter (Fig. 4) or refraction (not shown). In general, accommodative eye movements were larger than wandering eye movements (111 OS), but the largest wandering eye movement (Fig. 4, 38 OS) recorded was larger than any of the accommodative eye movements recorded during stimulation (Fig. 4); still, it resulted in no change in measured lens diameter.

Discussion

Surgical iridectomy is necessary for direct visualization of the lens diameter as performed in this study. Previous studies have shown that surgical iridectomy does not alter EW-stimulated accommodative amplitude in rhesus monkeys, though iridectomy does reduce supramaximal, pharmacologically stimulated accommodative amplitude.³⁶ Direct action of the pharmacologic agents on the iris and strong pupil constriction may result in the ciliary body being pulled inward more than it is when the iris is not present. Surgical iridectomy is unlikely to alter the rhesus monkey accommodative mechanism.

EW stimulation of accommodation produces bilateral accommodation, convergence, and, if the irides are present, pupil constriction. The accommodative amplitude achieved and the maximum stimulus current amplitude required to elicit maximum accommodation may differ between monkeys or between eyes if the electrode is not centered down the midline or possibly for other physiologic reasons. The EW nucleus contains neurons that innervate the ciliary muscles and the iris, and the EW neurons are in proximity and dorsal to the oculomotor nucleus.^{40–42} Stimulation of accommodation also stimulates the oculomotor neurons and produces unavoidable accommodative convergence eye movements.²¹ These eye movements can be reduced with sutures or injections of botulinum toxin in the extraocular muscles,²¹ but even in the complete absence of convergent eye movements, movements caused by heart beat and respiration still occur.²¹ The analysis shown here demonstrates that measurements of lens diameter are unaffected by the extent of eye movements observed. The large accommodative decrease in lens diameter, the systematic correlation between refraction and lens diameter, the reproducibility of these relationships between responses of different amplitudes, experimental sessions and monkeys, the absence of an effect caused by eye movements, and the similarity between the results reported here and those reported previously²¹ leave little doubt that the lens diameter decreases with accommodation.

The gonioscopy lens used in these experiments was designed to reduce corneal power by replacing the curved cornea/air interface with a plano PMMA/air interface. Any resultant optical effects of movements of the eye and any shallowing of the anterior chamber are, therefore, negligible. The lens equator in monkey eyes may move forward, if at all, during accommodation but likely by no more than 150 μm .³⁴ A simple model (ZEMAX; ZEMAX Development Corporation, Bellevue, WA) of the monkey eye with a gonioscopy lens of this kind on the cornea shows that a 150- μm forward movement of the lens equator would result in a 0.4% increase in diameter of the crystalline lens image. This, together with the eye movement controls, demonstrates that eye movements, optical effects, artifacts, and experimental variation cannot account for the systematic 600- μm decrease in lens diameter with accommodation reported here.

The systematic and relatively linear relationships between change in lens diameter and refraction show, in accordance with other such relationships,³⁴ that the optical and physical changes of the lens are highly correlated during accommodation. Some variation and nonlinearities are present, even comparing the results from the same eye in two different sessions. This is because accommodation and lens diameter are measured sequentially and not simultaneously. Some variation occurs in the accommodative response from one stimulation to the next, and the correlations are imperfect.³⁴ Further, variation in accommodative responses from the same monkey may occur from one session to the next because of slight variation of the electrode location in the brain from day to day, depending on many physiologic factors, including hydration of the monkey or level of anesthesia. However, in spite of this variability, lens diameter decreased relatively consistently with accommodation in all eyes.

Efforts aimed at modeling the accommodative mechanism^{43–46} and in vitro experiments using mechanical stretching to induce accommodative changes^{24,47–49} will benefit from knowledge of the actual changes in lens diameter during accommodation in vivo. For example, Burd and colleagues⁴⁵ show a nonlinear, analytically derived relationship between equatorial strain and absolute optical power for a human lens. This is in contrast to the relatively linear changes of 1.15 to 1.77 (D/%) throughout the full range of accommodation, with an overall change of approximately 7% shown here in monkey eyes. The change in lens diameter with accommodation reported here for monkey eyes is contrary to and 5 times larger than that in analytical models of human accommodation used in support of the Tscherning/Schachar theory.^{43,44,50,51} Physiologically relevant conclusions can only be drawn from models that are based on accurate starting assumptions.

Knowing how much the lens diameter decreases per diopter of accommodation provides an indication of the range of movements occurring in the lens equator during accommodation. The performance of artificial accommodative IOLs that rely on a movement of an optic, a pair of optics, or changes in lens surface curvatures can be predicted with knowledge of the extent of changes in lens diameter. If the volume or dimensions of an IOL are known, the relationship between the change in diameter and the movements of the optics or the change in surface curvature may be derived analytically. This information may be useful in the design of accommodative IOLs and will enable finite element analysis models to better predict the theoretical capabilities of IOL designs.

Schachar and coauthors^{18,25,48,52,53} have suggested that lens diameter increases during accommodation in primates, resulting in a movement of the lens equator toward the sclera by 40 to 60 μm and that zonular stretching induces accommodative increases in curvature and optical power in bovine and human lenses.^{24,48} Recent zonular stretching experiments in human cadaver lenses in support of the Tscherning/Schachar theory of accommodation provide no information on the extent of stretch applied or the resulting increase in lens diameter.⁴⁸ This absence is notable because the theory these experiments are suggested to support relies critically on small changes in lens diameter.^{50,51} In accordance with the Helmholtz accommodative mechanism, many previous in vitro zonular stretching experiments with quantitative measurements of changes in lens surface curvature and focal length show that zonular traction causes a flattening of the lens surface curvatures and an increase in lens focal length with an increase in lens diameter in accordance with the results shown here in living monkey eyes.^{47,49,54–56}

The 600- μm decrease in lens diameter reported here in monkeys is similar to accommodative changes in lens diameter measured in vivo in young human eyes. Studies in humans have consistently shown a decrease in lens diameter with accommodation of 6.6% in eight of the youngest subjects studied using MRI,⁷ 8.8% with photography in a subject with congenital aniridia,^{4,5} 7.4% with retroilluminated videography in a carrier of ocular albinism,⁶ and 6.6% with ultrasound in healthy human subjects.⁵⁷ Similarly, a 6% decrease was shown previously in monkeys with pharmacologic and EW stimulations,²¹ and a 7% decrease is reported here. Slight variation exists because of the accommodative response amplitude, age of the subjects, methods of accommodation stimulation, measurement methods, and magnification issues related to optical measurements through the cornea. Schachar⁴⁸ has criticized these previous results as subject to error because of eye movement and absence of controls. However, the results from those studies are surprisingly consistent, and the criticisms appear to be unfounded. Pharmacologic stimulation of accommodation causes a decrease in lens diameter of a magnitude similar to that for EW-stimulated accommodation but, unlike EW stimulation, is not subject to systematic eye movements.²¹ Imaging at the nasal and the temporal quadrants of the eye during EW stimulations shows the lens equator moves away from the sclera at both quadrants despite a consistent

convergent eye movement toward the nasal quadrant.²¹ It is highly unlikely that i) random eye movements during pharmacologic stimulation while viewing the entire lens diameter, ii) convergent eye movements during EW stimulation while viewing the entire lens diameter, iii) convergent eye movements during EW stimulation while imaging the nasal quadrant, and iv) convergent eye movements during EW stimulation while imaging the temporal quadrant could all consistently produce the same artifactual accommodative movement of the lens equator. These represent the controls for eye movements that Schachar suggested are missing.^{48,58}

Accommodative movement of the lens equator has been measured previously with UBM and goniovideography.^{11,18,20,21,25} In UBM experiments performed by Schachar and colleagues,^{18,25} the lens equator reportedly moved toward the sclera, whereas in others using both UBM and higher resolution goniovideography, the lens equator moved away from the sclera during accommodation.^{11,20,21} These studies imaged only one edge of the lens; therefore, it is unknown what happens concurrently at the opposite edge of the lens. When the entire lens diameter is measured, as in this study and others, the problem is avoided.^{5,6} The reference is the unaccommodated lens diameter rather than one edge of the sclera, and, as we show, small eye movements are immaterial. Even in the presence of eye movements (Figs. 1C, 1D, 4), there is a clear and pronounced decrease in lens diameter. Eye movements are not the cause of the decrease in lens diameter. Anomalous movements of the lens equator toward the sclera do occur²¹ and are likely to be caused by asymmetric accommodative movements of the lens or by lack of appropriate controls.^{18,25}

Lens diameter, as shown here, and lens axial thickness, as shown previously,³⁴ change systematically and linearly with accommodative refractive changes. However, these findings do not require that the lens surface curvatures simply become more “spherical” with accommodation. How the lens surface curvatures change with accommodation is the fundamental point of contention between the Helmholtz and Tscherning theories of accommodation.^{1,23} Tscherning was led to postulate that zonular tension must increase during accommodation to explain the observed flattening of the lens periphery during accommodation.^{23,59} It is now well established that the lens and eye do not simply undergo a uniform increase in optical power across the full diameter. Accommodative changes in wavefront aberrations in monkey eyes after iridectomy measured across the full diameter of the eye show that the eye undergoes a strong accommodative change in power near the optical axis but that little change in power occurs near the periphery.²² The same result is seen from wavefront measurements of zonular traction/relaxation-induced accommodative changes in isolated human and monkey lenses^{47,49} or in vivo during accommodation in human eyes.⁶⁰ Thus, although lens diameter decreases and lens axial thickness increases systematically with accommodation, the lens surfaces undergo a greater steepening centrally than at the periphery.^{61,62} This is probably because of the nonuniform molding pressure that the capsule, with regional variations in thickness and elasticity, imparts to the lens.^{3,22}

Coleman^{63,64} has disputed the capsular basis of accommodation in favor of hydraulic-, pressure differential-, or catenary-based forces. However, accommodation still occurs after vitrectomy,⁶⁵ and accommodative changes, essentially identical to those occurring in vivo, occur in vitro in the absence of vitreous, pressure differentials, or catenary forces in mechanical stretching experiments when zonular tension is released.^{47,49,56,66,67} This argues in favor of the Helmholtz/Gullstrand/Fincham capsular basis of accommodation.

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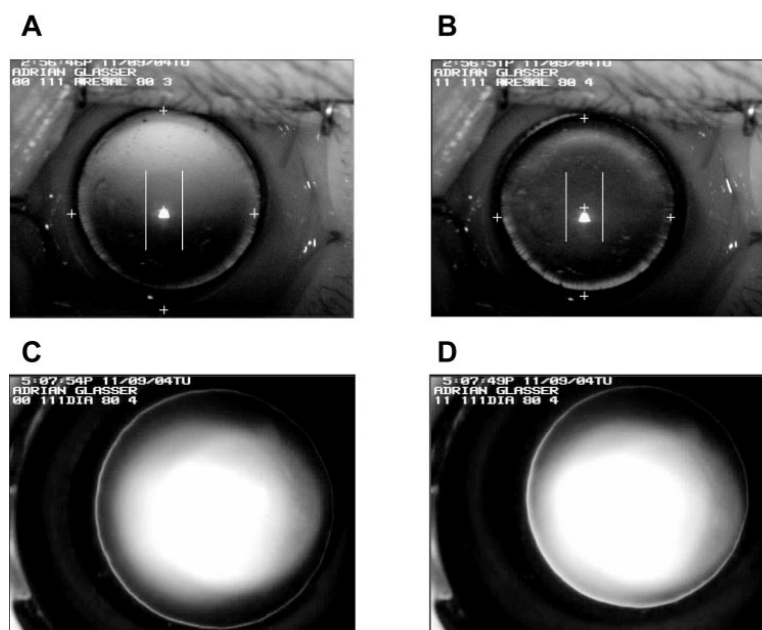


Figure 1. Photorefractive images of an (A) unaccommodated and (B) an accommodated eye, and images from which lens diameters were measured in the (C) unaccommodated and the (D) accommodated states. (A, B) Vertical lines show the points from which the vertical luminance profiles were extracted. (C, D) A slight upward eye movement and a clear decrease in diameter can be seen. Images are from monkey 111, left eye, at 0 D and approximately 13.5 D of accommodation.

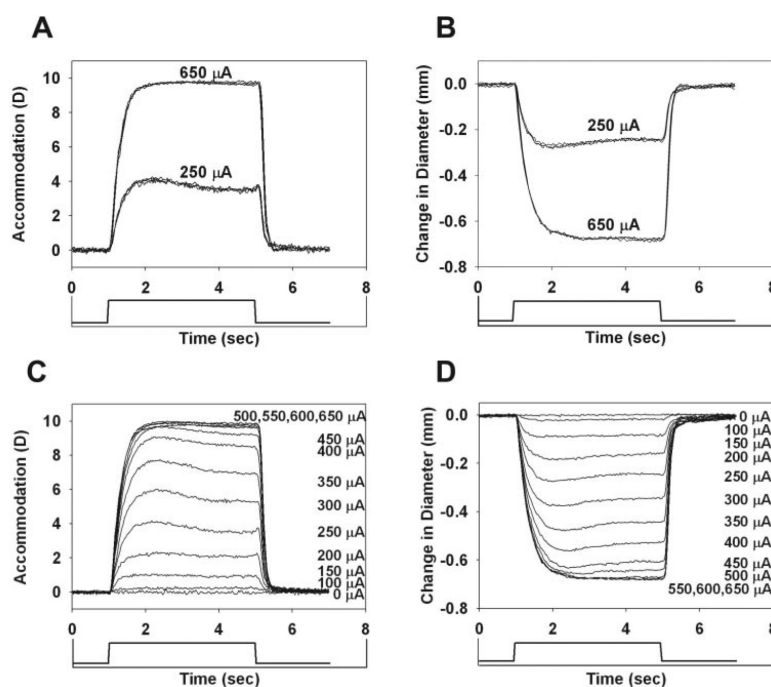


Figure 2.

Accommodative refractive changes (**A, C**) and diameter changes (**B, D**) from monkey 111, left eye. (**A, B**) Three individual raw traces (essentially superimposed) from three successive stimulations at 250 and 650 μ A. (**C, D**) Mean traces covering the full range of responses available to this eye.

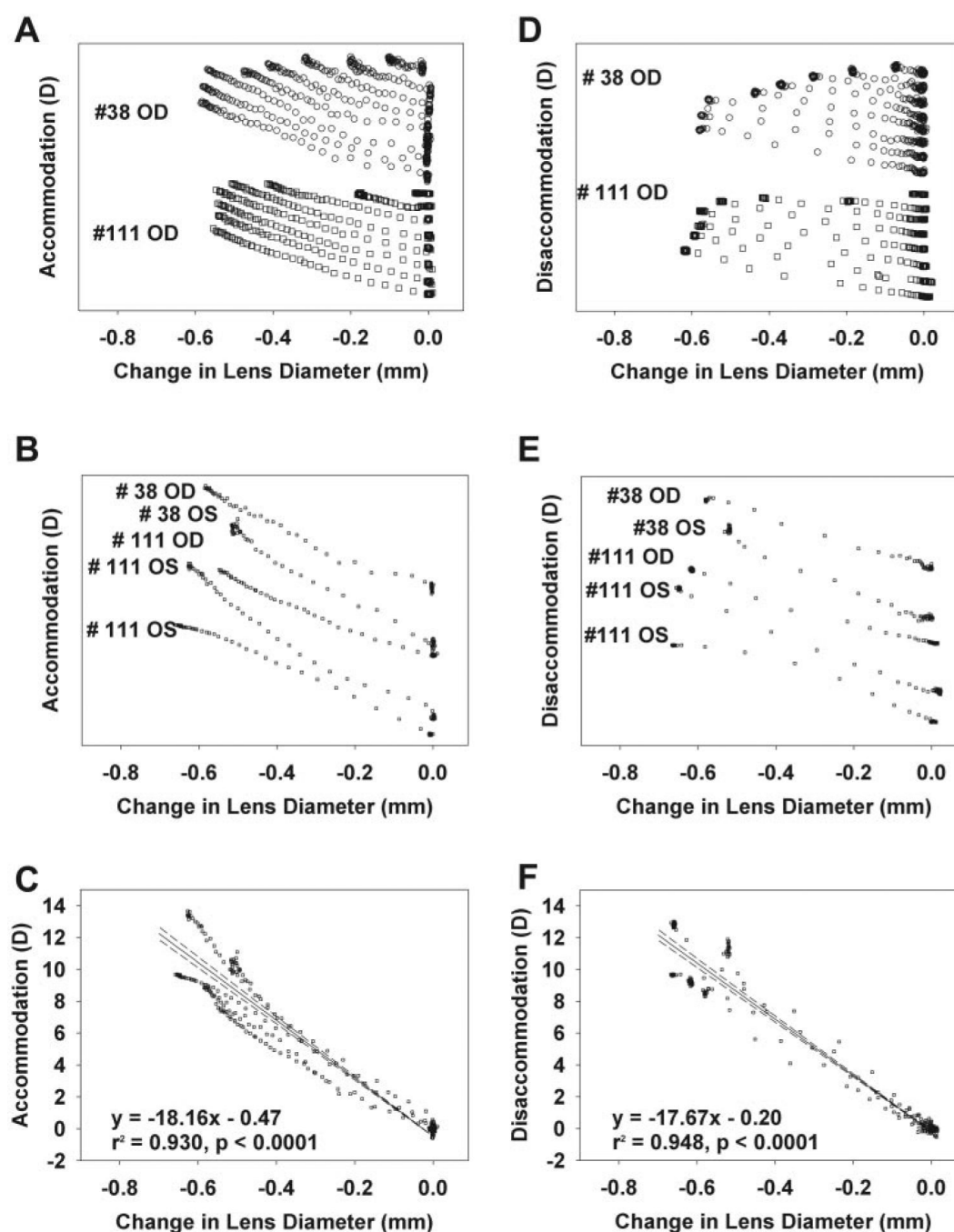


Figure 3.

Relationship between refraction and lens diameter for accommodation (A–C) and disaccommodation (D–F). (A, B) Full range of responses from the lowest stimulus amplitude to the maximum stimulus amplitude from one eye each of two monkeys. Data for each different response is distributed vertically by an arbitrary amount for visibility (hence, no vertical scale is shown). (B, E) Maximum responses from each eye, also distributed vertically by arbitrary amounts for visibility. (C, F) Orthogonal regressions (with 95% confidence intervals) fitted through all the maximum responses from each eye.

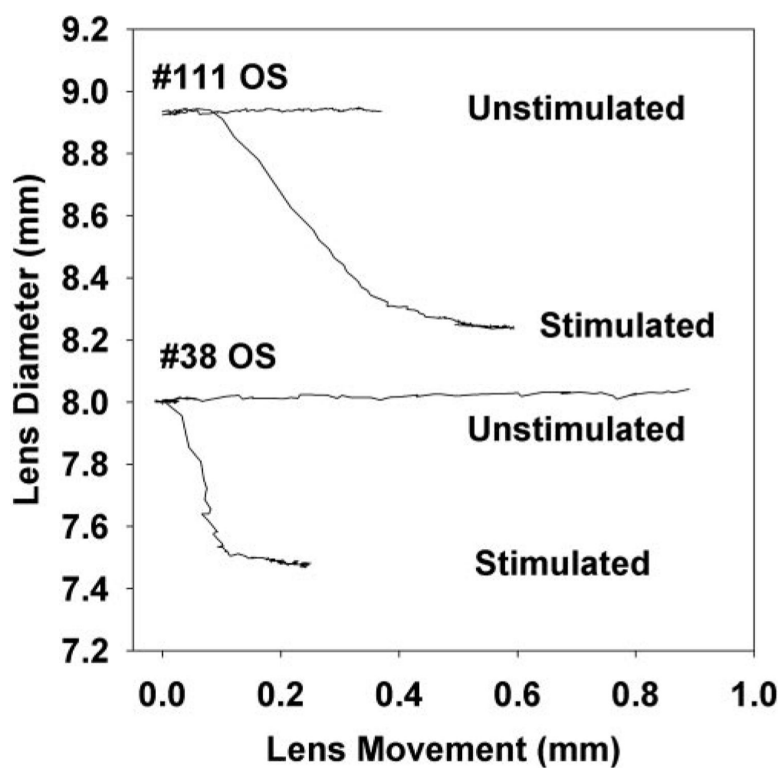


Figure 4.

Analysis of lens diameter as a function of movement of the center of the circumference of the lens. In two different eyes, EW stimulation produces an accommodative decrease in lens diameter and movements of the lens center (stimulated). Between stimulations, wandering eye movements result in a change in the lens center, but without a change in lens diameter (unstimulated).

Table 1

Individual Data from Each Eye Measured in This Study

Monkey Number and Eye	Accommodative Amplitude (D) \pm SD	Unaccommodated Lens Diameter (mm) \pm SD	Accommodated Lens Diameter (mm) \pm SD	Percentage Decrease in Lens Diameter	Decrease in Lens Diameter per D of Accommodation (mm/D)
111 OS	9.71 \pm 0.03	8.73 \pm 0.00	8.06 \pm 0.00	7.67	0.069
111 OS	12.86 \pm 0.13	8.83 \pm 0.00	8.19 \pm 0.00	7.25	0.050
111 OD	9.14 \pm 0.13	8.87 \pm 0.00	8.28 \pm 0.00	6.65	0.065
38 OS	10.84 \pm 0.25	8.07 \pm 0.00	7.57 \pm 0.01	6.20	0.046
38 OD	8.53 \pm 0.09	8.21 \pm 0.00	7.60 \pm 0.00	7.43	0.072
Mean \pm SD	10.216 \pm 1.70	8.542 \pm 0.37	7.94 \pm 0.33	7.04 \pm 0.60	0.060 \pm 0.01

Values are means \pm SD obtained from an analysis of 20 consecutive image frames from videotape when the eye was unaccommodated just before stimulus onset or accommodated just before termination of the stimulus. Values in the bottom row represent data from all eyes even though data from one eye are repeated.

Table 2

A-Scan Data from Each Monkey

Monkey Number and Eye	Anterior Chamber Depth (mm) \pm SD	Lens Thickness (mm) \pm SD	Vitreous Chamber Depth (mm) \pm SD	Axial Length (mm) \pm SD
111 OS	2.86 \pm 0.38	3.07 \pm 0.35	12.87 \pm 0.20	18.80 \pm 0.74
111 OD	3.22 \pm 0.08	3.25 \pm 0.08	13.02 \pm 0.04	19.49 \pm 0.05
38 OS	2.63 \pm 0.21	3.31 \pm 0.05	11.86 \pm 0.25	17.79 \pm 0.39
38 OD	2.66 \pm 0.20	3.11 \pm 0.41	12.17 \pm 0.11	17.95 \pm 0.48

Each measurement is a mean \pm SD from five measurements.