The Mechanism of Accommodation in Primates

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Objective: To study the accommodative mechanism in primates using monkeys, in light of a recently proposed novel accommodative mechanism in primates and a concomitant controversial surgical procedure for the reversal of presbyopia,

Design: Experimental study.

Methods: Accommodation was induced by stimulation of an electrode surgically implanted in the midbrain and by topical ocular application of muscarinic agonists. Pharmacologic disaccommodation was achieved by topical application of a muscarinic antagonist. Movements of the lens equator and the ciliary body were imaged during accommodation and disaccommodation using ultrasound biomicroscopy and goniovideography, and the images were analyzed to determine the direction and the extent of the movements.

Results: Despite the systematic eye movements occurring with electrical stimulation and the nonsystematic eye movements occurring with pharmacologic stimulation, in all instances the ciliary body and the lens equator moved away from the sclera during accommodation.

Conclusions: Movement of the accommodative structures is consistent with the classic mechanism of accommodation described by Helmholtz, and contrary to that recently proposed by Schachar. *Ophthalmology 1999;106:863–872*

In light of a recently proposed novel mechanism of ocular accommodation in primates,[1] we undertook a comprehensive series of experiments to study the accommodative mechanism in subhuman primates. Accommodation induced by electrical stimulation of the midbrain and topical application of drugs to the eye, and pharmacologic reversal of accommodation, have been used in conjunction with videographic imaging to identify the direction and extent of the movements of the accommodative structures within the eyes of rhesus and cynomolgus monkeys. A preliminary report of these findings was abstracted and presented at the 1998 meeting of the Association for Research in Vision and Ophthalmology [Glasser A, Kaufman PL. Invest Ophthalmol Vis Sci 1998;39(Suppl):S311].

The classic Helmholtz[2] mechanism of accommodation posits that a contraction of the ciliary muscle releases the resting tension on the zonular fibers that span the circumlental space extending between the ciliary body and the lens equator. This releases the outward-directed equatorial tension on the lens capsule and allows the elasticity of the capsule to "round up" the lens substance. This causes a decrease in the circumferential lens diameter and increases the curvature of the anterior and posterior lens surfaces. When the ciliary muscle relaxes after the accommodative effort ceases, the zonular tension on the lens equator is again increased. This pulls on the capsule at the lens equator and causes a flattening of the lens and a decrease in the curvature of the anterior and posterior lens surfaces. The movement of the equatorial edge of the lens is thus away from the sclera during accommodation and toward the sclera during disaccommodation.

Schachar et al[1] recently proposed an alternative accommodative mechanism for the primate eye that is similar to a theory originally proposed by Tscherning.[3] They believe that the equatorial zonule inserts to the anterior aspect of the ciliary muscle at the root of the iris, and the posterior zonule inserts into the posterior ciliary body. This description of the insertion of the zonule conflicts with evidence from fresh human tissues[4] and from scanning electron microscopy[5] that shows no insertion of equatorial bundles or any other zonular fibers at the iris root and anterior ciliary muscle. Schachar and Anderson[6] contend that contraction of the ciliary muscle causes a posterior-outward movement of the anterior ciliary muscle toward the sclera at the iris root, increasing tension on the equatorial zonular fibers while releasing tension on the anterior and posterior zonular bundles. Schachar believes that this provides a net outward-

directed force at the lens equator through the equatorial zonular fibers. This force, putatively, would pull the lens equator toward the sclera during accommodation and, together with the concurrent relaxation of the anterior and posterior zonular bundles, would cause a flattening of the peripheral lens surfaces while increasing the central anterior and posterior lens surface curvatures. From a theoretical standpoint, pulling on the lens equator could cause an increase in the central lens curvatures, depending on the viscoelastic properties of the lens. Schachar's theory, unlike that of Tscherning, identifies no role for the vitreous.

The significance of Schachar's theory relates to presbyopia and a proposed surgical procedure for its reversal and for the reintroduction of accommodation in humans.[7] Schachar believes that presbyopia is due to the continued growth of the lens throughout life, which results in an increased lens equatorial diameter, a crowding of the posterior chamber, and a reduction in tension of the zonular fibers at the lens equator with increasing age. On the basis of Schachar's theory of accommodation, this would result in a failure of zonular tension to increase sufficiently during a contraction of the ciliary muscle. Schachar's surgical procedure for the reversal of presbyopia, which has been performed on monkeys[1] and humans[7] (Yang GS, Yee RW, Chuang AZ, Ruiz AG. Invest Ophthalmol Vis Sci 1998;38 [Suppl]:S753; Yang GS, Yee RW, Cross WD, et al. Invest Ophthalmol Vis Sci 1997;39[Suppl]:S735), is intended to increase the scleral diameter at the ciliary region, reintroducing zonular tension at the lens equator.

Schachar's theory of accommodation predicts that the lens equator will move toward the sclera and that the lens equatorial diameter will increase during accommodation.[8] This theory also predicts that because of the increased equatorial zonular tension in the accommodated state, accommodative amplitude will not be altered by gravity; i.e., it will be the same in a supine subject looking up or looking down.[9]

We have undertaken experiments to determine the accommodative mechanism in rhesus monkeys. Rhesus monkeys have high amplitudes of accommodation, which can be stimulated by cholinomimetic drugs applied topically to the eye[10] and by midbrain electrical stimulation.[11,12] Presbyopia develops in monkeys with the same relative age course as in humans.[10,12] Electrical stimulation by an electrode surgically implanted in the Edinger-Westphal (EW) nucleus of the midbrain produces accommodation, convergence, and pupil constriction via the normal afferent parasympathetic pathways to the eye.[11] Pharmacologic stimulation of the ciliary muscle by a topically applied cholinomimetic agent induces accommodation,[10,13] which can be reversed (disaccommodation) with muscarinic antagonists.

Centrally stimulated accommodation is rapid in onset and reversal (on the order of seconds), repeatable, and reliable, and it can be induced frequently in an experimental session. Its disadvantage is that stimulation also induces systematic convergence eye movements. Pharmacologically stimulated accommodation, on the other hand, can be achieved only once in an experimental session and is of relatively slow onset (30 to 45 minutes). It does not induce *systematic* eye movements and typically produces higher accommodative amplitudes than centrally stimulated accommodation. Pharmacologic reversal of pharmacologically stimulated accommodation is also slow (30 to 60 minutes) and can also be achieved only once in an experimental session. Because both methods of inducing accommodation offer distinct advantages and disadvantages, we have used them both.

Materials and Methods

Animals

We used six cynomolgus monkeys (*Macaca fascicularis,* estimated ages 10 to 13 years) and eight rhesus monkeys (*Macaca mulatta,* ages 6 to 17 years) with centrally stimulated (described below) accommodative amplitudes ranging between 7 and 18 diopters (D). The monkeys had previously undergone complete removal of the irides bilaterally by tearing them away at the root over the entire 360° circumference,[14] and surgical implantation of stimulating electrodes into the EW nucleus.[11]

Several other young cynomolgus and rhesus monkeys, some surgically iridectomized, others not, were used for the pharmacologic stimulation experiments.

Anesthesia

Animals were initially anesthetized with intramuscular ketamine (10 mg/kg), followed by surgical depth sodium pentobarbital (Nembutal [Abbott Laboratories, Chicago, IL]; 15 mg/kg intravenously or 35 mg/kg intramuscularly, with supplements of 10 mg/kg hourly or as required).

Edinger-Westphal Nucleus-Stimulated Accommodation

Stimulating electrodes were permanently surgically implanted in the EW nucleus by use of stereotaxic localization procedures.[11] A 2-second stimulus train (500-microsecond duration, 10-millisecond interval, amplitude range 200 to 2,000 mA) was used to induce varying amplitudes of accommodation. Prior botulinum toxin injections (6 units/50 μl/muscle) in the medial and inferior rectus muscles, and 4-0 sutures placed beneath the medial and lateral rectus muscles during each session, with tension applied by micrometers, were used to reduce convergent eye movement.

Corneal Sutures

For precise visualization of the cornea and identification of eye movements during accommodation, 9-0 black nylon sutures were placed at the nasal and temporal lateral limbal margins, the knots were internalized in the cornea, and the sutures were left in place. In addition, three to eight 9-0 black nylon partial-thickness crossed corneal sutures were placed in clear cornea approximately midway between the corneal apex and the limbus at the start of each pharmacologic experiment. These sutures were removed at the end of each experiment while the animals remained anesthetized.

Videographic Imaging

Videographic recordings of the accommodative movements of the ciliary body, ciliary muscle, and lens equator were made during

each experiment with a variety of imaging techniques. Goniovideography of the iridectomized eyes allowed visualization of the tips of the ciliary processes, the anterior zonular fibers, and the lens equator.[12] An ultrasound biomicroscope (UBM) (Humphrey Instruments, San Leandro, CA) was used to image the ciliary muscle, the lens equator, and the posterior zonular fibers through the sclera.[1,8] For gonioscopy, a Swan-Jacob gonioscopy lens, a Goldmann lens or a custom-designed Plexiglas perfusion cell lens (described below) was placed on the cornea. Each lens was held with a flexible external clamp to orient the lens on the eye. Imaging was performed by use of a slit-lamp microscope (Carl Zeiss, Thornwood, NY) with a monochrome Cohu couple charge display (CCD) video camera attached. The output from the CCD camera or from the UBM was recorded on a SONY S-VHS video recorder.

Ultrasound Biomicroscopy

For UBM imaging of the ocular anterior segment during centrally stimulated accommodation, the anesthetized monkey was stabilized supine in a head holder. The body was placed on a vacuum-extractable stabilization polystyrene beanbag. The facial hair around the orbit was cut with hair clippers. Colloidon (Sigma, St. Louis, MO) was applied to the skin around the eyelids with a cotton-tipped applicator, and an adhesive sterile drape (3M Medical, St. Paul, MN) was pressed onto the eye and orbit.[15] A hole was cut in the drape around the eyelids to expose the eye. A circular ring stand was clamped above the head, and the edges of the drape were lifted over the sides of the ring to form a funnel-shaped well around the eye. The eyelids were held open with a lid speculum, and 18-inch long 4-0 sutures were placed beneath the medial and lateral rectus muscles, pulled over the sides of the well, and clamped with hemostats to allow rotation, orientation, and stabilization of the eye. The well was filled with sterile saline. The eye was rotated into extreme adduction to orient the temporal ciliary region upward or into extreme abduction to orient the nasal ciliary region upward, for UBM imaging. The transducer of the UBM was clamped above the eye in such a manner that the tip was submerged in the saline and positioned above the ciliary muscle. The transducer was then manipulated to image the ciliary region of the eye and the lens equator.

Image Analysis

A PC-based image analysis system, consisting of an IC-PCI (Imaging Technology, Inc., Bedford, MA) frame grabber board and Optimas Image Analysis software (Media Cybernetics, Silver Springs, MD), was used to acquire, store, subtract, and enhance individual image frames or continuous real-time sequences of image frames off the videotape. Image sequences were played back on the computer to analyze and measure the movements of the accommodative structures. Image pairs were subtracted from each other to identify movements that occurred during accommodation, and the image contrast was enhanced with standard filters to increase image quality. Individual image frames were identified with the VCR frame counter. A digital signal was recorded onto the videotape during the EW stimulation experiments to identify the onset, time course, and end of the electrical stimulation.

Image subtraction was used to determine the extent of the movement of the accommodative structures relative to eye movements. Central stimulation often caused eye movements, and superimposable images from the *completely* unaccommodated and *maximally* accommodated states were sometimes not found. In such cases, an image several frames (1 frame = 33.33 milliseconds) after the stimulus onset (i.e., before maximal accommodation was reached, but after eye movements had ceased and the eye

was stabilized in its new position) was compared with the image just before the end of the stimulus (i.e., the image of the eye in the maximally accommodated state). In this manner, completely superimposable image pairs could be identified.

Measurements of the dynamic movements of the lens equator and the ciliary processes were obtained from image analysis of goniovideography sequences.[16] A continuous sequence of 100 to 120 images during stimulation was recorded to disk. The positions of the lens equator and of six to eight ciliary processes were manually identified for the entire sequence. The change in the positions of these structures during the electrical stimulation provided a measure of the extent and direction of their movement.

Measurement of Accommodation

A Hartinger coincidence refractometer (Jenoptik, Jena, Germany) was used to measure objectively the refractive state of the eye during electrically induced accommodation. A plano polymethylmethacrylate contact lens was placed on the cornea. Baseline refraction and maximal accommodated refraction achieved at each stimulus amplitude were recorded. Accommodative amplitude at each stimulus was the difference between these two refractions.

For pharmacologically stimulated accommodation, a polymethylmethacrylate contact lens was initially placed on the cornea, and baseline resting refraction was recorded. The contact lens was removed, the pharmacologic agent was applied (see below), and the imaging was performed. At the end of the experiment, the contact lens was repositioned and the refractive state was measured. The difference between the predrug and postdrug refractions represented the pharmacologically stimulated accommodative amplitude. The refractive state was again measured after pharmacologic reversal of accommodation (see below).

Infrared Photorefractive Dynamic Measures of Accommodation

To measure dynamic changes in refractive state during centrally stimulated accommodation, infrared photorefraction was used.[16–18] A prior calibration of each eye, to relate the slope of the vertical brightness profile through the pupil to the absolute refractive state of the eye, was performed.[19] Accommodation was stimulated by a range of stimulus voltages, and maximal accommodation at each voltage was measured with a Hartinger coincidence refractometer. A regression curve describing the slope of the pupil brightness profile versus the measured accommodative amplitude was calculated for each eye. The dynamic optical changes in the eye occurring during centrally stimulated accommodation were recorded onto videotape with an infrared photorefractor, and subsequent image analysis was performed to measure the pupil brightness profile. The regression curve was then used to relate the dynamic changes in the pupil brightness profile to the accommodative amplitude.

Infrared photorefraction was also used to assess the effect on accommodative amplitude of applying tension to sutures beneath the extraocular muscles. Accommodation was measured with infrared photorefraction before and after the application of tension to the superior, medial, and lateral rectus muscles.

Pharmacologic Induction and Reversal of Accommodation

Carbachol chloride iontophoresis,[20] topical pilocarpine hydrochloride, and systemic pilocarpine hydrochloride were used to induce accommodation. Systemic and topical atropine sulfate were used to reverse pharmacologically stimulated accommodation. A cus-

tom-designed perfusion cell lens was used to topically apply and perfuse the pharmacologic agents over the cornea during continuous imaging. The perfusion cell lens was made from a tapered Plexiglas cylinder 15 mm long with a 22-mm diameter opening at one end and a 7-mm diameter opening at the other end. A plano, circular cover slip was glued over the larger opening with silicone glue to form a plano window perpendicular to the viewing axis. The smaller opening had a lip that was placed beneath the eyelids in contact with the conjunctiva to form a watertight seal. A polyethylene tube entered from below and exited above to allow solutions to flow through the cell. The corneal power was effectively neutralized by the plano window and fluid-filled perfusion lens, and the ciliary processes and the equatorial diameter of the crystalline lens were visible through the perfusion lens. Various protocols were used to induce and reverse accommodation. The most effective protocol (greatest amplitude and maximal reversal of accommodation) was as follows: Solutions of saline, 10% pilocarpine hydrochloride in sterile buffered saline, and 0.5% atropine sulfate in saline, matched for refractive index by use of glucose, were made up; baseline refraction was measured through a plano contact lens; 9-0 nylon marking sutures were placed in the cornea; the perfusion cell lens was placed on the eye; saline was perfused through the lens; baseline imaging was performed for 5 minutes; pilocarpine solution was perfused through the lens; continuous imaging was performed for 2 hours; the perfusion cell lens was removed; the contact lens was replaced; accommodated refractive state was measured; the contact lens was removed; the perfusion cell lens was replaced; saline was perfused through the lens; imaging was performed for 5 minutes; atropine solution was perfused through the lens; continuous imaging was performed for 45 minutes; the perfusion cell lens was replaced by the contact lens; and final refraction was measured.

These investigations conform to the Association for Research in Vision and Ophthalmology Statement for the Use of Animals in Ophthalmic and Vision Research.

Results

Ultrasound biomicroscopic imaging of the ciliary muscle during central stimulation showed that the inner apex of the muscle moved anteriorly and toward the anterior-posterior axis of the eye (i.e., centripetally) and that the equatorial edge of the lens moved away from the sclera during accommodation (Fig 1). In addition, the distance along the posterior zonular fibers extending between the inner apex and the posterior insertion of the ciliary muscle increased, presumably stretching the posterior zonular fibers during accommodation. Movements of the same magnitude and direction were observed during imaging of either the nasal or the temporal ciliary region of the eye, despite the tendency for convergent eye movement to cause a systematic adduction.

Goniovideography showed that the tips of the ciliary processes and the lens equator moved away from the sclera during accommodation. Sufficient eye stabilization was achieved to obtain virtually completely superimposable images (Fig 2). Imaging of both the nasal and temporal sides of the eye showed movements away from the sclera despite the tendency for convergent eye movements.

Goldmann lens imaging allowed visualization of the entire circumferential diameter of the crystalline lens (Fig 3), which was reduced during accommodation and increased during disaccommodation. In the monkey shown in Figure 3, there was an 11% decrease in lens cross-sectional area for 10 D of accommodation.

Several difficulties were encountered with the pharmacologic methods used to induce and reverse accommodation. Whereas
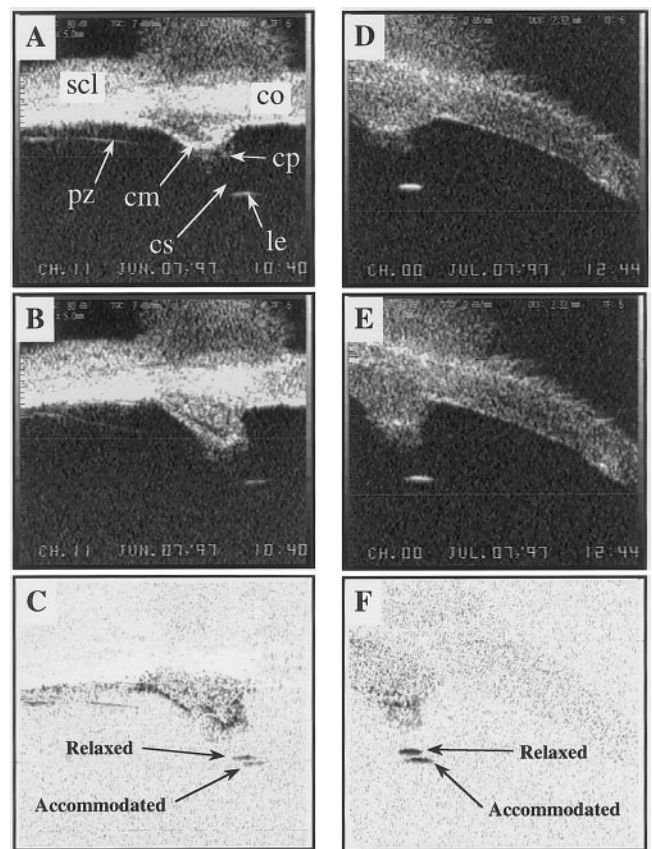

Figure 1. Ultrasound biomicroscopic images of the temporal ciliary region of an iridectomized ~13-year-old cynomolgus monkey eye on two separate occasions. Accommodation was induced by electrical stimulation of the midbrain. Scl = sclera; co = cornea; pz = posterior zonule; cm = ciliary muscle; cs = circumlental space; le = lens equator; cp = ciliary processes. The equatorial edge of the lens, visible as a short horizontal line, reflects ultrasound back to the transducer, but the anterior zonular fibers and the anterior and posterior lens surfaces do not and thus are not visible. **A,** the temporal sclera and underlying ciliary muscle are seen in the unaccommodated eye. The posterior zonular fibers extend between the inner apex and posterior attachment of the ciliary muscle. **B,** in the accommodated state, the inner apex of the ciliary muscle moves forward and toward the axis of the eye. The posterior zonular fibers are stretched, and the equatorial edge of the lens moves away from the sclera and toward the anterior-posterior axis. **C,** the subtracted image pairs show a virtual absence of eye movement. Dark areas show movement of structures between images; white areas are stable. The only movement visible is of the ciliary muscle and lens equator. The lens equator has moved ~100 μm away from the sclera. **D,** unaccommodated, (**E**) accommodated, and (**F**) subtracted image pairs from the temporal side of the same animal on another occasion.

carbachol iontophoresis induced 25 to 30 D of accommodation, it required touching the iontophoretic gel to the cornea, which prohibited continuous unimpeded imaging from predrug to postdrug application without eye movements. Pilocarpine administered systemically caused substantial reductions in blood pressure and substantial eye movements, making useful prolonged ocular imaging impossible. Systemic atropine only partly reversed accommodation induced by systemic pilocarpine, topical pilocarpine, or carbachol iontophoresis of the cornea. The most reliable and effective means of pharmacologically inducing and reversing accommodation during the maintenance of ocular stability for imag-
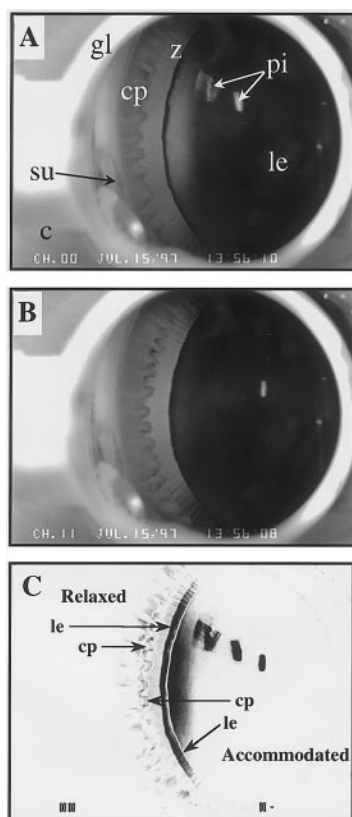
Figure 2. Swan-Jacob goniovideography, nasal side of left eye of a 6-year-old totally iridectomized rhesus monkey. **A,** relaxed, **(B)** ~10 D of centrally stimulated accommodation, **(C)** image pairs (**A** and **B**) subtracted. gl = gonioscopy lens; cp = ciliary processes; z = zonular fibers; pi = III Purkinje images; le = lens; c = conjunctiva; su = suture. **A,** ciliary processes tips and lens equator visible through Swan-Jacob gonioscopy lens. Reference for eye movements provided by 9-0 nylon marking suture in nasal limbus. **B,** during accommodation, ciliary process tips and lens equator move away from sclera toward anterior-posterior axis of the eye by ~250 μm. **C,** subtracted image pairs show movement of ciliary body and lens equator but virtual absence of eye movement during accommodation.

ing was the topical application of the agents through the perfusion cell lens.

Imaging of the entire circumferential diameter of the crystalline lens with the perfusion cell lens during pharmacologically stimulated accommodation demonstrated movement of the lens equator away from the sclera (Fig 4). The crystalline lens cross-sectional area decreased by ~12% for 11.5 D of accommodation. The paired images were taken 55 minutes apart and, despite the prolonged interval, were virtually superimposable. Pharmacologic reversal of accommodation resulted in a circumferential increase in lens diameter. Whereas carbachol iontophoresis and systemic pilocarpine caused eye movements and prevented comparison of the unaccommodated and maximally accommodated states, accommodation ensued rapidly, and superimposable image pairs separated by relatively short time intervals were compared to show substantial lens equator movement away from the sclera (Fig 4E–G).

Dynamic infrared photorefraction and image analysis of the movements of the lens equator and ciliary body showed the time course of the refractive changes and the direction and extent of the accommodative movements during centrally stimulated accommodation (Fig 5A). At stimulus onset, accommodation increased to a maximum and then remained relatively constant until the stimulus ended. The lens equator and the tips of the ciliary processes, as measured by gonioscopy, moved away from the sclera after the stimulus onset and were maintained at the position of maximal excursion with relative stability until the stimulus ended. Plotting the lens and ciliary body movements as a function of the refractive change during accommodation (Fig 5B) showed a linear movement of the ciliary process tips and the lens equator away from the sclera with a change in refraction. The direction and the extent of the movement were similar for both the nasal and the temporal sides of the eye.

We observed anomalous movements of the ciliary processes and lens equator during centrally stimulated accommodation after

substantial tension was applied to the extraocular muscle sutures. In the right eye of a cynomolgus monkey, tension applied to the lateral rectus muscle suture to prevent convergence substantially reduced movement of the lens and ciliary process, and movement of the lens equator was *toward* the sclera during the latter half of the stimulus (Fig 6A). With tension still applied, the ciliary processes and lens equator on the nasal side of the eye moved away from the sclera at stimulus onset, but both continued to move throughout the stimulus duration (Fig 6B). Parts B and C of Figure 6 together show that there is actually a horizontal translation of the lens toward the temporal side of the eye, resulting from the restricted movement of the temporal ciliary processes. After the tension was reduced, the expected lens and ciliary process movements returned (Fig 6C), although the amplitude of their movement was still somewhat reduced because of the remaining tension. In a rhesus monkey that normally had a maximum of 7.5 D of centrally stimulated accommodation, increasing the tension on the superior, medial, and lateral rectus muscles caused a myopic shift in the resting refraction of −2.5 D and a decrease in centrally stimulated accommodative amplitude to 2 D (Fig 6D). Thus, although the increased tension on the extraocular muscle sutures served to reduce eye movement, it also introduced anomalous results.

We also observed that gravity influenced the movement of the crystalline lens during centrally stimulated accommodation in a cynomolgus monkey on more than one occasion (Fig 7). A preexisting opacity on the anterior lens surface allowed visualization of the lens position during accommodation. At maximal accommodation, the lens sagged downward. This was clearly a result of
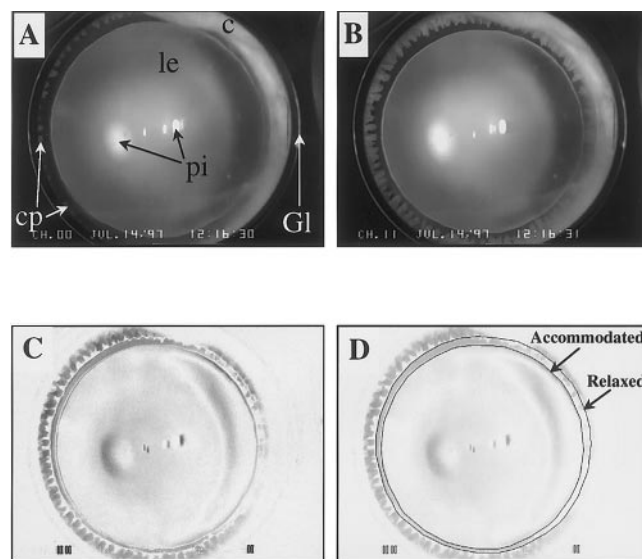

Figure 3. Goldmann lens imaging, left eye of 9-year-old rhesus monkey, showing entire circumferential diameter of lens. Accommodation is induced by central stimulation. Gl = inner edge of Goldmann lens; cp = ciliary processes; c = conjunctiva; pi = III Purkinje images; le = monkey lens. **A,** unaccommodated; the ciliary processes, conjunctiva, and entire lens equatorial diameter can be seen within the Goldmann lens. **B,** 12.5 D of accommodation; ciliary process tips move away from sclera toward anterior-posterior axis of the eye, and lens equator moves away from sclera to decrease lens cross-sectional area by ~11%. **C,** subtracted image pairs; the eye is essentially stable, but there is substantial accommodative movement of ciliary processes and lens equator. **D,** superimposed overlay drawings identify outer edges of lens equator from image **A** in the unaccommodated (outer circle) and image **B** in the maximally accommodated (inner circle) state.
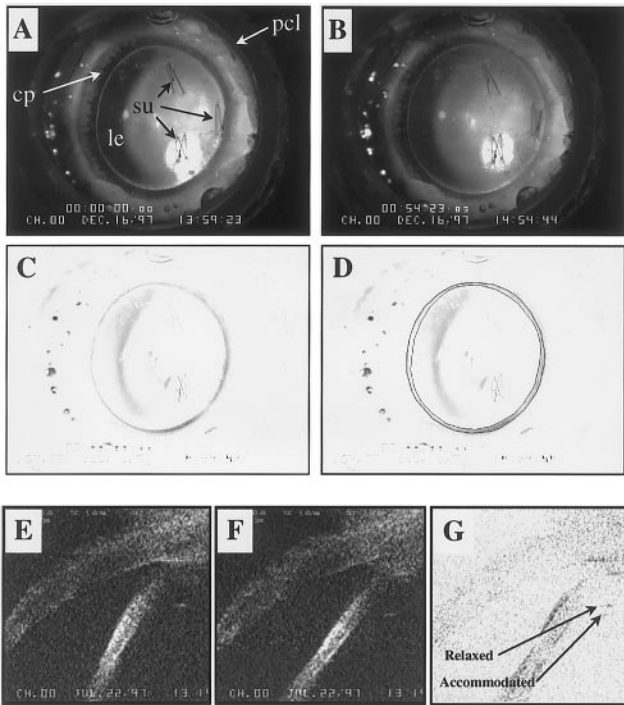
Figure 4. A through **D,** iridectomized left eye of ~12-year-old cynomolgus monkey imaged through a perfusion cell lens (pcl) during accommodation induced by perfusing refractive index-matched solutions through the cell for 30 to 45 minutes. su = 9-0 nylon cross marking sutures in cornea. Le = lens; cp = ciliary processes. **A,** relaxed and (**B**) accommodated 11.5 D ~53 minutes after continuous perfusion of 10% pilocarpine HCl solution. **C,** subtracted image pair shows small random, nonsystematic eye movement and concentric decrease in lens circumferential diameter. **D,** overlay of lens equator from image (A) in relaxed (outer circle) and image **B** in accommodated state (inner circle) shows a 12% decreases in lens cross-sectional area during accommodation. **E,** ultrasound biomicroscopic images of lens equator in an unaccommodated eye (refraction: −1.75 D) before and (**F**) 15 sec after iv pilocarpine administration (iv pilocarpine induces ciliary muscle contraction rapidly;[28] **F** is more accommodated as evidenced by anterior chamber shallowing). **G,** although iv pilocarpine causes systemic effects resulting in eye movements after longer time periods, the subtracted image pairs 15 sec apart show good ocular stability and substantial lens equator movement away from the sclera.

gravity, because the same downward movement was observed when the monkey was positioned upright, on its left or right side, or upside down. Similar lens sagging was also observed in this animal when the entire lens circumference was viewed with a Goldmann lens, as shown in Figure 3.

Discussion

Imaging of the accommodative structures during centrally or pharmacologically stimulated accommodation showed that the lens equator moves away from the sclera, in accordance with the classically described accommodative mechanism[2] and contrary to Schachar's proposed mechanism. Similarly, UBM imaging demonstrated movement of the inner apex of the ciliary muscle anteriorly and centripetally during accommodation; localized posterior or outward

movement of the anterior aspect of the ciliary muscle, as suggested by Schachar and Anderson,[6] and Schachar[21] from histologic analysis, was not visible.

Wilson[22] has shown lens equatorial movements away from the sclera during accommodation using transilluminated infrared light in a young human subject with ocular albinism. Glasser and Campbell[4] have shown that mechanically stretching the zonule of the human lens increases lens focal length in accordance with classic teachings. There has been no independent confirmation of the anatomic arrangements of the ciliary region, the accommodative mechanism, or the causes of presbyopia described by Schachar.

The entire extent of the ciliary muscle slid forward along the inner sclera during accommodation. Because the inner apex of the ciliary muscle where the posterior zonular fibers attach showed the greatest forward movement,[23] the posterior zonular fibers must be elastic and be stretched during accommodation. The entire choroid/zonule ciliary muscle system thus constitutes an elastic sling.[24] The active contraction of the muscle, anchored at the scleral spur, trabecular meshwork, and peripheral cornea,[25,26] provides the forward movement during accommodation, and the elastic choroid and posterior zonule provide the posterior movement when the muscle relaxes.

The extraordinary measures required to reduce convergent eye movements during accommodation produced anomalous results on occasion. Tension on sutures placed beneath the extraocular muscles reduced or reversed the expected lens movements, presumably because of deformation of the relatively thin monkey sclera, physical stretching of the choroid, and restriction of contraction and forward movement of the ciliary muscle. However, we never saw lens equator movements toward the sclera on both sides of the eye, or an increase in lens diameter with accommodation, as Schachar's theory predicts. Surgical expansion of the sclera might thus actually restrict ciliary muscle contraction; indeed, sufficient tension applied to the sutures caused a reduction of up to 73% in centrally stimulated accommodative amplitude.

The tendency for convergent eye movements to occur during centrally stimulated accommodation, although reduced through botulinum toxin injections and tension on extraocular muscle sutures, could not be completely avoided. During UBM imaging of the temporal ciliary muscle, a convergent eye movement might cause an apparent movement of the lens equator *away* from the sclera. During imaging of the nasal side of the eye, the convergent eye movement would tend to cause an apparent movement of the lens equator *toward* the sclera. However, the lens equator was seen to move *away* from the sclera during imaging of either the nasal or the temporal sides of the eye by use of both gonioscopy and the UBM, so this movement cannot be explained by eye movements. Similarly, the downward movement of the lens under the influence of gravity during central stimulation (Fig 7) cannot be a consequence of eye movements, because the same downward movement was observed regardless of the head orientation and despite the consistent convergent eye movement.

No credible eye movement can explain the circumferential decrease in lens diameter during centrally and
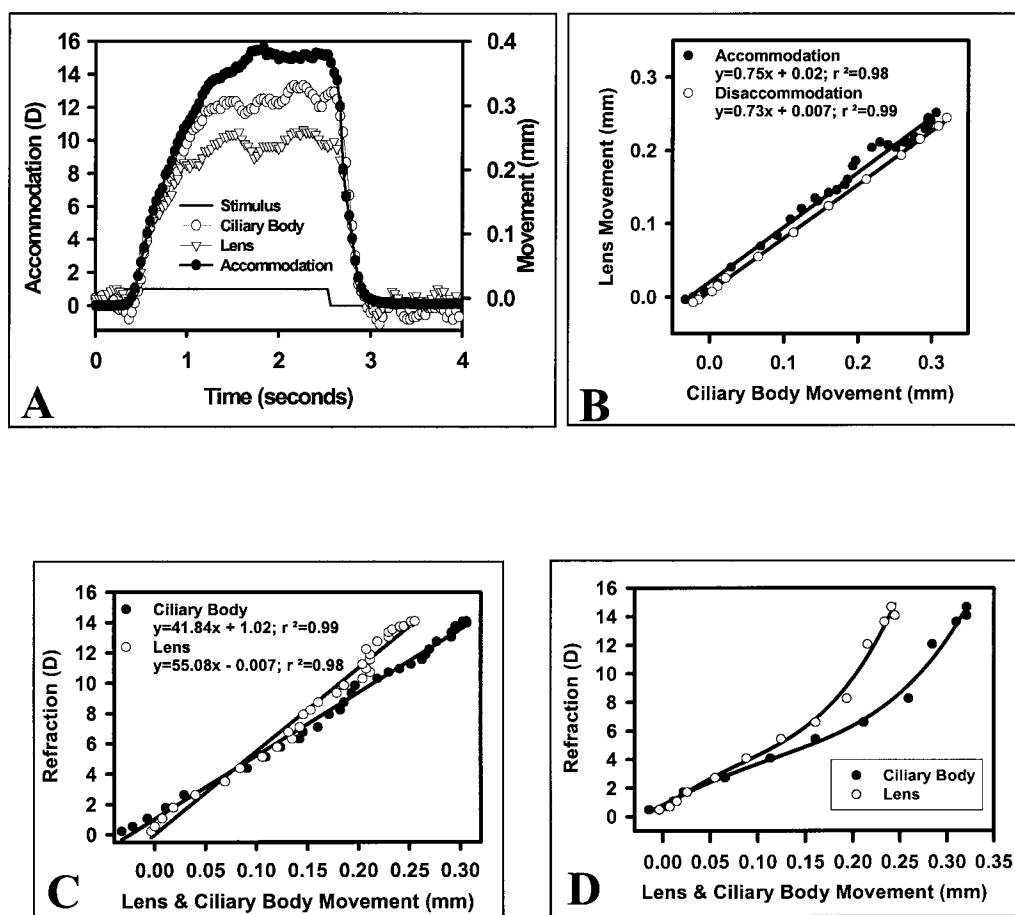
Figure 5. Graphs of lens and ciliary body movements and refractive changes in eye of 6-year-old rhesus monkey during centrally stimulated accommodation. Physical movements measured from goniovideography; refractive change subsequently measured by infrared photorefraction. **A,** accommodation (solid symbols; left axis) of ~15.5 D and movements of ciliary processes and lens equator (open symbols; right axis) are plotted together. Solid line shows onset, duration, and end of stimulus. Ciliary process tips and lens equator move away from sclera, and accommodative amplitude increases after stimulus onset. A relatively steady state is then reached, during which there are minor fluctuations in refractive state and maximally accommodated positions of lens equator and ciliary body. When stimulus ends, refractive state rapidly returns to baseline as lens and ciliary body move back toward the sclera. **B,** lens and ciliary body movement are highly linearly correlated during both accommodation and disaccommodation. **C,** lens and ciliary body movements plotted as a function of refractive change during accommodation. Lens equator and ciliary body movement away from the sclera are highly linearly related to refractive change, with slightly greater ciliary body movement per diopter. Thus, lens equator and ciliary body move in the same direction and at roughly the same rate and extent during accommodation in this monkey. **D,** lens and ciliary body movement during disaccommodation as a function of refractive change. During the early phase of disaccommodation, there is a relatively rapid decrease in accommodation for small movements of lens equator and ciliary processes. As accommodation nears baseline the lens and ciliary body movements become more nearly linear.

pharmacologically stimulated accommodation and the resulting 11% to 12% decrease in lens cross-sectional area. The only lens movement besides the classically described accommodative mechanism[2] that could cause this would be a backward translation of the lens. Such lens movement was never seen by UBM imaging. Further, by simple geometry (justified by neutralization of the corneal refractive power when the perfusion cell lens was used), a 12% decrease in cross-sectional area of an 8-mm diameter crystalline lens viewed at 90 mm from the slit lamp would require the crystalline lens to move 6 mm toward the retina. In an eye with an axial length of ~18 to 21 mm,[10] this is clearly impossible.

Our UBM findings in monkeys are opposite from those of Schachar et al[1,8] in humans and monkeys. Schachar et al[8] imaged the ciliary region of the unaccommodated eye, instilled topical pilocarpine, and then imaged the ciliary region of the accommodated eye at least 1 hour later to find an image superimposable over the first. It is extremely unlikely that exactly the same ciliary region could have been located again in this manner. Because localized regions of the

ciliary body may appear similar, it is possible that different regions of the ciliary body were identified before and after accommodation to give the appearance of very small (40–66 μm) lens movement toward the sclera. Close examination of the ciliary processes in the image pairs shown by Schachar et al[8] clearly reveal that the images are of regions with different ciliary processes and are not taken from *exactly* the same ciliary region of the eye. Given that our UBM experiments in monkey eyes enabled comparisons of the accommodated and unaccommodated images of the same ciliary region, we were able to identify images that superimposed at least as well as those shown by Schachar et al,[1,8] but with the opposite result and substantially larger lens equator movements. All told, several hours of dynamic video recordings clearly demonstrated movement of the lens equator away from the sclera.

Gonioscopic imaging is of substantially greater resolution than UBM imaging. Superimposable accommodated and unaccommodated images seconds apart show virtual absence of eye movement but movement of the lens equator away from the sclera. In addition, in sequences of 100
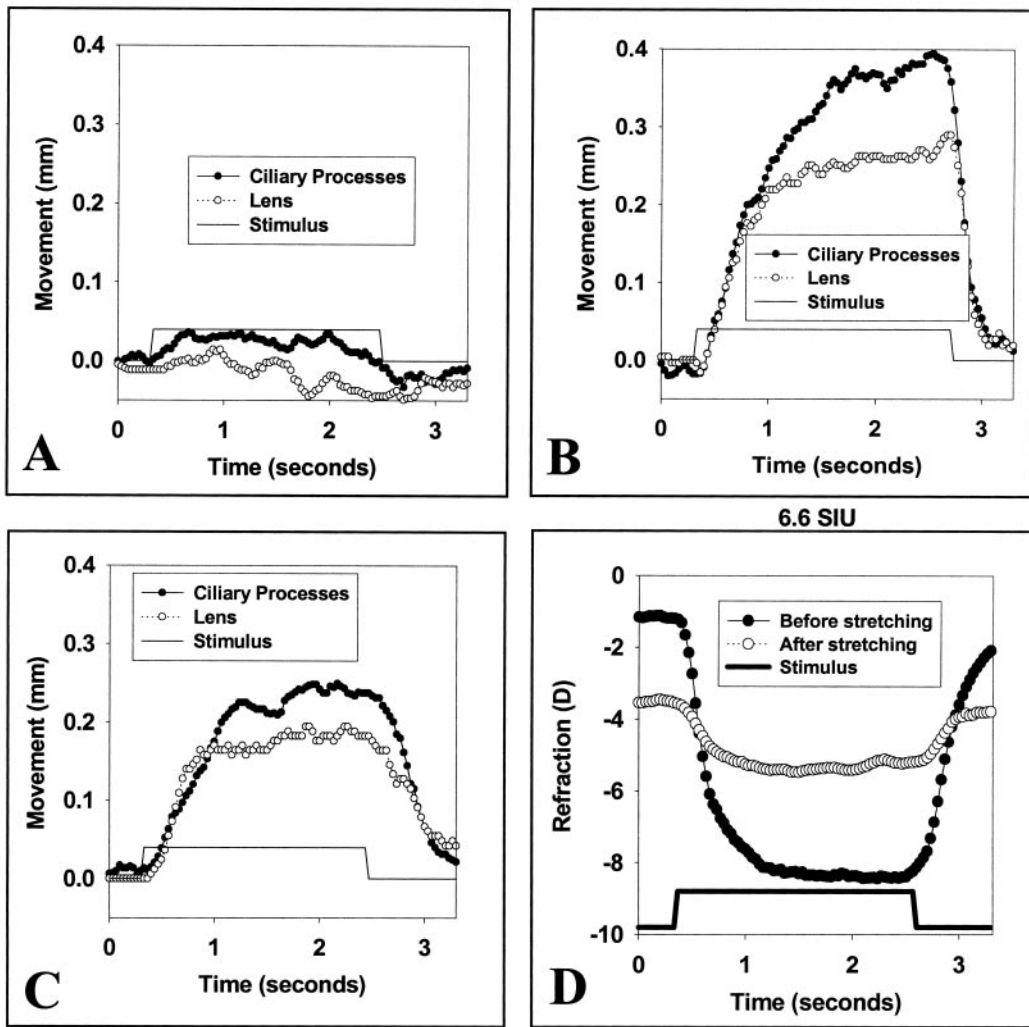
Figure 6. Anomalous movements of accommodative structures during central stimulation with tension applied to sutures tied beneath extraocular muscles. **A** and **B,** tension applied to lateral rectus of right eye of a cynomolgus monkey. **A,** temporal side: substantially reduced ciliary process movement, and movement of lens equator *toward* sclera during stimulation. **B,** nasal side: ciliary processes and lens equator move *away* from the sclera at stimulus onset. Movement of both structures continued throughout the stimulus. Together, **A** and **B** demonstrate a horizontal translation of the lens within the eye. **C,** temporal side, after reduction of tension on the lateral rectus muscle: return of normal movements of both structures. **D,** in a rhesus monkey, increasing the tension on the extraocular muscle sutures resulted in a more myopic resting refraction and reduced accommodative amplitude on central stimulation. A forward translation of the lens is one possible explanation for the myopic shift.

images taken in real-time showing progression of the lens movement, numerous image pairs are superimposable, all demonstrating lens movement away from the sclera.

Virtually superimposable image pairs from the accommodated and unaccommodated states were also obtained during pharmacologically stimulated accommodation, despite the length of time needed to achieve maximal accommodation. Small nonsystematic and random eye movements that occur as a consequence of respiration and heartbeat complicate the identification of completely superimposable images. Nonetheless, movement of the lens equator was in the same direction and of similar magnitude as that seen during centrally stimulated accommodation, and therefore cannot be explained by eye movements.

Our observation of a downward sag of the lens under the influence of gravity during centrally stimulated accommodation in the monkey, irrespective of head orientation and therefore irrespective of the direction of convergent eye movement (Fig 7), is inconsistent with Schachar's proposed accommodative mechanism. The demonstration by Schachar and Cudmore[9] of a lack of gravity effect on accommodative amplitude is unconvinc-

ing as evidence for absence of a gravitational influence on the lens; objective measures of accommodation were not used, and the subjective method used is unlikely to resolve small differences, let alone demonstrate whether anterior or posterior lens movement caused by gravity can occur during accommodation. Our findings do not address the issue of whether accommodative amplitude differs according to supine or prone position, but they do demonstrate that complete zonular relaxation can occur during accommodation, at least in monkeys, in contravention to Schachar's theory. The convergent eye movement that occurs with centrally stimulated accommodation ceases before maximal accommodation is reached (as evidenced by superimposable images), and the lens begins to sag only as maximal accommodation is reached, during a period of relative ocular stability.

The image subtraction from superimposable images for the UBM, gonioscopy, and perfusion cell lens techniques used to demonstrate movements of the accommodative structures should not serve as the only criteria to determine the direction of such movements. That our results are opposite those of Schachar attests to the fallibility of relying
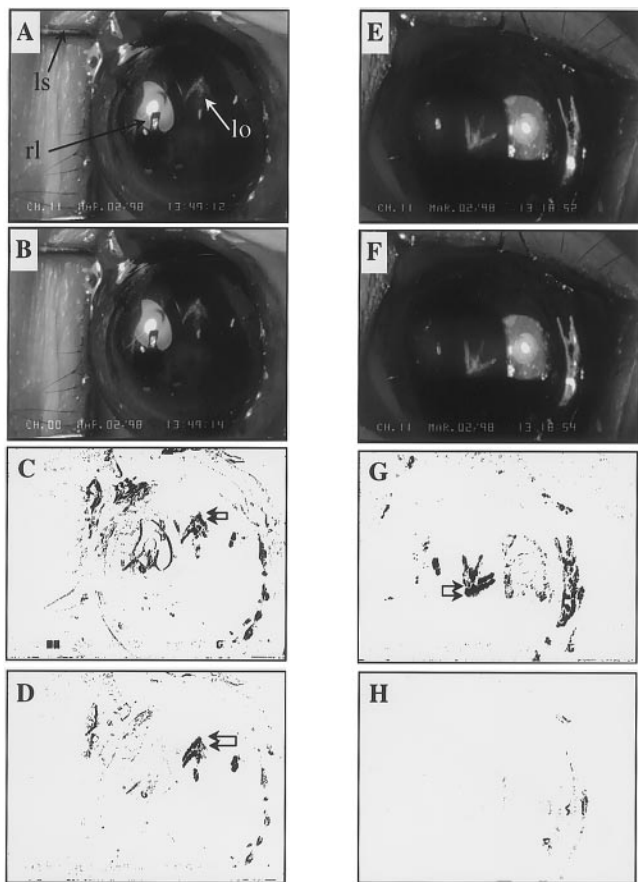
Figure 7. Effect of gravity on the lens of the left eye in a cynomolgus monkey during centrally stimulated accommodation. **A** through **D,** monkey is on left side; **E** through **H,** on right side. Eyelid held open with lid speculum (ls); reflection of room light (rl) seen on corneal contact lens. **A,** nearing maximal accommodation, after eye movements have ceased. **B,** 49 frames later, just before end of the stimulus. **C,** subtracted image pairs show incomplete ocular stability with predominantly horizontal eye movement (black detail), evidenced by absence of downward movement of the reflected light source, but lens opacity (lo) has moved down 129 μm as measured at the cornea (i.e., not accounting for corneal optics). Double arrow indicates extent of downward movement of lens opacity. **D,** during *disaccommodation,* two images, only three frames (1 millisecond) apart, show good eye stability and upward lens movement as depicted by double arrows. **E** and **F,** two images 51 images (1.7 seconds) apart with the monkey now on its *right* side demonstrate a 300-μm downward movement of lens opacity as measured at the corneal plane, but no downward movement of reflected room light. **G,** downward movement of lens opacity (double arrow), but not reflected room light, is seen. **H,** the monkey's heartbeat and respiration produced eye movement, as demonstrated by subtracting two images just two frames (67 milliseconds) apart in an unaccommodating eye. The identical image enhancement has been applied to panels **C, D, G,** and **H** to increase image contrast.

solely on image subtraction. Our image subtraction, image analysis, and graphs show not only the same direction of movements of the lens equator and ciliary processes but their extent as well. Complete ocular stability is rare. We have restricted our data presentation to a very small proportion of the experiments performed, in which eye movements do not occur. The major body of results, in which eye movements are present, demonstrate similar accommodative movements.

These complex experiments ideally require optimal eye positioning, illumination, ocular stability, and maximal accommodation simultaneously. Central stimulation does not produce maximal accommodative amplitudes as high as those resulting from pharmacologic stimulation,[10] and removal of the iris reduces the maximal accommodation achieved with either technique.[27] Although most experiments resulted in accommodative amplitudes (~10 D) considerably less than the maximal pharmacologically induced accommodative capabilities of young rhesus monkeys (30 to 40 D),[10] this was sufficient for the observation of considerable (250 to 300 μm) movement of the lens equator (Figs 5 and 6B, C). While the absolute magnitude of the gonioscopically recorded movements is subject to optical errors, this is not so for UBM imaging or imaging through the plano perfusion cell lens (which neutralizes corneal power). Although some variability was observed between results from the different techniques, attributable partly to optical (e.g., cornea, gonioscopy lens) and mechanical influences (e.g., orientation of the eye, tension on the sutures), in general, movements of the lens equator of 250 μm away from the sclera and decreases in lens cross-sectional area of 11% to 12% were observed for ~10 D of accommodation, in accordance with the classic mechanism proposed by Helmholtz.[2] The UBM findings, which were obtained from at least some noniridectomized monkeys, give the same conclusion as the video imaging, indicating that iridectomy does not alter the fundamental mechanism.

The Helmholtz accommodative mechanism, our reconfirmation of it, and our current understanding of the primary factors contributing to presbyopia[4,10,12,13,16,24] are inconsistent with Schachar's surgical procedure for the reversal of presbyopia[1,7] (Yang GS, Yee RW, Cross WD, et al. Invest Ophthalmol Vis Sci 38 [Suppl]:S497, 1997; Yang GS, Yee RW, Chuang AZ, Ruiz RS. Invest Ophthalmol Vis Sci 39 [Suppl]:S753, 1998). Although proponents of this surgical procedure have claimed to reintroduce accommodation in human subjects, only subjective near vision was used as an assessment of accommodation in these patients. No accommodation was found by objective infrared refractometry in three subjects examined by an independent observer.[29] It has been suggested on the basis of retinoscopic aberrations (David L. Guyton, M.D., personal communication) that surgical expansion of the sclera may induce lenticular aberrations resulting in a multifocal optical system, rather than true accommodation.

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