Accommodative Movements of the Vitreous Membrane, Choroid, and Sclera in Young and Presbyopic Human and Nonhuman Primate Eyes

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Purpose. We report, for the first time to our knowledge, dynamic movements of the vitreous membrane and peripheral choroid during accommodation, and age-related changes in the anterior sclera.

Methods. We studied 11 rhesus monkeys (ages 6–27 years) and 12 human subjects (ages 19–65 years). Accommodation was induced pharmacologically in human subjects and by central electrical stimulation in the monkeys. Ultrasound biomicroscopy, endoscopy, and contrast agents were used to image various intraocular structures.

Results. In the monkey, the anterior hyaloid membrane bows backward during accommodation in proportion to accommodative amplitude and lens thickening. A cleft exists between the pars plicata region and the anterior hyaloid membrane, and the cleft width increases during accommodation from 0.79 ± 0.01 mm to 1.01 ± 0.02 mm in young eyes ($n = 2$, $P < 0.005$), as fluid from the anterior chamber flows around the lens equator toward the cleft. In the older eyes the cleft width was 0.30 ± 0.19 mm, which during accommodation increased to 0.45 ± 0.20 mm ($n = 2$). During accommodation the ciliary muscle moved forward by approximately 1.0 mm, pulling forward the choroid, retina, vitreous zonule, and the neighboring vitreous interconnected with the vitreous zonule. Among the humans, in the older eyes the scleral contour bowed inward in the region of the limbus, compared to the young eyes.

Conclusions. The monkey anterior hyaloid bends posteriorly during accommodation in proportion to accommodative amplitude and the sclera bows inward with increasing age in both species. Future descriptions of the accommodative mechanism, and approaches to presbyopia therapy, may need to incorporate these findings.

Keywords: accommodation, presbyopia, vitreous membrane, lens, choroid

The exact manner in which the accommodative forces on the lens change during accommodation is unclear. The mechanism of accommodation in the human eye includes the antero-inward movement of the ciliary muscle during contraction. This allows the relaxation of the anterior zonule that suspends the lens, and thereby allows the lens to become thicker and more spherical in shape as the lens substance is molded by the capsule.

The vitreous, which is in close juxtaposition to the accommodative apparatus, also has been posited to be important to the accommodative change of the lens shape, either by pushing against the lens (according to Cramer in 1851[1]) or by forces of vitreous pressure that change the lens shape (suggested by Tscherning in 1904[2]), as cited by Fincham.[3] Coleman and Fish speculated that the lens, zonule, and anterior vitreous comprise a diaphragm between the anterior and vitreous chambers, and that a pressure gradient between the two chambers is initiated by muscle contraction, which, in turn, aids accommodative lens shape change.[4–6]

Reports exist that argue for and against a role for the vitreous in accommodation and presbyopia.[4,7,8] Some studies indicate that accommodative amplitude is not diminished in human patients following vitrectomy.[7] Another study reported a loss of approximately 2 diopters of accommodation in human patients (ages 33–41 years) following pars plana vitrectomy.[9] In both instances, the vitrectomy procedure avoids the anterior hyaloid membrane (vitreous face) and the periphery of the vitreous. The hydraulic theory posits that, during accommodative contraction, the ciliary muscle exerts pressure upon the aqueous in the posterior chamber, where it is confined by the iris as the pupil constricts onto the lens surface, compressing the lens equator and causing the anterior lens surface to bulge.[10–12] Fincham discounted this theory, due to the fact that accommodation is unimpaired by iridectomy or aniridia.[3] However, Crawford et al. reported a 40% loss in accommodative amplitude after iridectomy in the monkey eye.[13] To our knowledge, the accommodative movements of the vitreous/anterior hyaloid and peripheral choroid have never been observed in vivo in the human or

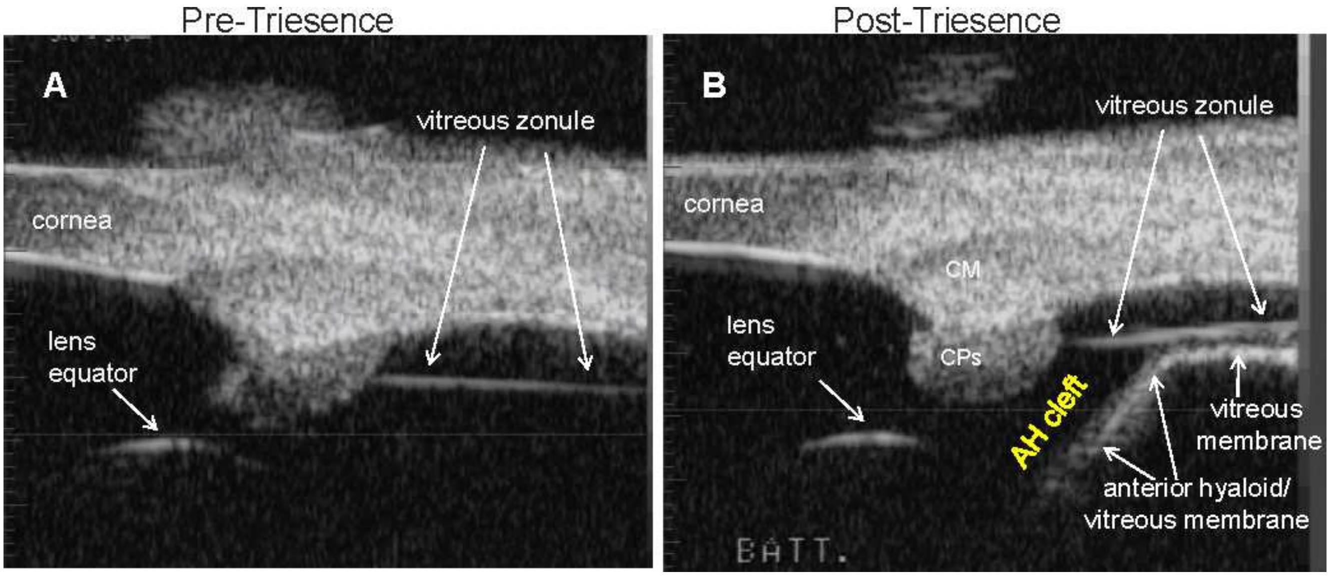

FIGURE 1. (A) Typical UBM image in an 8-year-old rhesus monkey before injection of triamcinolone (Triesence). The vitreous zonule was clearly visible, but the anterior hyaloid/vitreous membrane was not visualized. (B) UBM image 24 hours after injection of Triesence in the same monkey eye and quadrant as in (A). The location of the vitreous membrane and anterior hyaloid portion of the vitreous membrane are now clearly visible as the Triesence clings to the vitreous membranes. There is a cleft between the ciliary processes (pars plicata region) and the anterior hyaloid membrane; termed the AH cleft. CP, ciliary processes; CM, ciliary muscle.

monkey eye, not even in our recent ultrasound biomicroscopic (UBM) and scanning electron microscopic study, demonstrating the existence of the vitreous zonule.[14]

To visualize and record the dynamics of the accommodative mechanism, high-resolution imaging (i.e., UBM) is necessary and can be performed in anesthetized monkeys.[15–19] Magnetic resonance imaging (MRI)[20] cannot capture dynamic movements of the various intraocular structures during accommodation, and cannot image the vitreous zonule or the vitreous anterior hyaloid membrane, due to resolution limitations. The static images at rest, and after pharmacologic stimulation to induce accommodation, do supply some valuable information; however, they do not supply the visualization of the structures' dynamic movements and the analyses in real time that are available by doing the in vivo monkey experiments.

Our study sought to develop a technique, using contrast agents, to visualize the vitreous (anterior hyaloid) membrane, and determine its accommodative movement in young and old human and monkey eyes. We also report, for the first time to our knowledge, visualization of the dynamic movements of the peripheral choroid during accommodation/disaccommodation in the living monkey eye, along with changes in the anterior sclera at the level of the scleral spur.

MATERIALS AND METHODS

Measurements of accommodation, ultrasound biomicroscopy techniques, stimulation of accommodation, and so forth, for the monkey and the human have been described in our companion study.[21] Images from the same experimental sessions as described therein[21] were used for this study. We recruited 12 human subjects ranging in age from 19 to 65 years with normal eyes, and 11 rhesus monkeys (*Macaca mulatta*) ranging in age from 6 to 27 years with normal eyes were studied, as described in detail in the companion study.[21]

This research adhered to the tenets of the Declaration of Helsinki (human subjects) and to the ARVO Statement for the Use of Animals in Ophthalmic and Vision Research, and to institutionally approved animal protocols (rhesus monkeys).

Ultrasound Biomicroscopy

Triamcinolone acetonide (50 µL of 40 mg/mL, Triesence; Bristol-Meyers Squibb Company, Princeton, NJ), which adheres to the vitreous membranes/fibers,[22] was administered via pars plana injection to enhance visualization (by either UBM or endoscopy) of the intravitreal structures (i.e., anterior hyaloid) in 4 rhesus monkey eyes.

For the monkeys and human subjects, analogous images were collected, with the anterior/posterior ends of the ciliary body and vitreous zonule oriented in a horizontal direction within all images.

Endoscopy in the Monkey Eye During Accommodation

An endoscopic camera system (Model E2 endoscopic camera; EndoOptiks, Little Silver, NJ) with a fiberoptic light and a curved imaging probe to allow passage behind the lens, (the camera and the light source were contained within the 20-guage probe), was inserted via the pars plana in 3 rhesus monkey eyes to image the intraocular structures during centrally stimulated accommodation. The images were recorded to tape. Two entry points were required: one for the endoscopic probe and one for a sutureless 25-gauge infusion cannula (to maintain IOP). One to two weeks before endoscopy, a 50 µL bolus of an aminofluorescein dye (0.02% 5-[4,6-dichlorotriazin-2-yl]-aminofluorescein [DTAF] hydrochloride; Sigma-Aldrich, St. Louis, MO), which binds to collagen, and fluoresces with excitation and emission spectra similar to sodium fluorescein,[23] was injected via the pars plana into the vitreous cavity to enhance visualization of the vitreous fibers/anterior hyaloid membrane.

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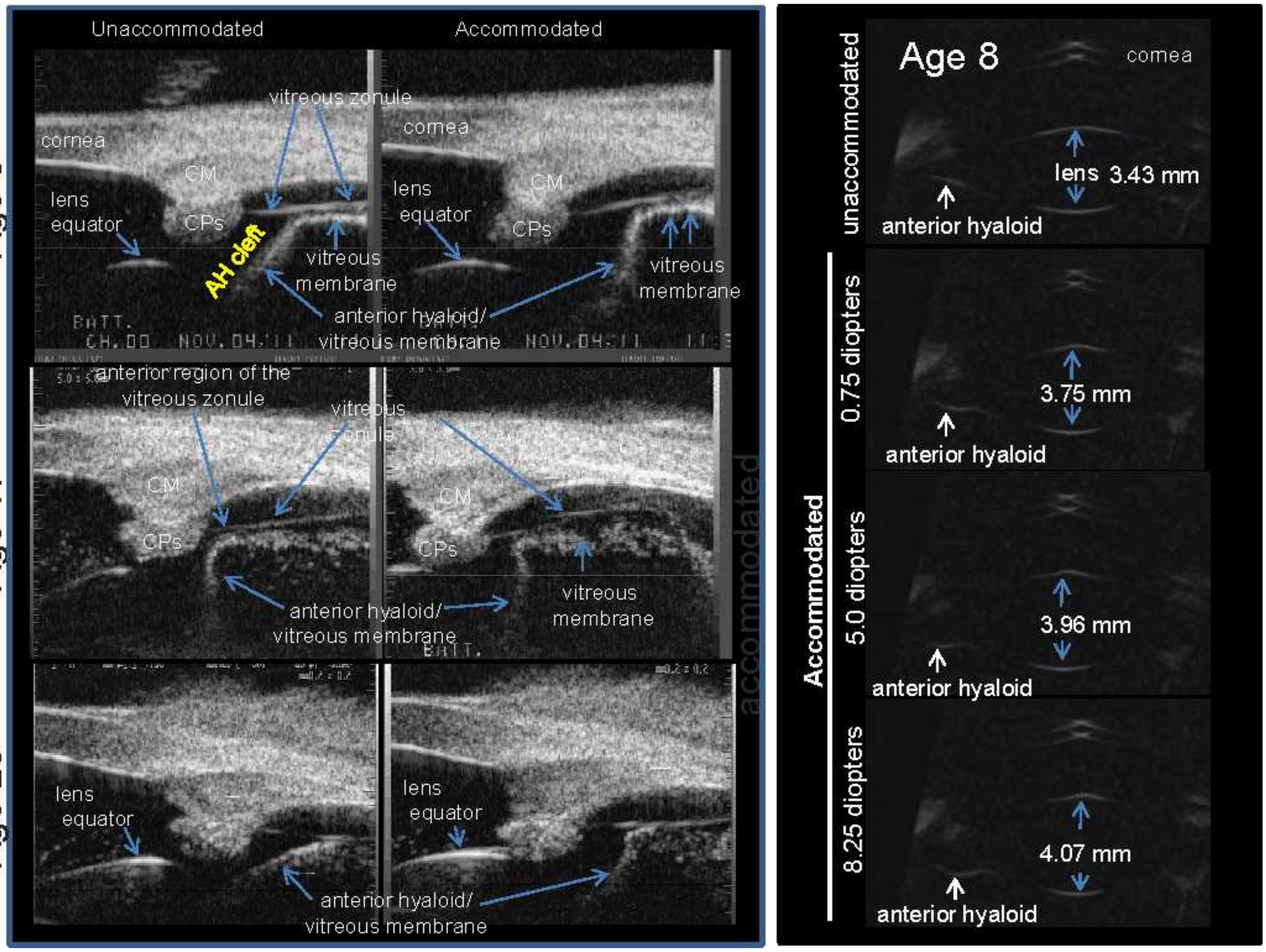

Figure 2. *Left* and *Middle*: UBM images in the temporal quadrant in 8-, 17-, and 25-year-old rhesus monkeys in the unaccommodated and maximally accommodated states following injection of Triesence (triamcinolone acetonide), which clings to the vitreous membrane. *Middle*: The anterior hyaloid relaxes/curves posteriorly during accommodation (see also Supplementary Video Clips S1, S3). The AH cleft, which lies between the ciliary processes and the anterior hyaloid, is reduced in the older eyes (ages 17 and 25) versus the young eye (age 8). *Right*: UBM images of the anterior segment in an 8-year-old rhesus monkey in the unaccommodated state and during various accommodative amplitudes. *Arrow* indicates the anterior hyaloid. The backward bowing of the anterior hyaloid is more pronounced as the amplitude of accommodation increases.

Results

Accommodative Movements of the Vitreous Face (Anterior Hyaloid Membrane) in Monkey Eyes

Following intravitreal injection, the triamcinolone acetonide clung to the vitreous membrane, allowing clear visualization of the vitreous membrane location and its movements using UBM imaging (Fig. 1, Supplementary Video Clips S1, S2).

In the young monkey eyes during accommodation, as the muscle and vitreous zonule moved forward (by approximately 1.05 mm[21]), the anterior hyaloid membrane bowed backward from the lens into a curved shape that extended between its deviation point from the vitreous zonule and its attachment point to the posterior lens/Wieger's ligament (Fig. 2, Supplementary Video Clips S1, S2). The anterior hyaloid/vitreous membrane did not push against the peripheral posterior lens during accommodation. There was a cleft between the posterior aspect of the ciliary processes and the vitreous membrane/anterior hyaloid (AH cleft, Fig. 1), possibly analogous to the Canal of Petit[24–26] or to the zonular chamber as reported by Minsky.[27] The thickness of the AH cleft measured 0.79 ± 0.01 mm and increased during maximum accommodation to 1.01 ± 0.02 mm, an increase of 0.20 ± 0.01 mm ($n = 2$, Fig. 2, Supplementary Video Clips S1, S2). In addition, during accommodation, material (likely triamcinolone acetonide) suspended in the aqueous humor of the anterior chamber angle could be visualized moving around the lens equator in a posterior direction (Supplementary Video Clip S2), toward the enlarging AH cleft. This indicated fluid flow into the AH cleft during accommodation.

In vivo images showed that the vitreous zonule and the vitreous membrane were adjacent to each other in the region of the pars plana of the ciliary body, but at approximately 0.80 mm posterior to the pars plicata they separated, forming the AH cleft. In this area, the anterior hyaloid turned in a centripetal direction toward the posterior lens equator, where it attached to Wieger's ligament.

During the accommodative response, the backward bowing of the anterior vitreous membrane and enlargement of the AH cleft began to occur immediately upon muscle contraction, along with centripetal lens equator movement and lens thickening (Supplementary Video Clip S3)—even during the smallest accommodative amplitudes (Fig. 2, right panels). Therefore, there was not a threshold position for the muscle/vitreous zonule to achieve for the vitreous membrane to bow backward. The posterior pole of the lens moved posteriorly

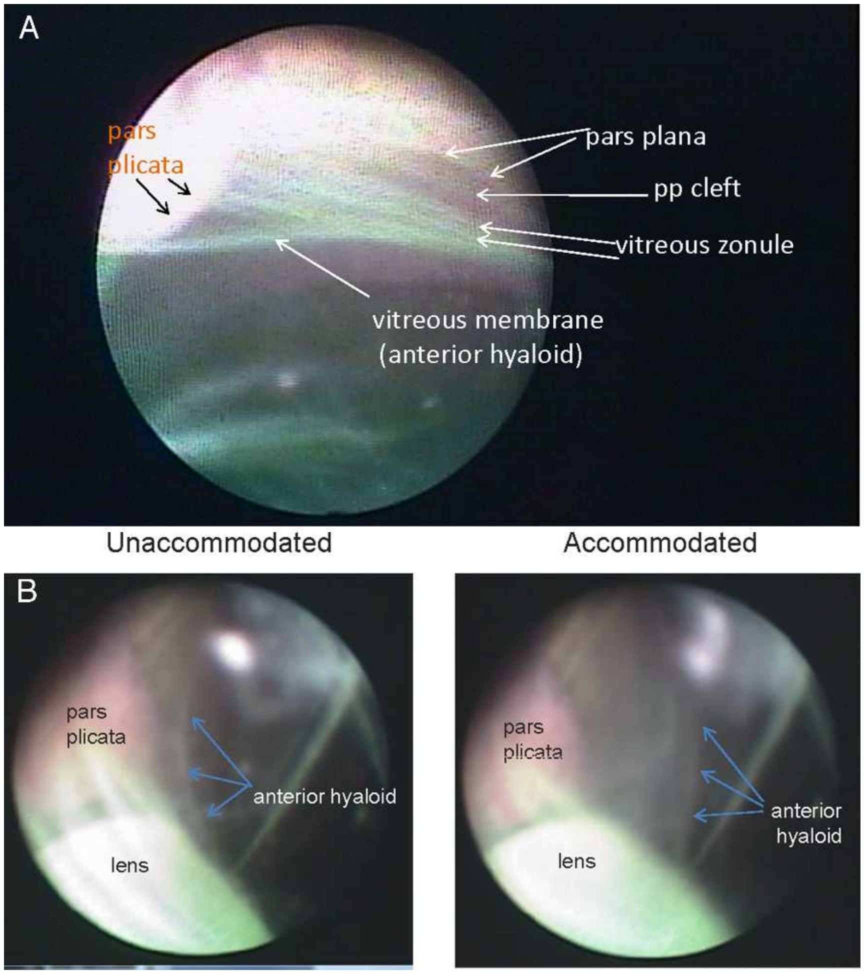

Figure 3. (**A**) Endoscopy in a 19-year-old rhesus monkey eye. Note the structure that extends from the posterior insertion zone of the vitreous zonule past the pars plicata internal to the vitreous zonule. An aminofluorescein dye was used as a contrast agent to facilitate visualization of the vitreous membrane or zonula. See Supplementary Video Clip S4 for movement of the vitreous membrane during accommodation. pp cleft, pars plana cleft, which is the cleft between the pars plana and vitreous zonule. (**B**) Endoscopy in a 19-year-old rhesus monkey eye. Note anterior hyaloid configuration bowing toward the lens and pars plicata in the resting state, whereas in the accommodated state the anterior hyaloid bows in a posterior direction. An aminofluorescein dye was used as a contrast agent to facilitate visualization of the vitreous membrane or zonula. See Supplementary Video Clip S4 for movement of the vitreous membrane during accommodation visualized using an endoscopic camera.

during the accommodative response, as visualized by UBM (Supplementary Video Clip S3) imaging. The anterior hyaloid and its accommodative backward bowing were observed by UBM (Fig. 2, Supplementary Video Clips S1–S3) and endoscopy (Fig. 3, Supplementary Video Clip S4). The portion of the vitreous membrane that was adjacent to and interconnected with the intermediate vitreous zonule[14] up to the AH cleft also was pulled forward with the vitreous zonule parallel to the curvature of the eye during accommodative muscle contraction (Supplementary Video Clip S1). The accommodative forward movement of this portion of the vitreous membrane (i.e., interconnected with the vitreous zonule[14]), in turn, pulled forward much of the neighboring inner vitreous near and posterior to the region of the ora serrata (Supplementary Video Clip S5), seen through movement of the triamcinolone acetonide particles.

In the two older monkey eyes (aged 17 and 25 years), the anterior hyaloid also curved posteriorly during accommodation. The AH cleft (between the anterior hyaloid and posterior region of the pars plicata region) was reduced, compared to the young eyes. The average thickness of the AH cleft in the resting eyes was 0.30 ± 0.19 mm and during accommodation increased to 0.45 ± 0.20 mm. Further, in some places, the older vitreous membrane appeared to form adhesions to the anterior region of the vitreous zonule (Fig. 2, Supplementary Video Clip S6).

Attachments Between the Posterior Insertion Zone of the Vitreous Zonule and the Posterior Lens Equator (PVZ INS-LE Strands)

In addition to the vitreous zonule in the eyes of the human subjects, there always was a prominent continuous structure between the posterior insertion zone of the vitreous zonule and the posterior lens equator (here termed PVZ INS-LE strands; Figs. 4A, 4B). The distance between the vitreous zonule posterior insertion zone and the posterior lens equator (PVZ INS-LE strand distance) did not change significantly during accommodation (Fig. 5). Therefore, the vitreous zonule and PVZ INS-LE strand moved anteriorly during accommodation.

The Monkey Peripheral Choroid

UBM imaging during central electrical stimulation of the E-W nucleus, at maximal stimulus settings, showed that the ciliary

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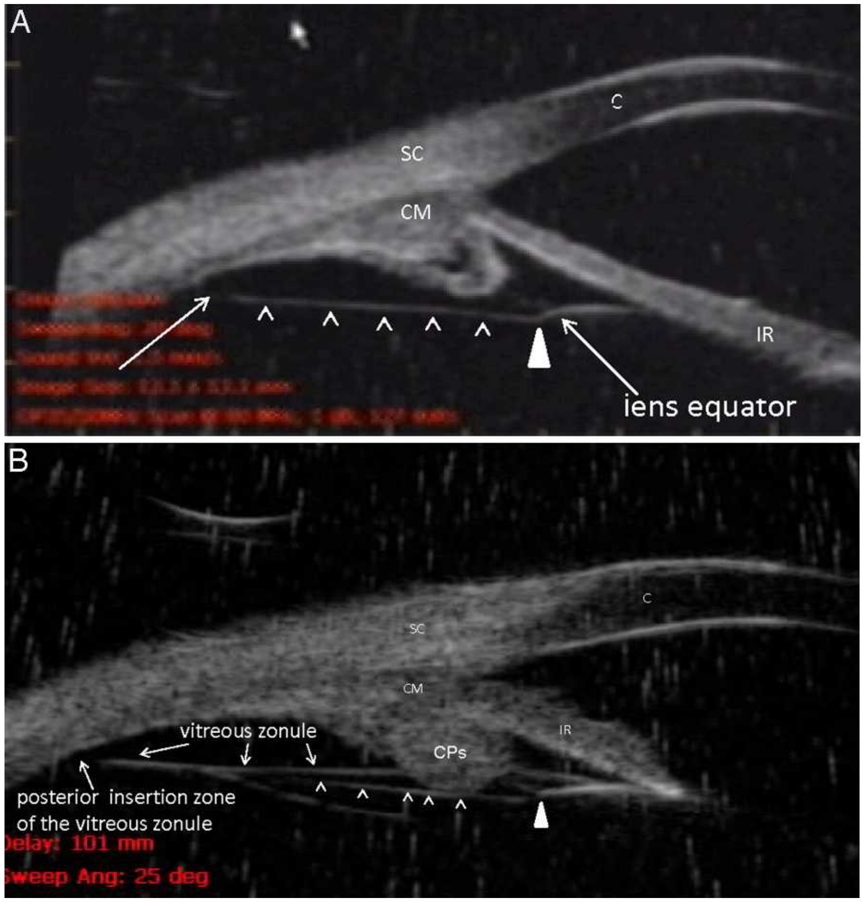

FIGURE 4. (**A**) UBM images (50 mHz, UBM-ER) in the nasal quadrant of a 19-year-old male human. Note the connection between the posterior insertion zone of the vitreous zonule (*arrow*) and the posterior aspect of the lens equator (*large arrowhead*), seen in all 12 human subjects, termed PVZ INS-LE strand (*arrowheads*). IR, Iris; C, Cornea; SC, Sclera. (**B**) UBM image in the resting eye of a 65-year-old human subject. Note that a portion of the PVZ INS-LE stand (*small arrowheads*) is visible that extends between the posterior insertion zone of the vitreous zonule and the posterior lens equator (*large arrowhead*), as in (**A**) with the strand passing immediately internal to the CPs. The PVZ INS-LE strand lies between the vitreous zonule and vitreous membrane.

muscle pulled forward not only the vitreous zonule and PVZ INS-LE strand, but also the peripheral choroid and retina, as the muscle contracted and moved forward during accommodation (Supplementary Video Clip S7). During disaccommodation, the muscle and choroid/retina returned to the resting posterior position. The accommodative forward movement included the choroid/retinal tissue at least 4 to 5 mm posterior to the region of the ora serrata (Supplementary Video Clip S7) and in some instances 6 to 7 mm beyond the region of the ora serrata. We were unable to visualize further posteriorly as this was out of the range of the UBM instrument.

During accommodation the young vitreous zonule was moved forward by 1.05 ± 0.067 mm,[21] pulled by the ciliary muscle apex to which it was attached, and it follows that the amount of forward movement of the interconnecting tissues to the vitreous zonule and ciliary muscle also were moved forward or were stretched forward by that amount (i.e., choroid and the neighboring vitreous interconnected with the vitreous zonule).

Sclera

In the human eyes, imaging of the sclera showed one striking difference between the young and older eyes during accommodation. In the accommodated state of all 4 young human eyes, there was a noticeable "notch," or localized scleral dip, in the limbal region of the nasal quadrant (Fig. 6), compared to the unaccommodated state. In all four older accommodated eyes, instead of this notch, we discerned an extensive limbal scleral depression. This gave the nasal quadrant in the older eyes the appearance of an "inward bowing" contour shape (Fig. 6), and this was more pronounced in the accommodated state versus the unaccommodated state of the older eyes. These phenomena were not present in the temporal quadrant in either the young or older eyes.

In the monkey eyes, the presence of the extraocular muscle sutures induced conjunctival swelling and, as a result, it was far more difficult to visualize distinct scleral edges. Nonetheless, this same phenomenon was present in two young and two older monkeys where proper images were obtained. The "inward bowing appearance" in the monkey eyes is demonstrated in Figure 7.

DISCUSSION

Vitreous Movements

To our knowledge, this is the first report of dynamic imaging of the anterior hyaloid membrane/vitreous face during accommodation in the rhesus monkey. Burian and Allen noted similar observations using a gonioscopy lens in two human subjects:

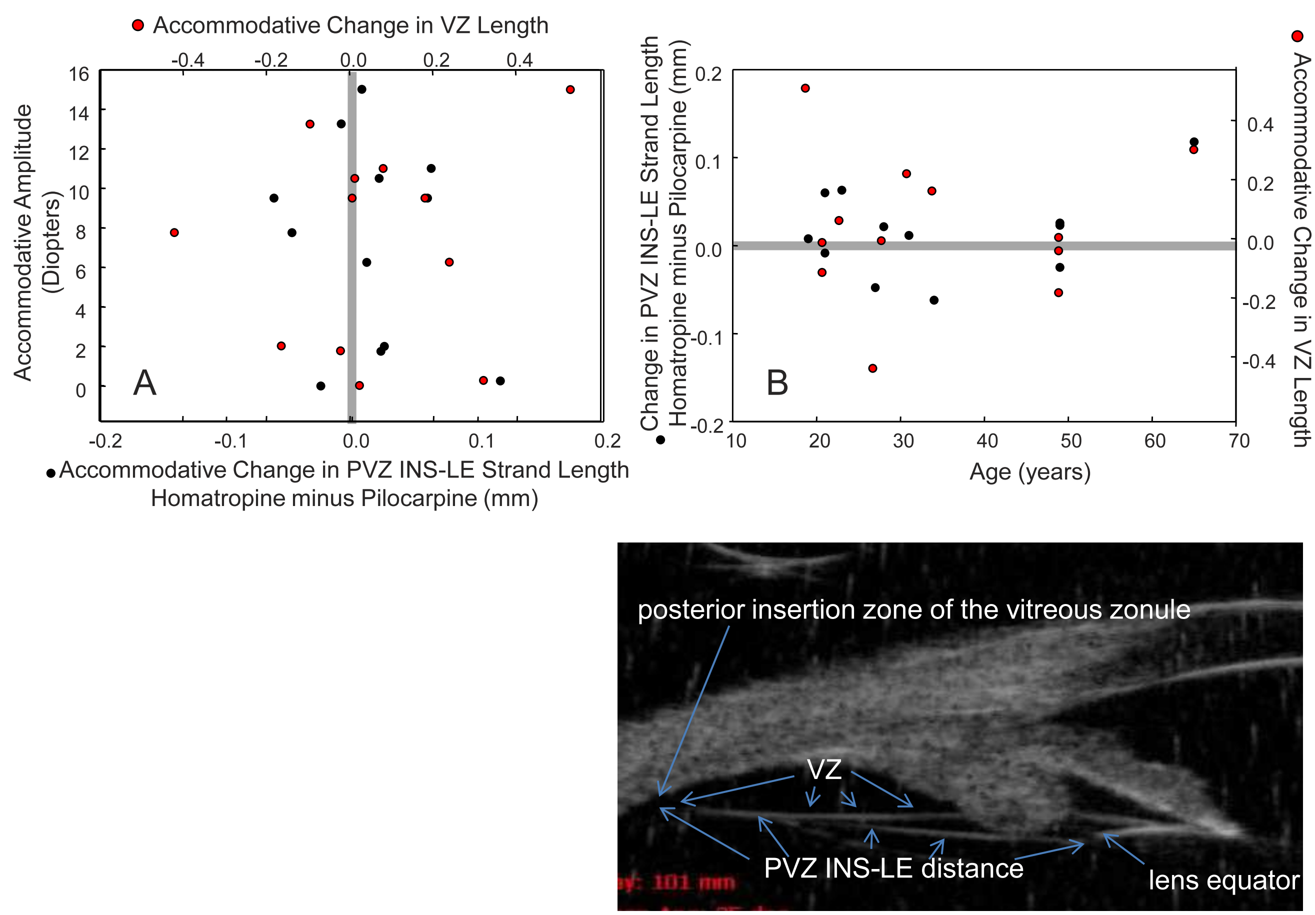

Figure 5. Accommodative change in vitreous zonule (VZ) length (unaccommodated minus accommodated) plotted versus accommodative amplitude (**A**) or age (**B**). In addition, there was a fiber/strand connecting the posterior VZ insertion zone to the posterior lens equator (PVZ INS-LE strand), and this distance was measured in the resting (homatropinized) and accommodated (pilocarpinized) states. The accommodative change in distance (change in length), unaccommodated minus accommodated, was calculated and plotted versus accommodative amplitude (**A**) or age (**B**). Given the age of the subject, the small accommodative change in VZ length (*red circles*), and the small accommodative change in PVZ INS-LE strand length (*black circles*) were important for predicting the small accommodative lens thickening.[21] Also, it is important to note that these two accommodative distance changes are dependent upon the position of the posterior insertion zone of the VZ, and this also may impact accommodative forward movement of the lens equator.[21]

that is, backward bowing/relaxation of the anterior hyaloid membrane during accommodation.[28]

The backward bowing of the anterior hyaloid in the in vivo images (Supplementary Video Clips S1–S3) during accommodation is in opposition to previous reports that the lens, zonule, and anterior hyaloid membrane act as a diaphragm during accommodation, according to Cramer,[1] as reported by Coleman[4] and Fincham,[3] which would imply that the anterior hyaloid (vitreous face) would be taut during accommodation and press against the posterior peripheral lens.[4] The vitreous membrane attaches to the vitreous zonule posterior insertion zone and courses anteriorly adjacent to the posterior vitreous zonule, until it veers away from the vitreous zonule in a centripetal direction to attach to Wieger's ligament, in agreement with previously reported morphologic findings.[14] We reported previously that Wieger's ligament moves centripetally during accommodation,[29] likely due to the slackening of the anterior hyaloid membrane. Posterior restriction of the forward movement of the vitreous zonule and ciliary muscle could restrict the backward bowing of the anterior hyaloid membrane during accommodation, and thereby dampen accommodative lens thickening and centripetal movement of Wieger's ligament.

The fluid flow from the anterior chamber angle around the lens equator toward the vitreous compartment indicates a change in anterior chamber pressure and volume induced by lens thickening and the redistribution of lens mass, as proposed by other researchers.[6] The Helmholtz theory of accommodation also would predict that the lens thickening would decrease the anterior chamber volume, and thereby fluid would flow around the lens equator toward the vitreous compartment.[30] The posterior bowing of the vitreous membrane during accommodation may be in response to or is allowing the influx of fluid from the anterior chamber. Likewise, the backward movement of the posterior pole of the lens (visualized by UBM in Supplementary Video Clip S3) and previously reported[4,31–34] as the lens thickens during accommodation may contribute to or be consequent to the backward bowing of the anterior hyaloid. Either sequence of events in turn would require that the vitreous fluid or vitreous structures posterior to the lens posterior pole and posterior to the anterior hyaloid would necessarily also move backward. Although the function of the anterior hyaloid during accommodation may not be as previously proposed by Cramer's theory[1] or by the catenary theory of accommodation,[5,6] it clearly is reconfigured in a "dose-dependent" (i.e., accommodative amplitude dependent) manner during the accommoda-

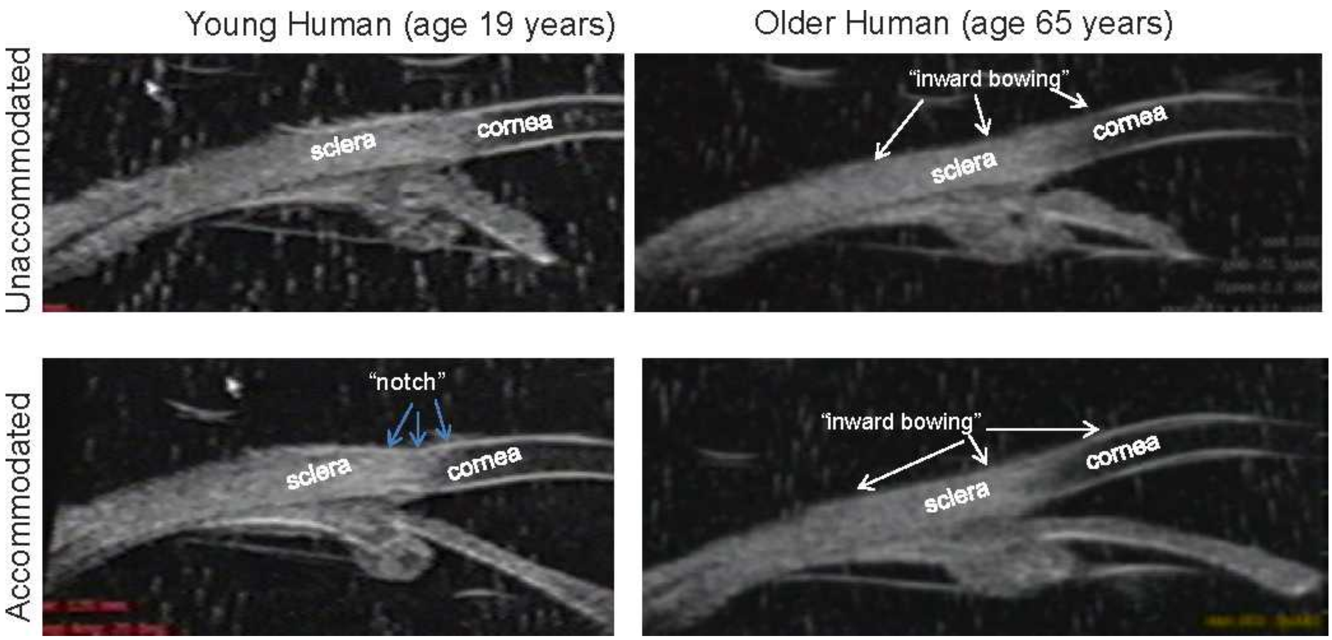

FIGURE 6. Age-related change in the geometry of the sclera, ciliary body, and zonula: human. Note the deformation of the outer limbus ("notch," *arrow*) in the accommodated young eye compared to the unaccommodated eye. In the older eye there is a discernible depression or "inward bowing" contour to the sclera. The notch appearance in the young sclera and the "inward bowing" of the older sclera occur in the nasal, but not the temporal quadrant. In the older eye there is not much difference between the unaccommodated and accommodated state with regard to the ciliary body/muscle shape. The young accommodated muscle clearly is in the anterior inward position compared to the unaccommodated eye. The "inward bowing" phenomena also is present in the monkey eye (see Fig. 7), although this has not been observed as frequently due to iatrogenic conjunctival swelling in the monkey eye.

tive/disaccommodative response and may have a role in accommodation.

Coleman has posited accommodative support to the posterior lens surface by "forward vitreous pressure due to a gradient of fluid or hydraulic pressure between the vitreous body, the lens and the anterior chamber."[4,5] One could argue that the flow of aqueous into the vitreous compartment from the anterior chamber during accommodation could supply hydraulic support to the peripheral posterior lens surface as it is trapped in the AH cleft by the anterior hyaloid membrane, with central vitreous support at the lens posterior pole—not unlike a piston. However, this is highly speculative and we did not measure pressure. Further, it has been documented that the posterior pole of the lens also moves posteriorly during accommodation, and after removal of the lens substance the capsule bows backward by 0.7 mm (Croft, et al. *IOVS* 2013;54:ARVO E-abstract 386). However, it is likely that the posterior movement of the posterior lens surface in the phakic eye is limited by the presence of the central vitreous.

Conversely, the results also could be interpreted in a different way. One could argue that during accommodation the capsule reshapes the lens, which in turn exerts force against the anterior chamber, producing a hydraulic pressure in a posterior direction. Given the direction of the aqueous fluid movement around the lens equator into the AH cleft of the vitreous compartment toward the anterior hyaloid, this flow could induce the backward bowing of the hyaloid. The posterior pole of the lens, and thereby central vitreous, also moves backward during accommodation.[4] Thus, the backward bowing of the anterior hyaloid and the posterior movement of the central vitreous could mean that the vitreous actually is making room, in a posterior direction, to allow for the accommodative response to occur. This could explain why the pressure increases in the midsagittal region of the vitreous, where Coleman measured pressure during accommodation. Another possibility is that the vitreous membrane may have a role in the flattening of the posterior lens surface during disaccommodation by the tension placed on Wieger's ligament. During accommodation, the vitreous membrane relaxes, which may facilitate the increase in curvature of the posterior lens surface.

At or near maximum accommodative amplitudes, the relaxation of the anterior, equatorial, and posterior zonules that suspend the lens explains the lens fall with gravity reported previously.[16,18] For the lens to fall with gravity, all suspensory membranes/fibers/zonules necessarily must be relaxed, with the lens being held loosely in place by the relaxed membranes/fibers/zonules. Therefore, the bending of the vitreous membrane, with the bow of the curved membrane pointed posteriorly, also may represent relaxation or slackening,[16,18] which would explain the lens fall with gravity.

Although the anterior hyaloid bends/relaxes even during minimal amplitudes of accommodation, the anterior zonule does not relax until at or near maximum accommodation, perhaps due to the concomitant centripetal movement of the lens. The bending posteriorly of the vitreous membrane also could be part of a pressure detection mechanism, in response to the influx of fluid due to the lens shape change. If this is the case, there may be pressure or mechanosensitive cells present, for example, such as those described in the stroma of the pars plicata ground plate next to the circular portion of the ciliary muscle.[35] Muscle contraction/relaxation then could be influenced by the described intrinsic nervous system in this region.[35,36] Further imaging of the anterior hyaloid in rhesus monkeys throughout the age range would be required to elucidate the accommodative function of the anterior hyaloid membrane and its change with age.

During accommodation, although the posterior pole of the lens moves slightly backward as the lens thickens, the lens equator moves slightly forward (i.e., the lens assumes a more

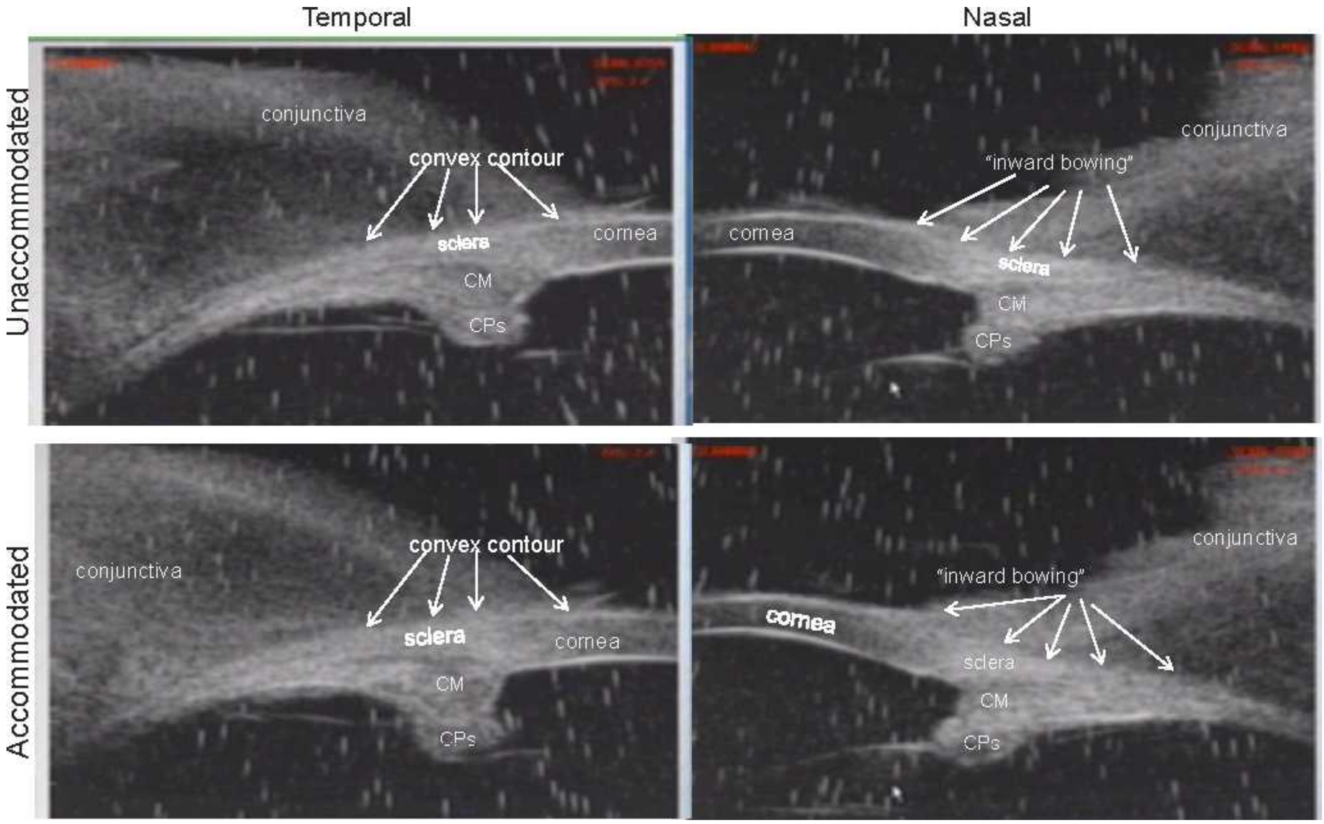

Figure 7. UBM images taken in a 22-year-old monkey eye in the unaccommodated and accommodated state. Note that the deformation of the outer limbus in the nasal quadrant is more pronounced in the accommodated eye compared to the unaccommodated eye. In the older eye there is a discernible depression or "inward bowing" contour to the sclera. The "inward bowing" of the older sclera occurs in the nasal, but not the temporal quadrant. Also, the cornea and sclera are thinner in the nasal quadrant compared to the temporal quadrant. The "inward bowing" phenomena as seen in the human has not been observed as frequently in the monkey eye due to iatrogenic conjunctival swelling.

spherical configuration).[21] For the first time, using UBM, we observed direct attachments between the posterior lens equator and the vitreous zonule posterior insertion zone in the human eye in vivo (PVZ INS-LE strands). These connections could impact accommodative forward movement of the lens equator,[21] creating a posterior "drag" on the ability of the lens equator to move forward and of the lens to thicken during accommodation.[21] The PVZ INS-LE strands that we imaged, without connections to the "plexus," were posited to exist by Rohen and are in a similar location, and have similar connections to one of the groups of the "posterior zonular fibers" reported by Farnsworth and Burke.[37] Whether the structures reported by Farnsworth and Burke that extend between the pars plana and posterior lens surface (termed posterior zonule) are the same as the PVZ INS-LE strands that we imaged in our study is unknown. Further study of the PVZ INS-LE strands would be necessary to determine the function of these strands during accommodation.

The Peripheral Choroid

Moses presented evidence, using transillumination of the eye, that the human retina stretches forward (by approximately 0.5 mm or 2%) in the region of the ora serrata during accommodation.[38] However, the results were variable and the technique could examine only the ora serrata region. Hollins (using techniques involving Badal optics) postulated that the central human retina stretches by 4.5%, but could not measure it directly.[39] We show, for the first time to our knowledge, the accommodative/disaccommodative movements of the choroid/retina by dynamic UBM imaging (Supplementary Video Clip S7) in the rhesus monkey eye, illustrating that the accommodative forward movement includes retina/choroidal tissue that is located at least 4 to 7 mm posterior to the region of the ora serrata. This demonstrated that the stretch/movement of the tissue is not confined to the region of the ora serrata and that this may have implications for accommodation-dependent distortions in visual perception. Rapid significant accommodative shear stress might create a retinal tear and subsequent retinal detachment. Sustained contraction of the ciliary muscle, induced by echothiophate, resulted in cystoid changes in the peripheral retina.[40–42]

The function of the vitreous zonule may be to avoid shear between the retina and vitreous and/or to facilitate the eye's ability to track smoothly the movement of objects (without distortions, i.e., minimizing over- or under-shoots) within its field of view. Alternatively, the role of the vitreous zonule may be related to some other accommodative function as yet undiscovered. Further imaging of the region is necessary to determine the exact mechanism of action.

Sclera

With age the scleral spur lies increasingly nearer to the lens equator, as reported in our companion study.[21] The scleral depression ("inward bowing") could contribute to this phenomenon and also may contribute to the age-related decrease in circumlental space. It is unknown why the age-related "inward bowing" in sclerocorneal contour occurs. It may be due to the lifelong contraction of the muscle placing stress on the corneosclera, perhaps thereby inducing the change in contour of the sclera. This is analogous to monkeys that undergo long-term pilocarpine treatment exhibiting an anterior-posterior shortening of Schlemm's canal[41] consequent to backward movement of the cornea toward the scleral spur, due to accommodative ciliary muscle contraction. The tips of the meridional muscle bundles provide the anterior attachment of the ciliary muscle to the scleral spur, and in addition to the presence of true tendons, these muscle fibers also ultrastructurally and biochemically somewhat resemble the fast fibers of striated muscle.[43] It was hypothesized that the meridional muscle tips can contract faster than the rest of the muscle and supply stiffness to "brace" the muscle for effective accommodation.[43,44] In any event, the change in scleral contour and the inner contour of the muscle clearly changes the geometry of the muscle/sclera system and its relationship to the lens. The age-related change in the scleral contour in humans has not been observed as frequently in the monkey, perhaps due to the conjunctival swelling (see Results) associated with the insertion of the extraocular muscle sutures; further imaging without conjunctival swelling is required to make definitive conclusions. Determining the importance of the age-related change in scleral contour (bowing inward) is beyond the scope of our study.

The rhesus monkey remains the best surrogate for studying human accommodation and presbyopia, as the similarities between the two species' accommodative mechanisms and changes with age far outweigh the differences.[14–16,21,32,45–50] In addition, the monkey model allows for the use of surgical procedures,[29,51] and insertion of contrast dyes and devices not possible in the human eye, to disturb and observe the accommodative apparatus and, thereby, elucidate accommodative function, presbyopia pathophysiology, and potential therapies.

Accommodating IOLs

Much effort has centered on designing an accommodating IOL to replace the enlarged/hardened lens in the presbyopic human eye. To date, this has been only modestly successful, with accommodative amplitudes of two diopters or less. Accommodating IOL function may be impacted by the age-related loss in ciliary body movement and by the changes in the eye's scleral, ciliary muscle, and zonular geometry.

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