8

ROLE OF THE CILIARY MUSCLE AND ZONULA IN ACCOMMODATION AND PRESBYOPIA

Mary Ann Croft, MS and Paul L. Kaufman, MD

BACKGROUND

Accommodation occurs by contraction (forward and inward movement) of the ciliary body and relaxation of the zonula that attach the ciliary body to the lens; as a result, the lens thickens and becomes more sharply curved, thus increasing the refractive power of the eye.[1,2] The lens capsule molds the lens into the accommodated state. As the muscle contracts, the tension on the anterior zonular fibers is released, while tension is placed on the posterior elastic tissues as the muscle moves forward and inward.[3] It has also been reported that the vitreous supplies support to the lens periphery and facilitates the lens shape change in combination with a change in the vitreous/anterior chamber pressure gradient, but other reports argue against a role for the vitreous in accommodation.[4-6]

Presbyopia (literally "old eye") is the age-related loss of the ability to accommodate and is the most common ocular affliction in the world. The ultimate cause of presbyopia is not yet known. Age-related changes in each component of the accommodative apparatus (either separately or combined) have been implicated in the pathophysiology of presbyopia, including lens hardening[7] and posterior restriction of the ciliary muscle.[8] However, although present and past studies of living and postmortem human eyes have provided useful and relevant information, the invasive surgical procedures necessary to uncover important information cannot be used in the living human.

Resolution of the issue is currently being facilitated by the use of a suitable animal model—the rhesus monkey. Although the mechanisms of accommodation in subprimate species are unlike those of the human (some subprimates do not accommodate at all[9]), the mechanism of accommodation in the rhesus monkey is very similar to that of the human,[10-12] and, adjusting for differences in lifespan, both species develop presbyopia at the same rate.[12] Rhesus monkey and human lenses grow throughout life, long after growth of the globe has ceased,[2-14] whereas lens and eye growth both cease relatively early in life in other mammalian species.[15]

Using the rhesus monkey model, several studies have applied electrical stimulation to the Edinger-Westphal (EW) nucleus in the rhesus brain to induce accommodation; during stimulation, imaging techniques such as goniovideography and ultrasound biomicroscopy (UBM) can be employed to evaluate the accommodative apparatus.[16-21] Surgical procedures such as intra- and extracapsular lens extraction and zonulolysis have been used to disturb the various accommodative components in the rhesus eye. Gonioscopy can be used to visualize the ciliary processes (CP; the tips of the ciliary body), zonula and lens equators, and their centripetal movements (Figure 8-1); and UBM allows visualization of the sagittal-sectional shape of the ciliary body and its forward movement, lens equator, and the course of the vitreous zonule (Figures 8-2 and 8-3).[2,16-20]

Pallikaris IG, Plainis S, Charman WN.
Presbyopia: Origins, Effects, and Treatment (pp. 69-76).

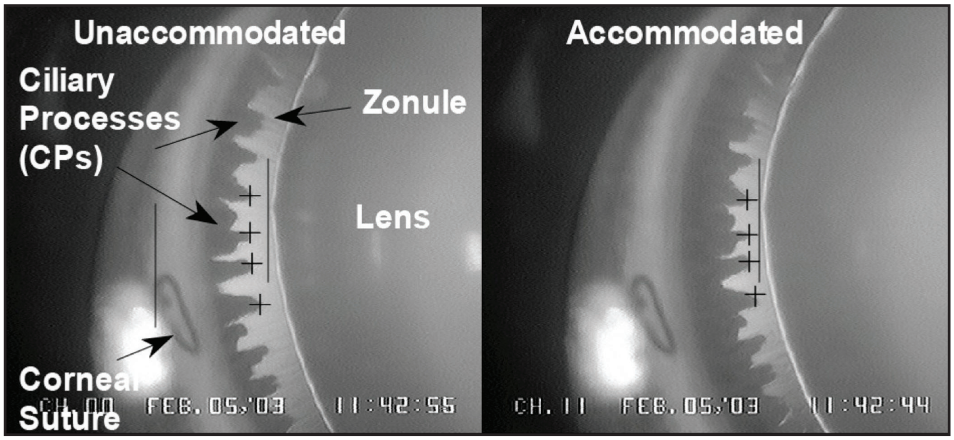

Figure 8-1. Goniovideography images of normal lens and CP configuration in the accommodated and unaccommodated states. To obtain quantitative measurements, a 9-0 nylon suture placed at the corneoscleral limbus served as a reference point (left solid vertical line) from which to measure distances to the lens equator (right solid vertical line) and the CPs (cross-hairs) for each image during a 2.2-sec stimulus period. The change in distance during stimulation represents centripetal (inward) movement of the lens equator and ciliary body. (Adapted with permission from Croft et al. Accommodative ciliary body and lens function in rhesus monkeys. I. Normal lens, zonule and ciliary process configuration in the iridectomized eye. *Invest Ophthalmol Vis Sci.* 2006;47:1076-1086; copyright Association for Research in Vision and Ophthalmology [ARVO].)

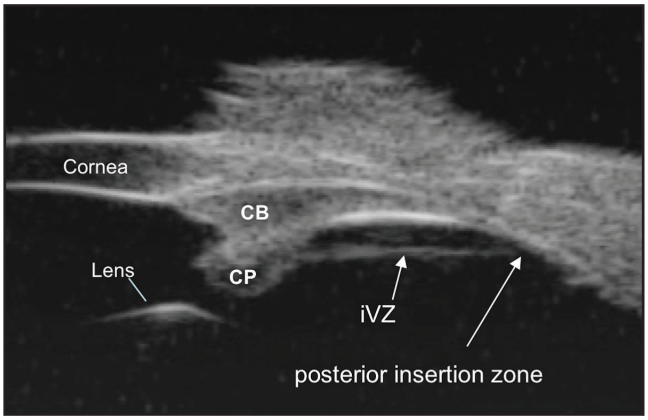

Figure 8-2. Ultrasound biomicroscopy (UBM) overview image (E-Technologies) of a live rhesus monkey shows the intermediate vitreous zonule (iVZ) extending from the pars plicata region of the ciliary body to the ora serrata region where it inserts (posterior insertion zone). CP = ciliary processes, CB = ciliary body. (Adapted with permission from Lütjen-Drecoll et al. Morphology and accommodative function of the vitreous zonule in human and monkey eyes. *Invest Ophthalmol Vis Sci* 2010;51:1554-1564; copyright Association for Research in Vision and Ophthalmology [ARVO].)

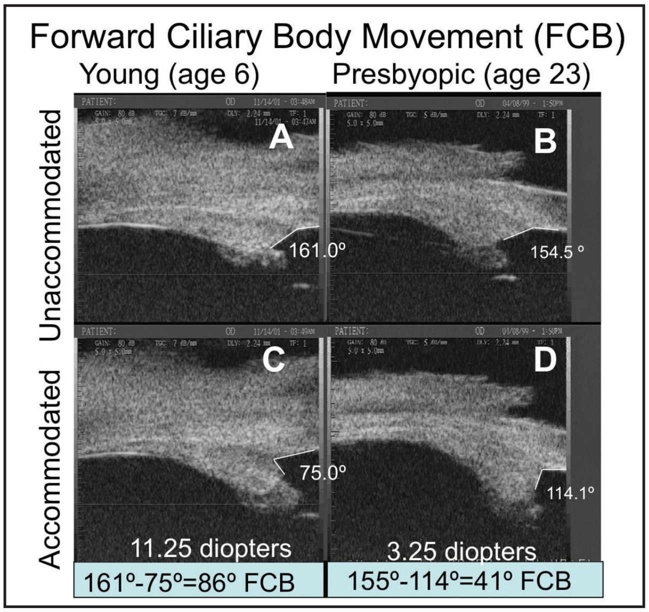

Figure 8-3. Ultrasound biomicroscopy images of 2 normal monkey eyes, aged 6 years (A, C) and 23 years (B, D), in the unaccommodated and accommodated states. The change in angle between the anterior aspect of the ciliary body and the inner aspect of the cornea during supramaximal central stimulation was used as a surrogate indicator of forward ciliary body movement (FCB). (Reprinted and adapted from *Exp Eye Res,* 89, Croft MA, McDonald JP, Nadkarni NV, Lin TL, Kaufman PL. Age-related changes in centripetal ciliary body movement relative to centripetal lens movement in monkeys, pp 824-832, Copyright 2009 with permission from Elsevier.)

In this chapter, we provide a brief overview and focus our attention on the newest and most pertinent information and its implications relating to the ciliary body/muscle and the zonula for accommodation and presbyopia.

THE LENS

Presbyopia is by definition the loss in accommodative amplitude due to the loss in the ability of the lens to change shape. In both human and monkey, the lens grows throughout life and does so primarily in an anterior/posterior direction (thickening) but not equatorially,[22-24] as some would claim.[25] Glasser and Campbell[7] measured the lens power in stretched and unstretched excised human eyes and demonstrated that the maximum change in lens power between the 2 states declined significantly with age. The decline was superimposable with the loss in accommodative amplitude in Duane's curve[26] (see Chapter 2, Figure 2-1), demonstrating that the lens can completely account for the age-related loss in accommodative amplitude.[7] Duane also established that, by the age of 40, more than two-thirds of the human accommodative ability has been lost.[26] Subsequent studies have shown that, after age 40, there is evidence of an age-related decrease in lens compliance,[27] an increase in lens resistance to deformation,[7] an increase in density of the lens nucleus, increased intraocular light scattering, and an increase in lens aberrations.[28] However, these changes cannot account for the loss in optical power change (between the stretched and unstretched states) in the human lens that occurs before the age of 40 years, although the age-related lens thickening (growth) that has been observed in the resting eye could be involved.

Clues to the presbyopia puzzle can be gleaned from studies of the monkey eye, where the decline in accommodative amplitude also parallels Duane's curve.[16] Croft et al[20] demonstrated that, for a given amount of lens movement, the ability of the lens to induce accommodation in middle-aged monkey eyes (aged 12 to 15 years; comparable human age 28 to 34 years) was not diminished compared to young animals (aged 5 to 9 years). However, the higher levels of lens movement were not achieved in this middle-age range, possibly due to the 50% reduction in forward muscle movement, which was measured in the middle-aged animals compared with the young animals (Figure 8-4).[20]

A decline in forward movement of the muscle would geometrically alter the lens/zonule/muscle relationship and thus directly affect the lens, dampening its capacity to change shape. All of the nourishment for the lens comes from the aqueous humor; Candia[29] reported that waste diffuses out of the equatorial regions and nutrients diffuse in from the anterior/posterior poles of the lens via a constant flow of fluid. This process is maintained by the Na+/K+ ATPase pumps located in the epithelial cells of the lens equator[29] and is but one of the known physiological processes that occurs in the lens. A remote possibility might be that the dramatic loss in forward muscle movement dampens normal lens movement, interrupting normal lens physiological processes and thus leading to or inducing secondary physiological changes in the lens. This could potentially contribute to the gradual decline in the accommodative optical power change of the lens in the human eye prior to age 40 years and eventual decreased deformability of the lens that occurs in the human eye after the age of 40 years. However, the exact cause of the loss in accommodative optical power change of the lens with aging remains unknown.

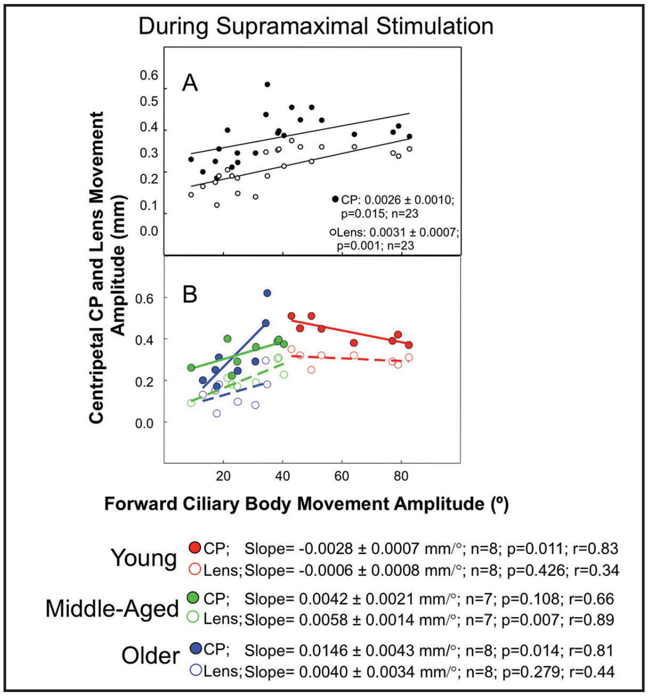

Figure 8-4. Ciliary body and lens movements during supramaximal stimulation. (A) Temporal accommodative forward ciliary body (FCB) movement versus centripetal CP and lens movement during a supramaximal stimulus current ~25% above the maximal stimulus in 28 eyes of 23 rhesus monkeys ranging in age from 6 to 27 years. (B) Same data as Panel A; however, the data were separated and analyzed according to age. For instances in which there were 2 eyes from 1 monkey, the data were averaged to provide 1 data point. Age ranges: young eyes (6 to 9.5 years, n=9 eyes, 8 monkeys); middle-aged eyes (12 to 15 years, n=8 eyes, 7 monkeys); and older eyes (17 to 27 years, n=11 eyes, 8 monkeys). The lines represent least squares linear regression of the amplitude of the CP (solid line) or lens (dashed line) centripetal movement versus FCB. Numbers represent slopes ± sem; P, probability that the slope=0.0; r=correlation coefficient. (A subset of the centripetal lens equator movement data [16 eyes of 12 monkeys] was reprinted and adapted from *Exp Eye Res,* 89, Croft MA, McDonald JP, Nadkarni NV, Lin TL, Kaufman PL. Age-related changes in centripetal ciliary body movement relative to centripetal lens movement in monkeys, pp 824-832, Copyright 2009 with permission from Elsevier.)

THE ZONULA

The anterior zonula attaches to and suspends the lens centrally within the eye. There are 3 subdivisions of the anterior zonula—anterior, equatorial, and posterior—and these 3 divisions attach to the anterior, equatorial, and posterior surfaces of the lens, respectively, and are referred to as the anterior zonula hereafter. There are literally hundreds[30] of these anterior zonula with some originating from the valleys of the ciliary processes, whereas others originate more posteriorly from the ciliary body, and others may exist that are as yet unknown.

THE VITREOUS ZONULE

Zonular fibers attach the ciliary processes to Wieger's ligament (the anterior face of the vitreous), and these are also involved in accommodation.[8] These fibers are termed *anterior vitreous zonules*,[8] and their role in the pathophysiology of presbyopia is not yet known.

Wasielewski et al[19] identified another segment of zonular fibers, both in the human eye and the monkey eye, and demonstrated that these fibers are clearly involved in accommodation and presbyopia. The fibers originate in the region of the ora serrata and course in a straight line through the vitreous to the ciliary processes where they branch and attach to the span fibrils between the walls of the ciliary processes (see Figure 8-2).[19] These fibers are termed the *intermediate vitreous zonule* (iVZ; Figure 8-5).

Several studies show that the iVZ does not stretch during accommodation and that the posterior and anterior ends move in concert during accommodation and are restricted in concert with increasing age in both the monkey and the human.[31-33] The posterior insertion moves forward, and the anterior attachment moves both forward and inward during the accommodative response. The posterior insertion zone of the iVZ in the young eye (as measured in both human and monkey) moves forward by approximately 1 mm, but this movement is reduced to 0.5 mm by the age of 28 to 34 years in the human and by the age of 12 to 15 years in the monkey (comparable age groups adjusted for lifespan)—a reduction of 50%.[31-33] This reduction in movement in the human eye occurs prior to age 40 years (before pronounced changes occur in lens deformability, compliance, etc [see "The Lens" section on page 70]). Lens deformability has yet to be measured in the monkey eye.

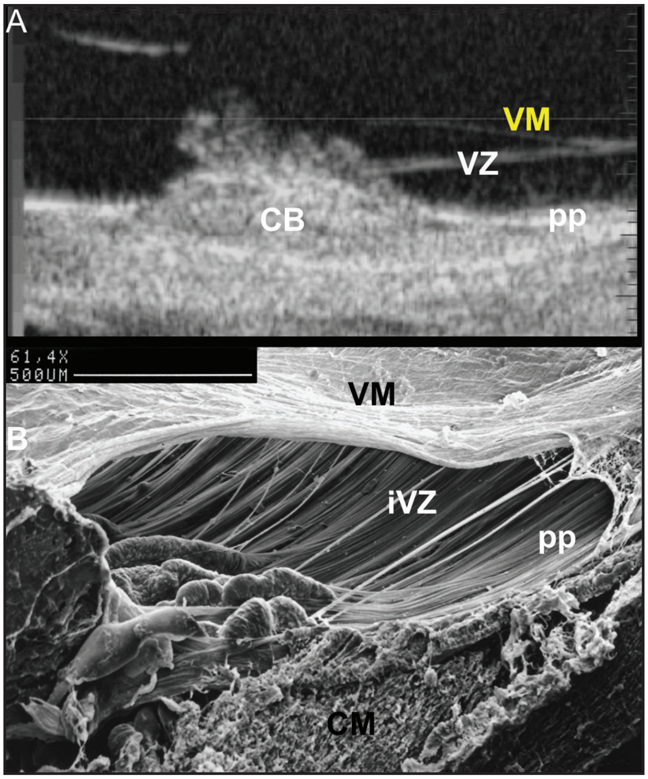

Figure 8-5. Ultrasound biomicroscopy (UBM) image (A) analogous to SEM (B), from the same 8-year-old rhesus monkey. CB = ciliary body, pp = pars plana zonule, iVZ = intermediate vitreous zonule, VM = vitreous membrane. The morphological specimen in panel B was prepared by Dr. Elke Lütjen-Drecoll's laboratory in Institute of Anatomy II, University of Erlangen-Nuremberg, Erlangen, Germany. (Reprinted with permission from Lütjen-Drecoll et al. Morphology and accommodative function of the vitreous zonule in human and monkey eyes. *Invest Ophthalmol Vis Sci.* 2010;51:1554-1564. Copyright Association for Research in Vision and Ophthalmology [ARVO].)

CILIARY MUSCLE

The loss of the lens' ability to change power[30] is clearly the proximate optical reason for presbyopia; however, it is unknown what the age-related loss in ciliary muscle mobility might contribute or how this loss in mobility might limit the efficacy of accommodating IOLs.

The ciliary muscle is the accommodative engine and, on contraction, it moves forward and centrally or inward, relaxing tension on the anterior zonula and lens capsule. The capsule putatively molds the lens into an accommodated state; the lens thickens, and the lens equator moves away from the sclera. The magnitude of ciliary muscle accommodative movement is reduced with increasing age in both monkey and human and in both movement vectors (forward and inward; see Figures 8-1 and 8-3).[31-33]

The ciliary muscle is composed of 3 muscle fiber groups, with longitudinal, radial (oblique), and circular orientations. In 1992, Tamm et al[34] reported that the area encompassing the circular portion of the ciliary muscle increases with age in excised human eyes, whereas the area of the longitudinal portion of the ciliary muscle decreases with age.

It is interesting to speculate that, due to the posterior restriction of the muscle movement in the aging human eye, the longitudinal portion of the muscle may undergo more of an isometric contraction than the circular portion—resulting in a decrease in the longitudinal area and a marked loss in forward movement. In a related study using the rhesus eye, Croft et al[18] suggested that the age-related increase of the circular portion may occur to allow a compensatory muscle movement in the centripetal direction to achieve a given level of zonular relaxation for a given level of accommodation. This concept of "system compensation" is supported by morphological evidence in the human eye (see "Evidence for Proprioception" section on page 74). This dynamic may be responsible for the anteroinward muscle positioning in the old human eye as reported by Tamm et al[34] and the age-related decline in the ciliary ring diameter, which Strenk et al[23] observed in 1999. However, anteroinward positioning of the muscle could be due to an aging, thickening lens that pulls the ciliary body anteriorly and inwardly.

Studies in both the human and the monkey eye provide evidence that the loss of ciliary muscle accommodative movement may be due to a decreased elasticity of the tissues that attach the ciliary muscle to the back of the eye (ie, posterior ciliary muscle tendons, choroid, and/or iVZ posterior insertion zone).[8,21,34] It is the elasticity/mobility of these tissues that allow the ciliary muscle to move forward and inward during contraction. The accommodative movement of the iVZ posterior insertion zone (see "The Vitreous Zonule" section on page 72) also likely reflects the forward movement of the muscle itself, as the iVZ itself does not stretch and anchors to the anterior and posterior ends of the muscle. It would be logical that a posterior restriction would have more of an impact on forward movement (it is in direct opposition to forward movement) than on centripetal muscle movement. Posterior restriction would have less of an impact on centripetal muscle movement because the restriction is perpendicular to the direction of movement. Indeed, Croft et al[16,20] reported an age-related loss in forward movement of the ciliary muscle in middle-aged monkey eyes (12 to 15 years) that was far more pronounced (50%) than the age-related loss in the muscle's centripetal movement (15%). Ocular geometry and dynamic UBM images of a middle-aged rhesus monkey eye during accommodation when compared with the young monkey eye shown in Figure 8-3 demonstrate an age-related loss in forward ciliary body movement even while significant centripetal movement remained. This finding was typical of the dynamic found in all the middle-aged monkeys compared with the young monkeys in these studies.[16,20] The finding above demonstrates that, at middle-age in the rhesus monkey (ie, ages 12 to 15 years, equivalent to a 27- to 35-year-old human), with the progressive, pronounced loss in forward movement, the system compensates in part by increasing the level of centripetal movement to achieve zonular relaxation and sustain lens rounding.[20] In the human eye, ciliary muscle mobility is also reduced in early presbyopes, with some mobility still retained as the eye ages.[23]

THE CILIARY MUSCLE, ZONULA, AND LENS SYSTEM IN CONCERT

To clarify how the components of the accommodative system function together, several studies have applied surgical procedures to the rhesus eye. In a preliminary study, Lütjen-Drecoll et al[21] disturbed/severed the iVZ, which resulted in increased forward muscle movement in presbyopic monkey eyes, thus demonstrating another indication of posterior restriction of the ciliary muscle.

Croft et al[18] and Wasielewski et al[19] performed a number of surgeries on the lenses of rhesus monkeys to demonstrate the existence of agonistic tractional forces supplied by the attachment of the anterior zonula/lens complex to the ciliary muscle during accommodation, which enhance muscle movements that are more important to forward movement than to centripetal movement of the ciliary muscle.

Croft et al[20] demonstrated that ciliary body and zonular function begin to change with age before lens function changes, at least in the monkey eye. In that study, the lens accommodative response (ie, the centripetal lens movement required to induce a given level of accommodation) was not significantly changed in the middle-aged monkeys (aged 12 to 16.5 years) compared with the young monkeys. The authors reasoned it was unlikely that the resting lenses of the middle-aged monkeys changed in refractive power or deformability compared with the young animals; rather, the age-related loss in ciliary body function (ie, loss of forward ciliary body movement) measured in the study could be due to decreasing elasticity of the choroid, of the posterior ciliary muscle tendons, or of the iVZ. Further, the authors suggested that chemical or physical lysis or other treatment of these inelastic attachments may sustain the ability of the ciliary body to move forward during accommodative effort and thus prevent or delay secondary age-related lenticular changes and perhaps facilitate the mobility/deformability of accommodating IOLs.

Although the lens clearly plays a major role in presbyopia, altered lens function could be, in part, secondary to extralenticular age-related changes such as dampened forward muscle movement or dampened zonular elasticity/mobility. Loss of elasticity of the ciliary muscle posterior attachments may be an important factor contributing to presbyopia. Even if loss of ciliary muscle mobility is not causally related to presbyopia, it may limit the performance of putatively accommodating IOLs now being developed by academic and industrial groups.

EVIDENCE FOR PROPRIOCEPTION

Morphological findings by Flügel-Koch et al[35] demonstrated that there are proprioceptors lining the internal periphery of the ciliary muscle, which are functionally different depending on location in the human eye. Large receptor organs located at the anterior muscle tips resemble mechanoreceptors, measuring shear stress, and receptors located at the posterior muscle tips could measure stretch of the tendons. In addition, there are numerous intrinsic nerve cells located in the circular portion of the muscle, and contraction of the circular portion could be modulated locally through a self-contained reflex arc (Figure 8-6). Could this sort of system lead to the increased circular portion observed with age to maintain focus and thereby lead to a diminished ciliary ring diameter?

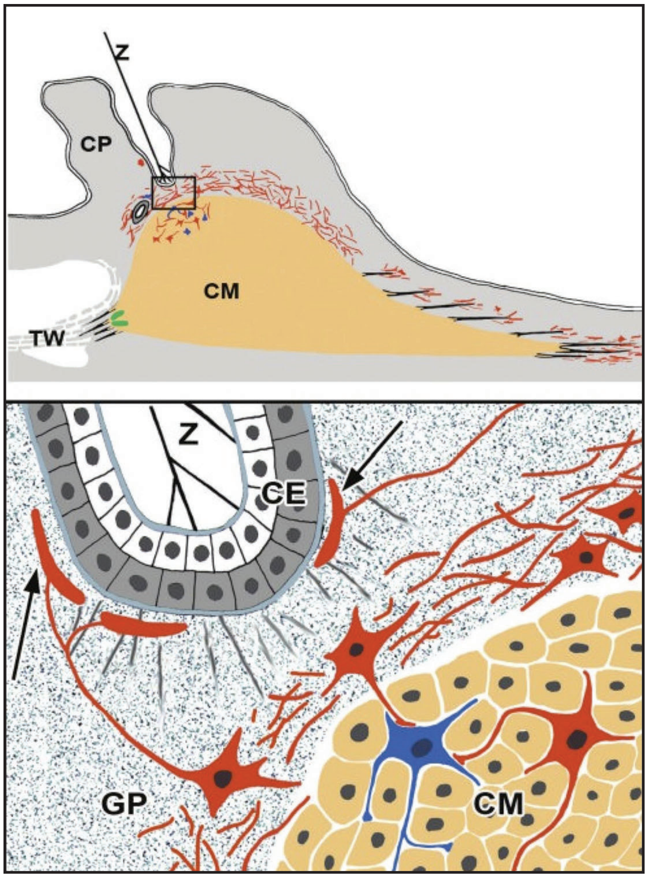

Figure 8-6. Schematic drawing summarizing our results on calretinin-IR. Top: the posterior tendons (black lines) of the ciliary muscle (CM) are surrounded by calretinin-IR terminals (red). At the anterior muscle tips (black lines), these calretinin-IR endings are absent, but large mechanoreceptor-like endings (green) are present between the muscle tips and in the scleral spur region. The circular muscle portion is covered by a cap-like net containing numerous ganglion cells. Calretinin-IR ganglion cells are also present within the inner portions of the muscle itself (bottom; magnified inset from top). These cells (red) form contact with nicotinamide adenine dinucleotide phosphate-oxidase diaphorase-positive cells (blue) within the circular and reticular muscle portions. Some ganglion cells within the ground plate (GP) are in contact with Ruffini-like structures (arrows) next to the pigmented ciliary epithelium (CE) in areas where zonular fibers (Z) are attached to the inner limiting membrane of the nonpigmented CE. CP = ciliary process; TW = trabecular meshwork. The drawing was prepared by Dr. Casandra Flügel-Koch, Institute of Anatomy II, University of Erlangen-Nuremberg, 91054 Erlangen, Germany. (Reprinted with permission from Flügel-Koch et al. Morphologic indication for proprioception in the human ciliary muscle. *Invest Ophthalmol Vis Sci*. 2009;50:5529-5536. Copyright Association for Research in Vision and Ophthalmology [ARVO].)

THERAPEUTIC IMPLICATIONS

Therapeutic approaches may need to take into account the diminished ciliary muscle movement with age. Failure to do so may explain the small accommodative amplitudes typically associated with current “hard” accommodating IOLs. Depending on the characteristics of the artificial lens inserted, enough ciliary body movement will likely exist to allow at least a few diopters of accommodation, which is sufficient for most near work. Replacing the elderly "hardened" crystalline lens material with a "moldable" polymer, leaving the capsule largely intact with the normal neuromuscular/lenticular/capsular mechanism still functional, has been envisioned for decades (see Chapter 28). Alternatively, some researchers seek to return pliability to the aged, hardened lens as a cure for presbyopia (see Chapter 27).

In the longer term, with an appropriately targeted surgical, pharmacologic, or genetic approach, it may be possible to sever the offending posterior attachments of the ciliary muscle or restore their elasticity to restore muscle movement.[21]

SUMMARY

Although some species differences exist, the rhesus monkey remains the best model with which to study human accommodation and presbyopia. Although the lens plays a major role in presbyopia, the dampened change in lens optical power and subsequent decreased lens deformability could be secondary to extralenticular age-related changes, such as loss of ciliary body forward movement or loss in mobility of the iVZ insertion zone. Accommodative centripetal movements of the ciliary processes and, thus the ciliary muscle, are reduced, but some movement ability remains in the old rhesus monkey eye and in the presbyopic human eye.[23] Whether the remaining movement is sufficient to power the system and produce accommodation after IOL implantation will depend on the approach and the characteristics of the accommodating IOL material. If accommodating IOLs rely primarily on centripetal ciliary body movement rather than forward ciliary body movement, they may be more effective in restoring accommodation in the presbyopic eye.

REFERENCES

1. von Helmholtz HH. Helmholtz's treatise on physiological optics. In: Southall JPC, ed. Handbuch der Pysiologishen Optik. Southall JPCT, trans-ed. *Mechanism of Accommodation.* Vol I, II. New York, NY: Dover Publications; 1909:143-172.
2. Glasser A, Kaufman PL. Accommodation and presbyopia. In: Kaufman P, Alm A, eds. *Adler's Physiology of the Eye, Clinical Applications.* Vol 5. 10th ed. St. Louis, MO: Mosby; 2003:197-233.
3. Rohen JW. Scanning electron microscopic studies of the zonular apparatus in human and monkey eyes. *Invest Ophthalmol Vis Sci.* 1979;18(2):133-144.
4. Coleman DJ. On the hydraulic suspension theory of accommodation. *Trans Am Ophthalmol Soc.* 1986;84:846-868.
5. Fisher RF. Is the vitreous necessary for accommodation in man? *Br J Ophthalmol.* 1983;67(3):206.
6. Koretz JF, Handelman GH. A model for accommodation in the young human eye: the effects of lens elastic anisotropy on the mechanism. *Vision Res.* 1983;23(12):1679-1686.
7. Glasser A, Campbell MCW. Biometric, optical and physical changes in the isolated human crystalline lens with age in relation to presbyopia. *Vision Res.* 1999;39(11):1991-2015.
8. Tamm E, Croft MA, Jungkunz W, Lütjen-Drecoll E, Kaufman PL. Age-related loss of ciliary muscle mobility in the rhesus monkey: role of the choroid. *Arch Ophthal.* 1992;110(6):871-876.
9. Duke-Elder S. *The Eye in Evolution.* Vol 1. St Louis, MO: Mosby; 1958:650-665.
10. Neider MW, Crawford K, Kaufman PL, Bito LZ. In vivo videography of the rhesus monkey accommodative apparatus. Age-related loss of ciliary muscle response to central stimulation. *Arch Ophthalmol.* 1990;108(1):69-74.
11. Lütjen-Drecoll E, Tamm E, Kaufman PL. Age changes in rhesus monkey ciliary muscle: light and electron microscopy. *Exp Eye Res.* 1988;47(6):885-899.
12. Bito LZ, DeRousseau CJ, Kaufman PL, Bito JW. Age-dependent loss of accommodative amplitude in rhesus monkeys: an animal model for presbyopia. *Invest Ophthalmol Vis Sc.* 1982;23(1):23-31.
13. Koretz JF, Neider MW, Kaufman PL, Bertasso AM, DeRousseau CJ, Bito LZ. Slit-lamp studies of the rhesus monkey eye: I. survey of the anterior segment. *Exp Eye Res.* 1987;44(2):307-318.
14. Koretz JF, Kaufman PL, Neider MW, Goeckner PA. Accommodation and presbyopia in the human eye. I. Evaluation of in vivo measurement techniques. *Appl Opt.* 1989;28(6):1097-1102.
15. Bito LZ, Miranda OC. Presbyopia: The need for a closer look. In: Stark L, Obrech G, eds. *Presbyopia: Recent Research and Reviews From the Third International Symposium.* New York, NY: Churchill-Professional Press; 1987:411-429.
16. Croft M, Glasser A, Heatley G, McDonald J, Ebbert T, Kaufman PL. Accommodative ciliary body and lens function in rhesus monkeys. I. Normal lens, zonule and ciliary process configuration in the iridectomized eye. *Invest Ophthalmol Vis Sci.* 2006;47(3):1076-1086.
17. Croft MA, Glasser A, Heatley G, et al. The zonula, lens, and circumlental space in the normal iridectomized rhesus monkey eye. *Invest Ophthalmol Vis Sci.* 2006;47(3):1087-1095.
18. Croft M, McDonald JP, James RJ, et al. Surgical intervention and accommodative responses: I. centripetal ciliary body, capsule, and lens movement in rhesus monkeys of various ages. *Invest Ophthalmol Vis Sci.* 2008;49(12):5484-5494.
19. Wasielewski R, McDonald JP, Heatley G, Lütjen-Drecoll E, Kaufman PL, Croft MA. Surgical intervention and accommodative responses: II. forward ciliary body accommodative movement is facilitated by zonular attachments to the lens capsule. *Invest Ophthalmol Vis Sci.* 2008;49(12):5495-5502.
20. Croft M, McDonald JP, Nadkarni NV, Lin TL, Kaufman PL. Age-related changes in centripetal ciliary body movement relative to conetripetal lens movement in monkeys. *Exp Eye Res.* 2009;89(6):824-832.
21. Lütjen-Drecoll E, Kaufman P, Wasielewski R, Ting-Li L, Croft M. Morphology and accommodative function of the vitreous zonule in human and monkey eyes. *Invest Ophthalmol Vis Sci.* 2010;51(3):1554-1564.
22. Strenk SA, Stenk LM, Semmlow JL, DeMarco JK. Magnetic resonance imaging study of the effects of age and accommodation on the human lens. *Invest Ophthalmol Vis Sci.* 2004;45(2):539-545.

23. Strenk SA, Semmlow JL, Strenk IM, Munoz P, Gronlund-Jacob J, DeMarco JK. Age-related changes in human ciliary muscle and lens: a magnetic resonance imaging study. *Invest Ophthalmol Vis Sci.* 1999;40(6):1162-1169.
24. Wendt M, Croft MA, McDonald J, Kaufman PL, Glasser A. Lens diameter and thickness as a function of age and pharmacologically stimulated accommodation in rhesus monkeys. *Exp Eye Res.* 2008;86(5):746-752.
25. Schachar RA, Tello C, Cudmore DP, Liebmann JM, Black TD, Ritch R. In vivo increase of the human lens equatorial diameter during accommodation. *Am J Physiol - Reg Int Comp Physiol.* 1996;271(3 part 2):R670-R676.
26. Duane A. Studies in monocular and binocular accommodation with their clinical applications. *Am J Ophthalmol.* 1922;5:867-877.
27. Weeber H, Eckert G, Soergel F, Meyer CH, Pechhold W, van der Heijde RGL. Dynamic mechanical properties of human lenses. *Exp Eye Res.* 2005;80(3):425-434.
28. Alió J, Schimchak P, Negri HP, Montés-Micó R. Crystalline lens optical dysfunction through aging. *Ophthalmology.* 2005;112(11):2022-2029.
29. Candia O. Electrolyte and fluid transport across corneal, conjunctival and lens epithelia. *Exp Eye Res.* 2004;78(3):527-535.
30. Glasser A, Campbell MCW. Presbyopia and the optical changes in the human crystalline lens with age. *Vision Res.* 1998;38(2):209-229.
31. Croft M, McDonald J, Kaufman P. Age-related changes of the posterior zonule and the ciliary body at rest during accommodation. Paper presented at: Association for Research in Ophthalmology meeting; April 27-May 1, 2008; Fort Lauderdale, FL; Abstract #4028,.
32. Croft MA, McDonald JP, Kaufman PL. The posterior vitreous zonule (pvz) does not stretch during accommodation. Paper presented at: Association for Research in Vision and Ophthalmology Meeting; May 3-7, 2009; Fort Lauderdale, FL.
33. Croft MA, McDonald JP, Kaufman PL. Configuration of the ciliary body: accommodation and presbyopia. Paper presented at: Association for Research in Vision and Ophthalmology Meeting; May 2-6, 2010; Fort Lauderdale, FL.
34. Tamm S, Tamm E, Rohen JW. Age-related changes of the human ciliary muscle. A quantitative morphometric study. *Mech Ageing Dev.* 1992;62(2):209-221.
35. Flügel-Koch C, Neuhuber WL, Kaufman PL, Lütjen-Drecoll E. Morphologic indication for proprioception in the human ciliary muscle. *Invest Ophthalmol Vis Sci.* 2009;50(12):5529-5536.