Magnetic Resonance Imaging Study of the Effects of Age and Accommodation on the Human Lens Cross-Sectional Area

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PURPOSE. To evaluate the effect of age and accommodation on lens cross-sectional area (CSA).

METHODS. High-resolution magnetic resonance images of the eye were acquired from 25 subjects ranging in age from 22 to 50 years during accommodation and with accommodation at rest. The images were analyzed to obtain the total lens CSA and the CSAs of the anterior and posterior portions of the lens.

RESULTS. The total lens CSA and the CSA of the anterior portion increased with age in both accommodative states. With accommodation, the CSA was larger in these portions of the lens; however, this difference decreased with age. Conversely, the CSA of the posterior portion of the lens remained statistically independent of both age and accommodative state.

CONCLUSIONS. This preliminary study documents, in vivo, that the lens grows with age. This growth appears to be confined to the anterior portion. A quite unexpected finding is that both the total lens CSA and the CSA of the anterior portion are greater during accommodation when zonular tension is minimized. This accommodative change in CSA, which decreases with age, may be due to compression of the lens material during relaxed accommodation when zonular tension is greatest. That both age and accommodative changes in CSA appear to be limited to the anterior portion of the lens may be related to properties of the anterior capsule and lens material, the position of the zonular attachments, and the location of the fetal nucleus. 

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Despite the ubiquity of presbyopia and a long history of study, the factors most significant in its development have not yet been resolved. One unique feature of the accommodative system is its reliance on a single-muscle mechanical system: ciliary muscle contraction. Perhaps the tight confines between the lens and sclera prohibit the typical agonist–antagonist muscle mechanism. A second unique feature of the accommodative system is lifelong lens growth. We have reported our findings regarding the effect of age and accommodation on the activity of the ciliary muscle1 (Strenk LM, et al. IOVS 2000;41:ARVO Abstract 2993). In the current study we examined the changes in lens cross-sectional area (CSA) that occur as a result of both aging and accommodation to add to our previously reported observations on the dimensions and shape of the aging lens1 (Strenk SA, et al. IOVS 2000;41:ARVO Abstract 17) and provide additional clues regarding the underlying mechanism of presbyopia. Because all the major accommodative structures (lens, muscle, and choroid) change their mechanical properties to some degree with age, they have all been considered at one time or another to be significant in the development of presbyopia. Modifications to Gullstrand’s2 basic concepts of accommodation have been developed—in particular, the essential role of the vitreous in supporting the lens3,4 and a geometric model of presbyopia.5 Several multifactorial theories of presbyopia implicate both lenticular and extralenticular mechanisms as important contributors.6–8 and involvement of the iris has been suggested.7 Age-related changes in zonular architecture and angle of insertion have also been reported.9 Mechanical changes most commonly cited as influencing presbyopia include increases in the stiffness10 and the thickness11 of the lens; reduced elasticity in the lens capsule12,13, a decrease in the ability of the passive elastic restoring elements to return the lens to the unaccommodated state14, a decrease in ciliary muscle mechanical advantage15, and ciliary muscle remodeling.8 Changes in lens size and characteristics are intimately involved with the development of presbyopia and have also been implicated as causal factors.5,11 Under the classic theory developed by Fincham16 an increase in the stiffness of the lens substance is a primary candidate for the inability to reshape the lens that occurs in presbyopia.17 However, this theory does not account for the early onset of accommodative loss. Fisher1,2,13 derived Poisson’s ratio and Young’s modulus for the anterior capsule, showed that capsule elasticity decreases almost linearly with age, and calculated that this decrease in elasticity leads to a reduction in the energy available to reshape the lens. For earlier ages, Krag et al.17 and van Alphen and Graebel18 have measured an increase in capsular elastic constant in vitro up to age 35. Measuring overall lens elasticity, van Alphen and Graebel showed that the effective lens-spring constant nearly tripled between ages 18 and 49 years. In several in vitro studies, researchers have applied radial stretching forces to the lens and correlated these forces to a change in lens shape.19–25 Pau and Kranz23 measured the resistance of different lens layers to penetration of a fine conical probe and found that the increased hardening occurs primarily in the nucleus. Ultrasound,25 Scheimpflug,15,20–27 and MRI experiments1 have shown that the lens increases its thickness with age, and this increase in thickness comes at the expense of anterior chamber depth.27 One of the most striking facts about the aging lens is that lens thickness and curvature increase with age—the so-called “Brown’s lens paradox.”27–29,30 A decrease in the effective index of refraction of the lens has been proposed as a compensatory or concomitant mechanism that preserves far vision.29,30

Much of the data on age-related changes in mechanical properties of the lens come from in vitro studies. As noted by Weale,31 such studies can present their own set of method-
ological problems, including tissue handling and changes post-mortem and artifactual deformation of the lens. Moreover, such studies may not accurately reproduce the forces acting on the lens. In vitro studies cannot provide information on the actual dimensions and relative positions of the various accommodative structures as they exist in the intact eye. Such critical information as the size of the ciliary muscle ring, the equatorial diameter of the lens, and the changes in these dimensions with accommodation and with age in the intact eye was not known before our image-based studies. It is possible to obtain this information with high-resolution MRI, because, unlike other modalities, MRI allows in vivo visualization of the entire undistorted lens and its relationship to the accommodative structures in the intact eye. Furthermore, MRI offers unparalleled soft tissue contrast and the ability to acquire images in any desired plane without obscuring vision. We have reported that ciliary muscle contraction, present in all subjects, reduces only slightly with advancing age and that the diameter of the ciliary muscle ring decreases with advancing age.1 We found that accommodative changes in the diameter of the ciliary processes ring do not track those of the ciliary muscle ring (Strenk LM, et al. IOVS 2000;41:ARVO Abstract 2993) and that the length of the lens equator is age independent in the unaccommodated eye but that increasing lens thickness correlates highly with age.1 We have described age and accommodative changes in lens shape (Strenk SA, et al. IOVS 2000;41:ARVO Abstract 17) and obtained in vivo images of the anterior zonular apparatus (Strenk LM, et al. IOVS 2001;42:ARVO Abstract 1533). In addition, we reported reduced circumferential space with advancing age.1 In the current study, we were able to examine total lens CSA and the CSAs of its anterior and posterior portions by the lens equator. The lens equator was found by first rotating the MR image until the iris was horizontal. The medial-most and the lateral-most pixels on the lens profile defined the lens equator. Because of resolution limitations and the digital nature of MRI, occasionally more than one pixel may be most medial. When this occurred, the coordinates of these pixels were averaged. An identical procedure was followed if more than one pixel was most lateral.

The anterior and posterior lens profiles were fitted to fourth-order polynomials. The choice of polynomial order was initially selected empirically. Specifically, polynomial order was evaluated by comparing cross-sectional areas determined using a range of polynomial orders. No change in the estimated area was found when polynomials higher than fourth order were used. This implies that fourth-order polynomials are sufficient to capture the shape of the lens.

The choice of a fourth-order polynomial is also supported by the underlying physics. The lens can be treated as a series of thin concentric shells subjected to bending by both the accommodative apparatus and the intraocular pressure acting as a distributed load (Strenk LM, et al. IOVS 1999;40:ARVO Abstract 4676). In this model, the concentric thin shells are best represented by fourth-order polynomials. These functions were integrated to determine the CSAs of the anterior and posterior portions of the lens as well as total lens CSA.

A repeatability study was performed on two subjects aged 22 and 49 years for minimum and maximum accommodation. Each subject was imaged during three different scanning sessions in each accommodative state. The image analysis consisted of measuring the anterior, posterior, and total CSA and equator for each image. The 22-year-old subject had an average total CSA of 24.369 ± 0.176 mm² for minimum accommodation and an average total CSA of 25.886 ± 0.183 mm² for maximum accommodation. A two-tailed Student’s t-test compared the difference between these mean areas and found it to be statistically significant (P = 0.027). The result for the average anterior total CSA research was approved by the institutional review board (IRB) of the University of Medicine and Dentistry of New Jersey (UMDNJ)-Robert Wood Johnson Medical School.

The images were analyzed on computer with NIH Image 1.62 software (available by ftp at zippy.nimh.nih.gov/ or at http://rsb.info.nih.gov/nih-image; developed by Wayne Rasband, National Institutes of Health, Bethesda, MD). The lens profiles were obtained by using interactive graphics. For examination of the anterior-posterior distribution of lens growth, lens CSA was divided into anterior and posterior portions by the lens equator. The lens equator was found by first rotating the MR image until the iris was horizontal. The medial-most and the lateral-most pixels on the lens profile defined the lens equator. Because of resolution limitations and the digital nature of MRI, occasionally more than one pixel may be most medial. When this occurred, the coordinates of these pixels were averaged. An identical procedure was followed if more than one pixel was most lateral.

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Figure 1. High-resolution composite axial image of the eye. Left: image at 0.1 D; right: image at 8 D.
was 9.368 ± 0.122 mm² for minimum accommodation and 10.635 ± 0.182 mm² for maximum accommodation. The difference between the average anterior CSAs was also statistically significant (P = 0.029). The result for the average posterior CSA was 15.002 ± 0.182 mm² for minimum accommodation and 15.251 ± 0.194 mm² for maximum accommodation. The difference between average posterior CSAs was not statistically significant (P = 0.454). Finally, the average length of the equator was 8.857 ± 0.093 mm for maximum accommodation, whereas the average length of the equator was 9.115 ± 0.052 mm for minimum accommodation.

RESULTS

Figure 2 shows that the total lens CSA increased with age during both minimum and maximum accommodation. The linear regression for minimum accommodation has a slope of 0.131 ± 0.043 mm² per year and an intercept of 19.660 ± 1.504 mm², and P = 0.006. Likewise, for maximum accommodation the linear fit has a slope of 0.100 ± 0.044 mm² per year, an intercept of 21.827 ± 1.523 mm² and P = 0.031.

Figure 3 shows the anterior and the posterior CSAs of the lens during minimum accommodation versus age. The anterior CSA has a slope of 0.098 ± 0.026 mm² per year and an intercept of 6.004 ± 0.903 mm² (P = 0.001). The posterior CSA has a slope of 0.033 ± 0.025 mm² per year and an intercept of 13.656 ± 0.864 mm². Unlike the anterior CSA, the linear fit to the posterior CSA has a P = 0.194. Thus, although a trend toward increasing posterior CSA may exist, it is not statistically significant for this sample. The mean posterior CSA is 14.772 ± 0.231 mm².

Figure 4 shows the anterior and posterior CSA for maximum accommodation. The anterior CSA has a slope of 0.064 ± 0.026 mm² per year and an intercept of 8.340 ± 0.916 mm² (P = 0.024). The posterior CSA has a slope of 0.036 ± 0.024 mm² per year and an intercept of 13.511 ± 0.837 mm². Unlike the anterior CSA, the linear fit to the posterior CSA has a P = 0.150. Thus, although a trend toward increasing posterior CSA may exist, it is not statistically significant for this sample. The mean posterior CSA is 14.713 ± 0.226 mm².

Figure 5 shows the anterior CSA at minimum and maximum accommodation. An analysis of the 95% confidence interval shows that the difference between intercepts is statistically significant, but the difference between the slopes is not. A weighted average of the slopes is 0.081 mm² per year.

Figure 6 shows the posterior CSA at minimum and maximum accommodation. The posterior CSA may show a trend toward increasing with of age for both accommodative states, but as noted earlier, this increase is not statistically significant for either accommodative state for this sample. Likewise, at the 95% level, the accommodative difference between the average CSA is not statistically significant; a weighted average of the CSAs of both accommodative states is 14.742 ± 0.325 mm².

The change in the relative CSA (the change in CSA divided by CSA at maximum accommodation) for the total lens is shown in Figure 7. A linear fit to this data has a slope of −0.001 ± 0.0004 mm² per year and an intercept of 0.097 ± 0.016 mm² (P = 0.003). Figures 8 and 9 show the change in relative CSA for the anterior and posterior portions of the lens, respectively. The anterior portion of the lens fits a line with a slope of −0.005 ± 0.001 mm² per year and an intercept of

![Figure 2](http://iovs.arvojournals.org/pdfaccess.ashx?url=/data/journals/iovs/933227/)  
**Figure 2.** The CSA of the entire lens as a function of age shows growth for both minimum (solid line) and maximum (dashed line) accommodation.

![Figure 3](http://iovs.arvojournals.org/pdfaccess.ashx?url=/data/journals/iovs/933227/)  
**Figure 3.** The anterior (solid line) and posterior (dashed line) CSAs as a function of age during minimum accommodation. The posterior CSA is statistically independent of age.
The anterior (solid line) and posterior (dashed line) CSA as a function of age at maximum accommodation. Just as in minimum accommodation, the CSA of the posterior portion of the lens is statistically independent of age, whereas the anterior portion shows growth:

\[ \frac{0.296 \pm 0.049 \text{ mm}^2}{H_11006} \left( P = 0.001 \right) \] whereas the posterior portion fits a line with a slope of \(-0.0002 \pm 0.0003 \text{ mm}^2\) per year and an intercept of \(0.010 \pm 0.010 \text{ mm}^2\) (\(P = 0.564\)). The lack of statistical significance implies that the change in the relative CSA of the posterior portion of the lens is independent of age:

\[
\frac{0.0002 \pm 0.0003 \text{ mm}^2}{H_11006}
\]

**DISCUSSION**

In vitro studies have shown that the lens grows throughout life\(^25,35,36\) and our in vivo data demonstrate lens growth over the age range studied. Our measured total lens CSA compares the average change in CSA of the posterior portion of the lens is calculated to be \(0.004 \pm 0.003 \text{ mm}^2\).
well with recently reported in vitro data. Specifically, for the accommodated state, which most closely corresponds to the state of the isolated lens, our values range between 22 and 30 mm$^2$ compared with 18 to 28 mm$^2$ reported for isolated human lenses. The smaller anterior portion of the lens appears to grow throughout life, whereas the CSA of the posterior portion of the lens is statistically independent of age. Lens growth appears confined to the anterior portion of the lens; however, a trend toward growth may occur in the posterior portion (the slope is increasing) and the lack of statistical significance could result from the limited sample size.

Another quite unexpected finding is that the lens CSA increased with accommodation. Because the CSA of the lens is larger in the accommodated state when external tension is minimal, the reduction in lens CSA must be produced by the increased zonular tension required to flatten the lens. Assuming symmetry of the lens about its polar axis, these accommodative changes in CSA reflect accommodative changes in lens volume and suggest that the lens material is slightly compressed when accommodation is relaxed and the external forces exerted on the lens are greatest. These results challenge a long-held belief that the lens is incompressible, a belief based on the fact that the lens contains a large amount of water, which is incompressible. However, it has been noted that lens mechanics cannot be modeled as a simple fluid filled sack. In fact, the compressibility of the lens (i.e., Poisson’s ratio) has never been measured, although Koretz and Handelman have conducted theoretical studies that indicate that the lens can be compressed, describing zonular stresses being converted by the capsule into a uniform compressive force on the lens material, and that the release of zonular stress results in the compressive force within the lens being reduced, allowing the lens to undergo elastic recovery. Koretz and Handelman also present a mathematical model of lens mechanics, valid over a range of Poisson ratios less than 0.5, thus indicating compressible material. Moreover, recent in vitro MRI studies of the lens have described a reversible, age-dependent, synergetic response, in which an increase in pressure leads to a conversion of a portion of the free water in the lens to bound water, implying a tighter packing of lens proteins. The accommodative change in CSA reported herein may be a manifestation of this synergetic response. A tighter packing of lens proteins could result in a decrease in the CSA during resting accommodation, when the lens is under greater pressure.

The age-dependent accommodative increase in lens CSA appears to be due entirely to an increase in the CSA of the anterior portion. The CSA of the smaller anterior lens portion displays significant accommodative changes in younger subjects, whereas the CSA of the larger posterior lens portion is statistically independent of accommodation. The smaller surface area of the anterior lens portion may result in greater compressive forces being applied to the anterior lens material with resting accommodation. The apparent independence of the posterior lens CSA with accommodation may also be related to the position of the fetal nucleus. The fetal and embryonic nuclei have been described as harder than the surrounding adult nucleus, juvenile nucleus, and cortex, and differences in cell morphology exist between these regions. Vibratome sections of a human lens show the bulk of the fetal nucleus below the equator of the lens. Recent in vitro MRI studies similarly indicate that the bulk of the fetal nucleus is posterior to the lens equator. If the bulk of the fetal nucleus is situated in the posterior portion of the lens, this portion of the lens may remain unresponsive to any pressure from the lens capsule.

Aside from possible differences in compressive forces and the proportion of fetal nucleus present, other differences exist between the anterior and posterior lens portions that may or may not play a role in the differing effects of age and accommodation on CSA. Both the anatomy and behavior of the
The decrease in the accommodative changes in lens CSA with advancing age could be due to the same mechanisms that have long been possible candidates for causing presbyopia: a reduction in the change in tension applied to the lens or a loss of lens compressibility due to changes in the mechanical properties of the lens material. It could also be due to the recently reported age related loss of reversible syneresis. Assuming symmetry about the polar axis, these findings on the CSA can be extrapolated to lens volume calculations. Future studies include examining the CSA in the sagittal plane to ascertain polar symmetry and recruiting additional subjects over the accommodative range to study the correlation between these CSA changes and other age-related changes in the accommodative structures.

CONCLUSION

High-resolution MRI is a useful tool with which to study the accommodative structures in the aging eye. The total lens CSA increases with both age and accommodation, as does the CSA of the anterior portion; however, the CSA of the posterior portion is statistically independent of both. The accommodative increase in total and anterior lens CSA decreases with age, whereas the CSA of the posterior portion apparently does not. These findings suggest that growth is confined to the anterior portion of the lens and that the anterior lens material may be slightly compressed with relaxed accommodation when zonular tension is greatest.

Acknowledgments

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References