Age-Related Changes in Human Ciliary Muscle and Lens: A Magnetic Resonance Imaging Study

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PURPOSE. To use high-resolution magnetic resonance (MR) images of the eye to directly measure the relationship between ciliary muscle contraction and lens response with advancing age.

METHODS. A General Electric, 1.5-Tesla MR imager and a custom-designed eye imaging coil were used to collect high-resolution MR images from 25 subjects, 22 through 83 years of age. A nonmagnetic binocular stimulus apparatus was used to induce both relaxed accommodation (0.1 diopter [D]) and strong accommodative effort (8.0 D). Measurements of the ciliary muscle ring diameter (based on the inner apex), lens equatorial diameter, and lens thickness were derived from the MR images.

RESULTS. Muscle contraction is present in all subjects and reduces only slightly with advancing age. A decrease in the diameter of the unaccommodated ciliary muscle ring was highly correlated with advancing age. Lens equatorial diameter does not correlate with age for either accommodative state. Although unaccommodated lens thickness (i.e., lens minor axis length) increases with age, the thickness of the lens under accommodative effort is only modestly age-dependent.

CONCLUSIONS. Ciliary muscle contractile activity remains active in all subjects. A decrease in the unaccommodated ciliary muscle diameter, along with the previously noted increase in lens thickness (the "lens paradox"), demonstrates the greatest correlation with advancing age. These results support the theory that presbyopia is actually the loss in ability to disaccommodate due to increases in lens thickness, the inward movement of the ciliary ring, or both. (Invest Ophthalmol Vis Sci. 1999;40:1162-1169)

Presbyopia, an inevitable consequence of growing older, is generally believed to be caused, at least in part, by a decrease in the ability of the lens to change its shape. Both contemporary and classic theories for presbyopia are based on the Gullstrand formulation of the accommodative (i.e., focusing) mechanism,1 a theory developed from concepts first described by Helmholtz in the mid-19th century. Under Gullstrand’s theory, the ciliary muscle alters the balance of two passive elastic elements: the elasticity of the lens and a restoring element thought to be the choroid. (This single muscle mechanical process is unique. Perhaps the tight confines between the lens and the edge of the eye prohibit the typical agonist-antagonist muscle mechanism. Evidence presented later indicates that presbyopia may be the price paid for this motor expedient.) These changes in balance alter the diameter of a suspensory ring formed from the ciliary muscle that surrounds and supports the lens. Decreases in ring diameter allow the lens to round up, increasing its dioptric power. Conversely, increasing ciliary ring diameter applies tension that flattens the lens. (Recently, some modifications of these basic concepts have been developed, in particular the essential role of the vitreous in supporting the lens2,3 and a geometric model of accommodation.4)

Changes in any of the three major accommodative processes, the lens, the ciliary muscle, or the restoring elasticity, could alter the balance of forces in this system, which in turn would change the equilibrium position of the ciliary ring and influence the maximum accommodative response. Because all these processes experience some change in their mechanical properties with age, they have all been considered, at one time or another, as potentially significant in the development of presbyopia.

Two classic theories have evolved from a long-standing debate to explain the mechanics of presbyopia.5,6 These theories differ with regard to ciliary muscle involvement and predict different relationships between ciliary muscle contraction and lens shape changes. The earliest theory for presbyopia placed all the responsibility on the lens: Presbyopia was believed to be caused by a decrease in the ability of the lens to change its shape. Under this lenticular theory, developed from early contributions by Hess7 and Gullstrand,1 muscle changes are not an important consideration in presbyopia. The muscle’s ability to modify lens shape is essentially normal in the region where the lens is still capable of response (the "manifest" region). Above this level, a latent region exists where the
muscle, although still capable of contracting, cannot produce a change in accommodation due to excessive stiffness.

In opposition to the lenticular theory of Hess-Gullstrand, the extralenticular theory of Duane placed the responsibility for presbyopia on the ciliary muscle. This theory was developed in response to experiments showing that the slightest weakening of the ciliary muscle (by topical application of diluted atropine) produced a decrease in maximum accommodative response. If a latent region existed as proposed by Hess-Gullstrand, some muscle weakening should be possible without a corresponding change in lens shape. In a modification of this theory by Alpern, the muscle-lens relationship has a latent region initially, but gradual atrophy through lack of use eliminates this latent region. This modification results in an essentially lenticular theory because muscle weakness becomes an effect not a cause of lens immobility.

Fincham proposed a theory that falls between these two extremes, suggesting that the decline in accommodation was primarily lenticular but that the amount of ciliary muscle contraction required for a given accommodative response also increases with age over the entire response range. Although the theories of Duane and Fincham postulate different underlying causes for presbyopia (muscle in the former, lens in the latter), they both predict the same muscle-lens relationship. Muscle activity should always produce some, however small, lens response, and the maximum accommodative response should always be associated with maximum muscle effort: If additional muscle contraction was made possible, a greater accommodative response should be achieved.

Although these early theories imply experimentally verifiable differences, none has gained unambiguous support. Under the lenticular theory ascribed to Hess and Gullstrand, the strength of the ciliary muscle (or other extralenticular processes) should not be diminished in the region where the lens is still capable of fairly normal responses (the "manifest") region. Above this level, a latent region should exist where the muscle, although still capable of contracting, cannot produce a change in accommodation due to limitations in mechanical properties of the lens. Because the responsiveness, or effectiveness, of the accommodative motor processes (both lenticular and extralenticular) would be normal in the nonpresbyopic or "manifest" response region, variables that involve accommodative responsiveness, such as AC/A stimulus ratios, will be unchanged in this region. Conversely, because responsiveness is negligible within the presbyopic or "latent" region, the AC/A stimulus ratio should be very large within this region.

Results from studies that track changes in the AC/A stimulus ratio with age have been mixed. Some show little change or even a gradual decrease with age, whereas others include two longitudinal studies showing a marked increase in stimulus AC/A with age. After a long history of conflicting findings, recent results clearly demonstrate that from 0 to around 45 years of age, the response AC/A ratio increases by approximately 0.1 prism diopter per year. After 45 years of age, this measurement is no longer reliable because of the small accommodative response. This modest change in the response AC/A ratio is most consistent with the Hess-Gullstrand theory.

The strongest support for the lenticular theory is found in evidence that indicates that the ciliary muscle does not weaken with age, a fundamental assumption of the extralenticular theory. Several researchers have shown that loss of accommodation begins at an early age, and Sun et al. have argued that this would be unusual for a disorder caused by muscle weakness. In addition, Fisher has determined that the strength of the ciliary muscle actually increases with age. Additional support for the lenticular theory is found in impedance cyclography experiments, which provide a qualitative measure of ciliary muscle activity. Saladin and Stark showed ciliary activity in the absence of an accommodative response, indicating a true latent region as required by the lenticular theory. Similarly, Swegmark showed that the amount of ciliary muscle activity required for a given accommodative response within the manifest region does not change with age as implied by the extralenticular theory.

Although it is commonly held that changes in the mechanical properties of the lens are an underlying cause of presbyopia, there is evidence that extralenticular processes do play a significant role in the apparent violation of the Hess-Gullstrand theory. For example, the lenticular theory assumes that maximum accommodation occurs well before maximum ciliary muscle contraction; hence, a modest increase in muscle contractile ability should have no effect on the maximum accommodative response. Careful studies by Fincham and later by Eskridge show that if the ciliary muscle activity is augmented or diminished (e.g., through the use of a parasympathomimetic or parasympatholytic drug) maximum accommodation changes accordingly. This finding implies that ciliary muscle weakness does contribute to the loss of accommodation. However, Semmlow et al. used computer simulations of the muscle-lens system to show that these results were also compatible with the lenticular theory when the highly nonlinear behavior of the presbyopic lens was taken into account.

Much of the controversy regarding the mechanism of presbyopia (and accommodation) results from an inability to directly measure the parameters in question. In this study, high-resolution magnetic resonance imaging (MRI) has been used to directly detect changes in the lens and the ciliary muscle. Of primary interest in this study is the relationship between the ciliary muscle and the lens. Specifically, we wished to determine whether the contractile ability of the ciliary muscle diminishes with age. We also examined changes in the resting (unaccommodated) dimensions of the ciliary muscle and age-related changes in lens equatorial diameter and thickness.

METHODS

High-resolution MRI is an extremely useful modality with which to study the relationship between ciliary muscle contraction and lens response, because it produces undistorted images of the entire anterior portion of the eye. Additionally, MRI offers excellent soft tissue contrast, thus the ciliary muscle is well visualized. MRI offers the ability to directly image intraocular structures during accommodation without obscuring vision and MR images can be acquired in any desired plane. Finally, MRI uses no ionizing radiation and has no known adverse effects. Nonetheless, to image structures as small as the ciliary muscle and lens using MRI presents a number of challenges, including resolution limitations, signal-to-noise ratio (SNR) limitations, image acquisition time constraints, the difficulty of presenting accommodative stimuli within the confines

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of the imager, and the need to limit head and eye movements during the scans.

Imaging Protocol

A 1.5-Tesla MR imager (1.5T-Signa, General Electric Medical Systems, Waukesha, WI) was used to obtain images from 26 subjects, 21 to 83 years of age. The research followed the tenets of the Declaration of Helsinki, informed consent was obtained after the nature and possible consequences of the study were explained, and the research was approved by the institutional review board of UMDNJ-Robert Wood Johnson Medical School.

Images were acquired using a T₁-weighted, single echo, multisequence spin-echo technique. The imaging protocol consisted of acquiring a 2.5-minute sagittal scout scan to ensure that the eye was properly positioned and that the axial scan that followed would bisect the lens. Great care was taken to position the eye so that it was not rotated with respect to the axial plane. Multislice axial scans were collected with a 4-cm field-of-view (FOV) and 256 X 256 pixel matrix, resulting in a 0.156 mm in-plane resolution. The contiguous 3-mm-thick axial slices ensured that the center of the lens was captured and allowed the desired slice and its adjacent neighbors to be evaluated to measure slice-centering accuracy.

Standard clinical MRI rarely uses a FOV less than 8 cm. Yet to obtain adequate in-plane resolution, a smaller FOV was required. By using a 4-cm FOV and standard clinical MR imaging receiver coils, we attained sufficient in-plane resolution, but the SNR of the resultant image was decreased to an unacceptable level. The SNR, which had been decreased by a factor of 4 because of the increase in FOV, could be restored to its original value by increasing the number of imaging averages by a factor of 16; however, this would result in an unacceptable increase the scan time from 5 to 80 minutes. We decided to address these SNR and scan time limitations by designing a custom receiver coil consisting of a two-turn solenoid with a 2.5-cm diameter. This small coil, positioned directly around the eye, restored the SNR in the region of interest to an adequate level and allowed high-resolution images of the ciliary muscle and lens to be acquired.

Stimulus Apparatus

An accommodative stimulus apparatus device was designed to present binocular (accommodative and disparity) stimuli and to provide a fixation target to reduce eye movement during the scan. The nonmagnetic apparatus consisted of a plastic frame that allowed the position of the visual target to be varied, a mirror to allow viewing of distant targets, and a simple black crosshair target that was backlit by a small incandescent bulb. The light was driven by a flasher circuit that periodically varied the bulb intensity between 100% and 50% at a rate of 2 Hz. Flashing the stimulus produced a compelling target and reduced the stabilized image phenomenon, which results in target image fading. The flashing target stimulus was effective in limiting eye movement during the scan. Standard MRI positioning cushions were used to limit head movement.

Visual targets were positioned at the appropriate distance from the eye to provide either a strong (8.0 D) or minimal (0.1 D) binocular accommodative stimulus during the MR scans. For presbyopic subjects, the near target was out of focus, but the effort to fuse produces disparity drive to the accommodative system. The initial scans were generally taken at the minimum stimulus at which point resting accommodation is expected. Scans taken under the 8-D accommodative stimulus followed. Images were acquired first with far target stimulation followed by near target stimulation to reduce possible effects from incomplete accommodative relaxation.

Image Analysis

The images were analyzed using the NIH Image 1.6 software package. The pixel coordinates for the major and minor lens axes were obtained. Within the ciliary body, the ciliary muscle was identified as a roughly triangular hypointense pixel cluster.
extending posteriorly from the iris root. A pixel corresponding to the medial apex of this triangle was identified for the nasal and temporal ciliary muscle cross sections. The distance between these points is taken as the apparent ciliary muscle diameter. Measurements of the apparent ciliary muscle diameter and those of the lens were corrected for finite slice thickness and slice-centering offsets to obtain the actual ciliary muscle diameter (see the Appendix for a description of these corrective algorithms).

RESULTS

Figure 1 shows representative images from one subject under near and far binocular stimuli. To assess the accuracy of the dimensional data extracted from these images, repeated images were taken from one subject. Table 1 shows dimensional data obtained from MR images of subject JS for three different trials with 8-D accommodative stimulus. The relative consistency of the data demonstrates that the dimensional measurements obtained from the MR images sets are repeatable to within the image resolution (0.156 mm).

<table>
<thead>
<tr>
<th>Condition</th>
<th>Ciliary Ring Diameter (mm)</th>
<th>Lens Diameter (mm)</th>
<th>Lens Thickness (mm)</th>
</tr>
</thead>
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<tr>
<td>JS-8 D</td>
<td>12.30</td>
<td>8.96</td>
<td>4.44</td>
</tr>
<tr>
<td>JS-8 D</td>
<td>13.27</td>
<td>8.89</td>
<td>4.49</td>
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<tr>
<td>JS-8 D</td>
<td>13.27</td>
<td>8.90</td>
<td>4.41</td>
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<tr>
<td>Average (SD)</td>
<td>13.28 (0.014)</td>
<td>8.92 (0.037)</td>
<td>4.45 (0.042)</td>
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</table>

Figure 2 A shows the change in ciliary muscle ring diameter produced by accommodative effort. For all subjects, the ciliary muscle continues to contract with accommodative effort, even for advanced presbyopes. Although some reduction in muscle contractility may occur, particularly in early presbyopes ($r^2 = 0.26; P < 0.015$), substantial contractile ability remains even in advanced age (note data point at 86 years of age). However, the most dramatic age-related change in the muscle is the decrease in unaccommodated ring diameter (Figure 2B; $r^2 = 0.74; P < 0.0001$).

The age-related loss in the ability of the lens to change shape is shown in Figures 3A and 4A, which plot the changes in lens thickness and lens equatorial diameter that occur with accommodative effort. In both plots, the ability to change diameter and thickness decreases to zero after 50 years of age. (Note that the negative values are within the resolution limits of the measurement process.) As noted previously, the accommodated lens thickens with age, as can be seen in Figure 3B, and a strong correlation was found between lens thickness and age ($r^2 = 0.53; P < 0.0001$). However, the maximum lens thickness attained under accommodative effort showed only modest correlation with age ($r^2 = 0.25; P < 0.12$). Similarly, the equatorial diameter of the unaccommodated lens is not a function of age as seen in Figure 4B ($r^2 = 0.0; P > 0.10$). For subjects under 40 years of age, changes in lens dimensions are age-independent; the diameter decreases an average of 5.7%, and the thickness increases an average of 12% during maximum accommodative effort. Table 2 summarizes the dimensional data obtained from all subjects.

DISCUSSION

Data were obtained from a limited number of subjects of both genders and varied races; consequently, significant individual variations are expected. Because of the limited number of subjects, our findings are of a preliminary nature. Nonetheless, a number of statistically significant findings are noted.
Maximum ciliary muscle contractile activity reduces only slightly with age and the ciliary muscle remains active in all subjects, well beyond the time when lens response is no longer possible. Because the restoring force of the choroid is known to increase with age, the contractile force of the ciliary muscle may actually increase with age. Within the context of classic theories of presbyopia, this finding supports the Hess-Gullstrand, or lenticular, theory of presbyopia because the extralenticular theory does not allow for muscle contraction in the absence of lens response.

Although lens diameter did not show any significant change with age, an age-related increase in the thickness of the lens was observed. The increase in lens thickness has been noted previously and has been termed the 'lens paradox.'

![Figure 3](https://iovs.arvojournals.org/pdfaccess.ashx?url=/data/journals/iovs/933213/)  
**Figure 3.** (A) Change in the lens thickness produced by an 8-D binocular accommodative stimulus as a function of age. The ability of the lens to change shape diminishes to zero with age. (B) Unaccommodated (relaxed) lens thickness as a function of age. Lens thickness continues to increase with age as described in the so-called lens paradox.

![Figure 4](https://iovs.arvojournals.org/pdfaccess.ashx?url=/data/journals/iovs/933213/)  
**Figure 4.** (A) Change in lens equatorial diameter produced by an 8-D binocular accommodative stimulus as a function of age. The ability of the lens to decrease its equatorial diameter decreases to zero with age. (B) Unaccommodated (relaxed) lens equatorial diameter as a function of age. The equatorial diameter of the lens does not change with age.
previously proposed by Bito and Miranda. 46 (Although the choroid appears to increase its elasticity with age,4' there is no evidence regarding changes in its resting length. An intriguing ciliary muscle with age would reduce tension on the lens, and length of the restoring elasticity (the choroid) as has been

Age 4^6
power, presumably because of the action of some compensatory mechanism.43'44
crease in lens thickness. There is evidence to suggest that the diameter. Under this scenario, the inward movement of the abnormal cortices.44'45 Such a process might lead to a shortening of the equatorial dimension that would, in turn, pull the ciliary muscle without altering lens diameter. Because a greater number of zonulas are attached to the anterior surface of the lens, an increase in the thickness of the anterior surface might develop an inward pull caused by the relative position of the muscle and lens. An inverse process is also possible: Lens thickening might be the result of the decrease in ciliary ring diameter. Under this scenario, the inward movement of the ciliary muscle with age would reduce tension on the lens, and this reduction in tension would enable processes that lead to increased thickness. In this case, the decrease in ciliary muscle ring diameter might be caused by an increase in the resting length of the restoring elasticity (the choroid) as has been previously proposed by Bito and Miranda.46 (Although the choroid appears to increase its elasticity with age,4' there is no evidence regarding changes in its resting length. An intriguing analogy is the elasticity in old underwear, which becomes stiffer but also expands in length. It is the latter feature that usually leads to its demise.) Alternatively, the decrease in ciliary ring diameter could be due to growth and/or realignment of the muscle itself.47 These alternatives are being addressed in another study.

Although data obtained from the limited number of subjects studied thus far indicate that the ciliary muscle remains active well after accommodation is lost, a longitudinal study would directly address this issue and is ongoing. Also, concerns regarding subject fatigue, image resolution, and the cost of another study.

<table>
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<th>Dimensional Data</th>
<th>Ciliary Muscle (mm)</th>
<th>Lens Equ. (mm)</th>
<th>Lens Thickness (mm)</th>
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<td>Age (y) 0.1 D 8 D</td>
<td>0.1 D 8 D 0.1 D 8 D</td>
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This term relates to the fact that while the lens increases in thickness and curvature, there is no increase in its refractive power, presumably because of the action of some compensatory mechanism.55'44

The ciliary muscle also showed a significant decrease in ring diameter for the unaccommodated state. It is possible that this decrease in ciliary ring diameter is secondary to the increase in lens thickness. There is evidence to suggest that the aging lens thickness due to increases in anterior and posterior lens cortices.44'45 Such a process might lead to a shortening of the equatorial dimension that would, in turn, pull the ciliary muscle inward.49 Although no statistically significant change was found in lens equatorial dimension, such changes could be missed because of our sample size. It is also possible that an increase in lens thickness could exert an inward pull on the ciliary muscle without altering lens diameter. Because a greater number of zonulas are attached to the anterior surface of the lens, an increase in the thickness of the anterior surface might develop an inward pull caused by the relative position of the muscle and lens. An inverse process is also possible: Lens thickening might be the result of the decrease in ciliary ring diameter. Under this scenario, the inward movement of the ciliary muscle with age would reduce tension on the lens, and this reduction in tension would enable processes that lead to increased thickness. In this case, the decrease in ciliary muscle ring diameter might be caused by an increase in the resting length of the restoring elasticity (the choroid) as has been previously proposed by Bito and Miranda.46 (Although the choroid appears to increase its elasticity with age,4' there is no evidence regarding changes in its resting length. An intriguing analogy is the elasticity in old underwear, which becomes stiffer but also expands in length. It is the latter feature that usually leads to its demise.) Alternatively, the decrease in ciliary ring diameter could be due to growth and/or realignment of the muscle itself.47 These alternatives are being addressed in another study.

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CONCLUSIONS

This study was structured to provide experimental differentiation between two long-standing theories of presbyopia: the Hess-Gullstrand, or lenticular theory; and the Duane-Fincham, or extralenticular theory. The approach used MR images to

This study was structured to provide experimental differentiation between two long-standing theories of presbyopia: the Hess-Gullstrand, or lenticular theory; and the Duane-Fincham, or extralenticular theory. The approach used MR images to
examine the relationship between the ciliary muscle and lens during accommodative effort with advancing presbyopia. Experimental limitations (resolution, SNR, motion artifacts, and the difficulty of controlling accommodative stimulation within the confines of the imager) were addressed. MR images were obtained and analyzed for of 25 subjects. Measurements of the ciliary muscle ring diameter, lens thickness, and lens equatorial diameter were obtained from MR images under minimum and maximum accommodative efforts for each subject. The data clearly show ciliary muscle activity with accommodative effort for all ages studied. This finding supports the Hess-Gullstrand possibility that lenticular changes are secondary to reductions however, a decrease in the unaccommodated ciliary muscle diameter was also strongly correlated with age, opening the possibility that lenticular changes are secondary to reductions in tension applied by the ciliary ring.

References

APPENDIX

Correction of the Ciliary Muscle Ring Diameter for Partial Volume Averaging and Slice-Centering Offset

Partial volume averaging occurs because the finite slice thickness of 3 mm is projected onto a single image. Slice-centering offset occurs if the center of the 3-mm slice is offset from the center of the lens. During volume averaging, the largest object dimension occurring in the slice is usually visualized in the resultant image. Consequently, as long as the center of the lens is captured somewhere within the 3-mm slice, its cross section will be correctly displayed in the resulting image. Although the lens dimensions in the resultant image are not altered by either partial volume averaging or slice-centering offset, both effects will cause the ciliary muscle ring diameter to appear smaller in the resultant image. Nonetheless, the actual ciliary muscle ring diameter is easily calculated from the apparent diameter measured in the image as described below.

Assuming radial symmetry of the lens and ciliary muscle, a slice passing exactly through the center of the lens produces an error in the diameter of the ciliary ring because of the finite thickness of the slice. The actual ciliary ring diameter, $D_c$, is given as $D_c = \sqrt{D_m^2 + (SLT)^2}$, where $D_m$ is the measured ciliary ring diameter and $SLT$ is the slice thickness. The error in the measured value of the ciliary ring is further increased if a slice-centering offset ($h$) exists (i.e., if the center of the slice does not correspond exactly with the center of the lens). Although slice-centering offset can be corrected, images that displayed significant slice-centering offset were discarded. (Obvious lens cross-sectional asymmetry in the two slices flanking the center slice was used as an indication of slice-centering offset). Correcting for small slice-centering offsets (generally <0.75 mm) was accomplished by calculating the width of the lens in each flanking slice, the superior and inferior lens chords, $C_s$ and $C_i$. Assuming lens symmetry, these chord lengths should be equal. The perpendicular offset, $h$, of the center slice can be determined from the difference in these chord lengths. Let $D_l$ be the actual diameter of the lens and $y_s$ and $y_i$ be the perpendicular distances from the center of the lens to the edge of the adjacent superior and inferior slices, respectively. Partial volume averaging results in the longest lens chord in an adjacent slice being visualized. This chord corresponds to the boundary between the center slice and an adjacent slice. By measuring chords $C_s$ and $C_i$ of adjacent slices, a corresponding distance $y_s$ and $y_i$ can be found $y_s = \sqrt{(D_l/2)^2 - (C_s/2)^2}$ and $y_i = \sqrt{(D_l/2)^2 - (C_i/2)^2}$. From the geometry, the slice offset $b$ is found to be $b = (1/2) (y_s - y_i)$.

By compensating for the partial volume-averaging error subsequent to correcting for slice offset, the true diameter of the ciliary muscle ring, $D_c$, can be found from the measured diameter of the ciliary muscle ring, $D_{m}$, by the Pythagorean theorem $D_c = \sqrt{D_m^2 + (SLT + b)^2}$.