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Magnetic resonance imaging of aging, accommodating, phakic, and pseudophakic ciliary muscle diameters

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Abstract

PURPOSE—To quantify in vivo accommodative changes in the aging human ciliary muscle diameter in phakic and pseudophakic eyes.

SETTING—Department of Surgery/Bioengineering, UMDNJ–Robert Wood Johnson Medical School, Piscataway, and the Institute of Ophthalmology and Visual Science UMDNJ–New Jersey Medical School, Newark, New Jersey, USA.

METHODS—Images were acquired from 48 eyes of 40 people between the ages of 22 and 91 years, 1 eye of 32 phakic volunteers and both eyes of 8 patients who had monocular implantation of a single-piece AcrySof intraocular lens (IOL) (Alcon Laboratories). Images were acquired during physiological accommodation and with accommodation at rest, and the diameter of the ciliary muscle ring was measured.

RESULTS—Results show the ciliary muscle remains active throughout life. The accommodative change in its diameter (mean 0.64 mm) ($P<.00001$) was undiminished by age or IOL implantation. Preliminary data showed that the accommodative decrease in muscle diameter in phakic and pseudophakic eyes was statistically identical. The phakic eyes had a marked decrease in ciliary muscle diameter with advancing age for both accommodative states ($P<.000001$ and $P<.000001$), which did not appear to be altered by IOL implantation. The lens equator was constant with age in the unaccommodated human eye, resulting in decreased circumlental space with advancing age in the phakic eyes.

CONCLUSION—Although the undiminished ability of the ciliary muscle to decrease its diameter with accommodation can be relied on in strategies for presbyopia correction, even in advanced presbyopia, the decreasing circumlental space and its potential effects on zonular tension must also be considered.

New strategies, including lens softening, lens refilling, scleral expansion, and potentially accommodating intraocular lenses (IOLs), are being developed to restore accommodation in presbyopic eyes.^{1–11} Because a functioning ciliary muscle is key to each procedure or device, it is increasingly important to quantify in vivo accommodative changes in the aging ciliary muscle of phakic and pseudophakic eyes. Although the iris obscures direct observation of the ciliary muscle in the normal, intact human eye, magnetic resonance

imaging (MRI) is not impeded by the iris and allows complete visualization of the anterior segment.

Although MRI is used clinically to diagnose a number of ocular disorders, because of its expense it is unlikely at present to be used preoperatively for IOL sizing or postoperatively for clinical IOL evaluation. Research applications of MRI include high-resolution retinal imaging and the study of extraocular muscles.^{12–20} In addition, Strenk et al.²¹ developed high-resolution anterior segment MRI techniques and instrumentation that permit observation of the geometric relationship between the accommodative structures during accommodation and with accommodation at rest. These studies yielded new information on lens growth²² and a new theory of presbyopia development: Life-long increases in lens thickness indirectly decrease circumlental space by displacing the iris and, hence, the ciliary muscle, ultimately leading to decreasing zonular tension and decreasing accommodative response.²³

This ability to observe the geometric relationship of the accommodative structures with MRI has also provided the only statistically significant demonstration that the Helmholtz theory²⁴ of human accommodation is correct. Strenk et al.²¹ found that in response to an accommodative stimulus, a decrease in the ciliary muscle ring diameter and the lens equatorial diameter occurred, with a corresponding increase in lens thickness. Although the lenticular changes decreased with advancing age, the accommodative change in the ciliary muscle ring diameter was undiminished throughout life, with a mean value of 0.661 mm. A possible trend toward a slight decrease in muscle contraction with advancing age was present but not statistically significant. However, only a limited number of people with advanced presbyopia were enrolled. The mean age of the 25 subjects in the study was 39.10 years (range 22 to 83 years). Only 1 subject was older than 62 years. Here, we expand the age range to 91 years and provide a more uniform age distribution to determine whether ciliary muscle contraction remains constant with advancing age in the phakic eye. Also, because most strategies for presbyopia correction remove or alter the crystalline lens, additional preliminary data from a subset of pseudophakic subjects are presented.

PATIENTS AND METHODS

Forty-eight eyes of 40 volunteers with emmetropia or mild myopia were included in the study. A subset of 8 volunteers was monocularly pseudophakic. The research followed the tenets of the Declaration of Helsinki. All subjects gave informed consent after the nature and possible consequences of the study were explained. The research was approved by the Institutional Review Board of University of Medicine and Dentistry of New Jersey–Robert Wood Johnson Medical School.

Surgical Technique

In the subset of 8 monocularly pseudophakic patients, a standard single-plane clear corneal incision was performed, after which a continuous curvilinear capsulorhexis was created. Next, hydrodissection was performed to separate the cataract cortex from the underlying lens capsule, which was followed by hydrodelineation to separate the nucleus from surrounding cortex. The cataract nucleus was split using the phaco-chop technique. Small pieces of cataract were emulsified and removed and the cortex was aspirated with the Infiniti phacoemulsification machine (Alcon Laboratories, Inc.). The IOL was inserted in the capsular bag. All patients received an AcrySof single-piece acrylic foldable IOL (SA60AT, Alcon Laboratories, Inc.).

Magnetic Resonance Imaging

Magnetic resonance imaging is a noninvasive, nonoptical imaging technique that uses nuclear magnetic resonance, a static magnetic field, magnetic field gradients, and the application of radio-frequency pulses. Magnetic resonance (MR) images are free of optical distortions and reflections. The technique also provides unsurpassed soft-tissue contrast that reflects the intrinsic properties of the tissue; this contrast can be varied through the appropriate selection of the radio-frequency pulse sequence timing parameters. Images can be collected in any desired plane. The high-resolution MRI method developed by Strenk et al. for imaging the anterior segment during accommodation provides visualization of the ciliary muscle and its geometric relationship to the crystalline lens in phakic eyes or to the optic and haptic in pseudophakic eyes.^{21,22} Moreover, this method does not obstruct vision and uses binocular physiological accommodation (Pharmacologically induced accommodation is reported to produce nonphysiological supra-accommodation,²⁵ probably as a result of the effect of the drug on iris contraction.²⁶)

High-resolution magnetic resonance ocular images were acquired using a clinical magnetic resonance imager (1.5 Tesla, General Electric), a custom-designed eye-imaging MR receiver coil, and a standard spin-echo radio-frequency pulse sequence (T1 weighted, single echo, multislice). A nonmagnetic accommodative stimulus apparatus was designed to present binocular (accommodative and disparity) stimuli within the confines of the imager. Visual targets were positioned at the appropriate distance from the eye to provide a strong (8.00 diopter [D]) or minimum (0.10 D) binocular accommodative stimulus during the MRI scans. The far target was viewed through a mirror to overcome the confines of the imager. The head was restrained and the room darkened during scanning. The subject was instructed to view the far visual target, which consisted of a black cross hair on a white background illuminated by a fiber optic; intensity varied between 50% and 100% at a rate of 2 Hz, providing a compelling visual stimulus and reducing the stabilized image phenomenon.

An initial series of orthogonal localization scans was simultaneously acquired in 3 dimensions and used to plan the location of the final series of contiguous, 3.0 mm thick, multislice axial scans with a 4.0 cm field of view, resulting in 0.078 mm in-plane resolution. The target was then repositioned for near viewing, and the entire localization and scanning procedure was repeated. Additional details of the data acquisition and stimulus apparatus have been reported.²¹

Images were acquired during accommodation and with accommodation at rest from 1 of the eyes of 32 phakic volunteers and both eyes of the 8 patients with monocular IOL implantation. Figure 1 is a representative image of a phakic eye; the soft-tissue contrast has been selected to highlight the differences between the ciliary muscle and processes; the ciliary processes display greater signal intensity than the ciliary muscle; similarly the lens cortex is brighter than the remaining lens material. Figure 2 is a representative image of a pseudophakic eye.

The images were analyzed using the National Institutes of Health Image 1.62 software package. The diameters of the ciliary muscle (from apex to apex) were obtained using interactive graphics. A repeatability study of the ability to measure the ciliary muscle ring diameter has been reported.²¹ Lens measurements obtained using this imaging protocol have been cross-validated with data collected by Scheimpflug imaging and other modalities.²⁷

RESULTS

The mean age of the 40 volunteers (21 women, 19 men) was 46.15 years (range 22 to 91 years). The mean age of the 8 monocularly pseudophakic subset (5 women, 3 men) was

68.40 years (range 61 to 76 years). The mean interval between surgery and MRI examination was 12.4 weeks (range 3.7 to 35.3 weeks).

Figure 3 shows the ciliary muscle ring diameter as a function of age for minimum and maximum accommodation in the phakic eye. The ciliary muscle ring diameter decreased significantly with age for both accommodative states. The linear regression for minimum accommodation ($P < .000001$, analysis of variance) had a mean slope of -0.0269 ± 0.004 mm per year (SE) and a mean intercept of 14.065 ± 0.208 mm. For maximum accommodation, the regression ($P < .000001$) had a mean slope of -0.0247 ± 0.004 mm per year and an intercept of 13.320 ± 0.180 . Although there was no statistically significant difference between these slopes, there was a statistically significant difference between the intercepts. This difference in intercepts was further analyzed by subtracting the accommodated ciliary muscle ring diameters from their unaccommodated counterparts. The linear regression for the change in ciliary muscle ring diameter with age (not graphed) was not statistically significant ($P = .37$), and the mean accommodative change in the ciliary muscle ring diameter of the phakic eye was independent of age with the ciliary muscle ring decreasing by a mean of 0.641 ± 0.047 mm with accommodation ($P < .000001$, Student *t* test). The corresponding accommodative change in the ciliary muscle ring diameter in the phakic eye (not graphed) in the subset of the 8 patients with monocular IOL implantation had a mean value of 0.625 ± 0.073 mm ($P < .000001$), which was statistically identical to that in the complete phakic eye data set.

Figure 4 shows the ciliary muscle ring diameter in the 8 pseudophakic eyes as a function of age for both accommodative states. The linear regression for minimum accommodation was not statistically significant ($P = .269$), and the mean ciliary muscle ring diameter was 12.073 ± 0.315 mm ($P < .000001$). Similarly, the linear regression of the ciliary muscle ring diameter versus age for the maximum accommodative state was not statistically significant ($P = .473$), and the mean ciliary muscle ring diameter was 11.598 ± 0.290 mm ($P < .000001$). The mean accommodative change in the ciliary muscle ring diameter (not graphed) in these pseudophakic eyes was 0.475 ± 0.089 mm ($P = .001$), which was statistically identical to that in the contralateral phakic eyes ($P = .21$, Student *t* test).

Figure 5 is a replotting of the unaccommodated ciliary muscle diameter in the phakic and pseudophakic eyes. Similarly, Figure 6 shows the accommodated ciliary muscle ring diameter in the phakic and pseudophakic eyes. The mean ciliary muscle diameter in the unaccommodated pseudophakic eye corresponded to that in a 74.0 ± 15.1 year-old phakic eye, while the mean accommodated ciliary muscle diameter in the pseudophakic eye corresponded to that in a 69.7 ± 15.1 year-old phakic eye.

DISCUSSION

Because the iris prevents direct observation of the ciliary muscle in the intact human eye, many attempts to study the accommodative behavior of the ciliary muscle have relied on in vivo and in vitro animal (primarily rhesus monkey) studies and in vitro human studies. Primate studies have provided a wealth of information as the accommodative systems of the rhesus monkey and human are similar and each species exhibits accommodative loss with advancing age.^{28,29} Nonetheless, significant interspecies differences in lens development and growth exist,^{30–32} leading to likely differences in the geometric relationship between the ciliary muscle and lens and the corresponding force vectors involved in accommodative mechanics.

Many species differences in the aging ciliary muscle itself exist, thus the underlying causes of presbyopia development in the rhesus monkey and human are likely very different. For

example, we report here that human ciliary muscle contraction is undiminished with advancing age, in contrast to the rhesus ciliary muscle, which exhibits reduced contractile response with age,³³ likely due to choroidal changes because rhesus ciliary muscle contraction is restored by severing its posterior choroidal attachment.^{34,35} These choroidal changes alone have been described as sufficient to explain presbyopia in this species.³⁵ This does not hold true for humans, as evidenced by the lifelong presence of undiminished accommodative ciliary muscle contraction. Similarly, the observations of accommodative IOL optic movement in the pseudophakic eye^{25,36-39} also indirectly indicate the ciliary muscle and its restoring force (the choroid) are capable, even in advanced presbyopia. In addition, while the aging human ciliary muscle apex displaces anteriorly,⁴⁰ the rhesus ciliary muscle becomes fixed in a position far posteriorly.⁴¹ With accommodation, the rhesus ciliary muscle moves anteriorly as well as inwardly with accommodation³³; conversely, the human ciliary muscle only moves inwardly with accommodation.⁴²

Finally, microscopy studies indicate that the aging human ciliary muscle develops more connective tissue, and in different regions, than in the rhesus monkey.^{40,41} Given these species differences in the aging ciliary muscle location and function, presbyopia correction strategies that work in the rhesus model may not be effective in humans.

A key finding in the present study is that human ciliary muscle contraction is undiminished throughout life. This holds true for phakic and pseudophakic eyes with advanced presbyopia. Although the ciliary muscle in the presbyopic eye contracts as much as a youthful muscle, a marked decrease in the ciliary muscle ring diameter also occurs with advancing age in both phakic and pseudophakic eyes. Because the length of the in vivo unaccommodated crystalline lens equator is constant with age,²¹ an age-dependent decrease in the ciliary muscle ring diameter also leads to decreasing circumlental space and decreasing zonular tension in the unaccommodated phakic eye. Ultimately, the zonular tension may reach zero in the unaccommodated state, in which case ciliary muscle contraction would not lead to a further decrease in zonular tension or an accommodative lens response.

In the pseudophakic eye, the decreasing ciliary muscle ring diameter and the resulting potential loss of zonular tension may be offset by the decreased IOL volume (compared to the crystalline lens) coupled with capsule contraction and a concomitant inward movement of the capsule's zonular attachments. Reports of anterior and posterior optic movement with accommodative effort^{25,36-39} indicate some level of zonular tension is likely restored after IOL implantation as ciliary muscle effort apparently affects optic position. Magnetic resonance imaging can visualize the optic and haptics in relation to the accommodative structures. We are investigating this question; because of the difficulties associated with subjective and objective measurement of accommodation, including the issue of pharmacological agents causing supra-accommodation, biometric measurement of accommodative changes in IOL position has been described as the most direct method of assessing accommodative IOL function.^{25,43} Scleral expansion strategies could increase the diameter of the ciliary muscle ring in presbyopic phakic eyes and thus provide an increase in circumlental space, and assuming both Helmholtzian accommodation and a sufficiently moldable crystalline lens, an increase in zonular tension and accommodative response. However, the continued growth of the crystalline lens and its effect on the uveal tract may reduce zonular tension and any potential accommodative response. Lens softening or refilling strategies that do not reduce the lens volume or equatorial diameter will not increase the circumlental space or restore zonular tension, without which accommodative lens response is unlikely regardless of the amount of ciliary muscle contraction.

In conclusion, we found that ciliary muscle contraction is undiminished by age or IOL implantation. In addition, the ciliary muscle diameter decreases with advancing age and this does not appear to be altered by IOL implantation. Thus, although strategies for presbyopia correction may rely on a functioning ciliary muscle, the effect of the age-dependent decrease in ciliary muscle ring diameter on zonular tension must also be considered.

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Figure 1.
A representative MR image of a phakic eye. Note that the ciliary processes are hyperintense to the ciliary muscle.

Figure 2.
A representative image of a pseudophakic eye.

Figure 3.
 Ciliary muscle ring diameter versus age for minimum (*diamonds*) and maximum (*squares*) accommodation in the phakic eye.

Figure 4.
 Ciliary muscle ring diameter versus age for minimum (*diamonds*) and maximum (*squares*) accommodation in the pseudophakic eye.

Figure 5.
 Ciliary muscle ring diameter at minimum accommodation for phakic (*diamonds*) and pseudophakic (*squares*) eyes.

Figure 6.
 Ciliary muscle ring diameter at maximum accommodation for phakic (*diamonds*) and pseudophakic (*squares*) eyes.